Epidemic modelling: aspects where stochasticity matters

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Abstract

Epidemic models are always simplifications of real world epidemics. Which real world features to include, and which simplifications to make, depend both on the disease of interest and on the purpose of the modelling. In the present paper we discuss some such purposes for which a *stochastic* model is preferable to a *deterministic* counterpart. The two main examples illustrate the importance of allowing the infectious and latent periods to be random when focus lies on the *probability* of a large epidemic outbreak and/or on the initial *speed*, or growth rate, of the epidemic. A consequence of the latter is that estimation of the basic reproduction number R_0 is sensitive to assumptions about the distributions of the infectious and latent periods when using the data from the early stages of an outbreak, which we illustrate with data from the SARS outbreak. Some further examples are also discussed as are some practical consequences related to these stochastic aspects.

Keywords: stochastic epidemic model, major outbreak probability, infectious period, latency period, exponential growth rate.

1 Introduction

Mathematical epidemic models describe the spread of an infectious disease in a community (e.g. Bailey, 1975, Anderson and May, 1991, Diekmann and Heesterbeek, 2000). A model can be used to derive various properties of an outbreak, such as: whether or not a big outbreak may occur, how big the outbreak will be, or the endemic level in case the

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disease becomes endemic. From a statistical/epidemiological point of view the model and its analysis may be used to estimate important epidemiological parameters from observed outbreak data. These estimates can then be used to study effects of potential interventions to stop or reduce the spreading of the disease. For example, an endemic disease may go extinct if a vaccination program is launched having high enough vaccination coverage (e.g. Anderson and May, 1991, pp87, and Gay, 2004), or an outbreak may be stopped during the early stages of an outbreak if spreading parameters are reduced enough by means of different sorts of intervention (e.g. Anderson et al., 2004, for an application to SARS).

Mathematical models are always simplifications of reality, but the hope is that the simplifications have little effect on the epidemic properties of interest. Simple models have the advantage of being tractable to analysis and quite often allow for explicit solutions admitting general qualitative statements. Their main disadvantage is of course that they may be too simplistic for the conclusions to be valid also for real world epidemics. Adding more complexity to the model increases realism but usually makes it harder to analyse and also introduces more uncertainty by having more parameters. More complex models are usually analysed by means of numerical solutions to differential equations, or from numerous stochastic simulations.

The most important features to include to make an epidemic model more realistic (and at the same time harder to analyse) are to incorporate individual heterogeneity (e.g. Anderson and May, 1991, pp 175) and/or structured mixing patterns (e.g. House and Keeling, 2008, for a deterministic household model). Another step in making a model more realistic is to make certain features random, for example the actual transmission/contact process but also possibly susceptibility, social structures, the latent period and/or the infectious period. Such stochastic models thus allow individuals to behave different from each other in a way that is specified by random distributions (e.g. Bailey, 1975, Andersson and Britton, 2000a).

Which complexities to include in the model, and which not to, depend both on the type of disease in question and on the scientific question motivating the study. The aim of the present paper is to illustrate some aspects where *stochasticity* matters. More precisely we focus on two features, the risk for an outbreak and the initial growth rate of the epidemic, and we illustrate that they depend heavily on assumptions about the latent and infectious periods; not only on their mean durations but also on their randomness. As a consequence, the (stochastic) distribution of these periods are important when addressing questions relating to these two features – using an over-simplified stochastic model or a deterministic model will give misleading results. For example, estimating R_0 from the initial phase of an epidemic is hard without additional knowledge about the distributions of the infectious and latents periods, a fact which we illustrate using data from the SARS outbreak. We illustrate our results using a simple epidemic model, but the qualitative conclusions hold also for more realistic models allowing other heterogeneities. We note that other features of the model, e.g. the basic reproduction number and the outbreak size in case of a major outbreak, hardly depend on the randomness of the latent and infectious periods at all, so having a deterministic latent and infectious period may be appropriate when addressing other questions.

Most results presented in this paper are not new but have appeared elsewhere or

are "folklore" among stochastic epidemic modellers, but are perhaps less known outside this community. The aim of the paper is hence to gather and present the results in a simple form reaching outside the community of stochastic epidemic modellers. The rest of the paper is outlined as follows. In Section 2 we present the standard stochastic SEIR epidemic model for a homogeneously mixing community of homogeneous individuals. In Section 3 properties of the model are presented and illustrated. In Section 4 we interpret the results in more epidemiologically relevant formulations and illustrate where it can make a difference. In the discussion we briefly describe, and give references to, some other situations where stochasticity of some form affect certain features of the epidemic model.

2 A simple stochastic epidemic model

2.1 Definition

We now define what we call the standard susceptible-exposed-infectious-removed (SEIR) epidemic model. Consider a homogeneously mixing community consisting of n homogeneous individuals, where n is assumed to be large. A transmittable disease is spread according to the following rules. Initially a small number, k, individuals are infectious and the rest of the community are susceptible to the disease (immune individuals are simply neglected). Each individual who gets infected is at first latent (exposed but not yet infectious) for a random period L with distribution F_L. After the latent period has ended the infectious period starts and lasts for a period I having distribution F_I. All infectious periods and latent periods are assumed to be mutually independent. While infectious an individual has random "infectious contacts" at rate λ, each contact is with a randomly chosen individual, so the contact rate with a specific individual is λ/n (or more correctly $\lambda/(n-1)$ but when n is large this distinction is irrelevant). Contacts with susceptible individuals result in infection (and their latent period starts); contacts with non-susceptibles have no effect. Once the infectious period is over the individual is said to be removed, meaning that the person has recovered and become immune, and plays no further role in the epidemic. The epidemic goes on until there are no more infectious or latent individuals, then the epidemic stops. Let T denote the (random) number of individuals who get infected during the outbreak, and that hence are removed at the end of the epidemic. T is often called the final size of the epidemic, and $\tilde{\rho} = T/n$ denotes the final proportion infected during the outbreak.

In what follows we will restrict ourselves to the case where L and I have different and independent Gamma distributions, this being a rather flexible family of distributions. We parametrise these distributions by their means, $\mu_L = E(L)$ and $\mu_I = E(I)$ (≥ 0), and their coefficients of variation $\tau_L = \sqrt{V(L)}/E(L)$ and $\tau_I = \sqrt{V(I)}/E(I) \geq 0$, where $V(\cdot)$ denotes the variance.

2.2 The basic reproduction number R_0

The perhaps most important property of an epidemic model is the basic reproduction number, denoted R_0, which for the present model can be defined as the average number of infections caused by a typical infective when the disease is introduced into the population. For the present model it is easy to show that

$$R_0 = \lambda E(I) = \lambda \mu_I.$$

The basic reproduction number determines both if a major outbreak is possible, and if so, also the final proportion infected in case there is a major outbreak. More precisely, it can be shown that $\tilde{\rho}$, the ultimate proportion infected, will in a large community be close to ρ, which solves

$$1 - \rho = e^{-R_0 \rho}. \tag{2.1}$$

It is easy to see that $\rho = 0$ (corresponding to a minor outbreak) is always a solution to (2.1). If $R_0 \leq 1$, this is in fact the only solution, meaning that a major outbreak is impossible. If $R_0 > 1$ there is also a unique strictly positive solution ρ^* $(0 < \rho^* < 1)$ corresponding to a major outbreak.

As was seen above, R_0 only depends on the *mean* of the infectious period – not on its randomness nor on the latency period. The model can be extended to allow for a (perhaps random) time-varying infectivity $\lambda(s)$ over the infectious period $(0 \leq s \leq I \leq \infty)$. Then $R_0 = E(\int_0^I \lambda(s)ds)$, the expected accumulated infectivity. As before, R_0 determines both if a major outbreak is possible, and if so, how big the outbreak will be. In fact, the complete (random) distribution of the final size, for any finite n, can be shown to depend only on the distribution of the accumulated infectivity $\int_0^I \lambda(s)ds$ (Ball, 1986), how the infectivity is distributed over time only affects the time dynamics of the epidemic and not the final size.

3 Model properties affected by randomness

In the previous section it was shown that R_0 only depends on the mean length of the infectious period and not at all on the latent period. In the present section we study two features, the probability of a major outbreak and the initial growth rate of the epidemic, where the randomness of the infectious period and also the latent period do matter. In the discussion we briefly mention some other aspects where stochasticity matters.

3.1 The probability of a major outbreak

When the community n is large, the initial phase of the epidemic may be approximated by a branching process (Ball, 1986). The reason for this is that new contacts will most likely be with not yet contacted people, so new infectives infect (="give birth" in branching process terminology) independently which is the crucial underlying assumption in branching processes. The branching process corresponding to our model is the Sevastyanov model (Jagers, 1975, p 8). Infections correspond to births in the branching process, the latency

period to infancy in the branching process and the infectious period to the reproductive life stage (life stages after the reproductive stage play no role for population growth just like with removed individuals in the epidemic).

Let π denote the probability of a large outbreak (corresponding to infinite growth of the approximating branching process) when starting with $k = 1$ infectious individual. From branching process theory it can be shown that π is the largest solution to the balance equation

$$1 - \pi = E[(1 - \pi)^X], \tag{3.1}$$

where X is the (random) number of births of a typical individual in the branching process. The balance equation is obtained by conditioning on the number of births of the first individual: if the first individual has $X = x$ births during her life, all these individuals must avoid causing infinite growth. They do this independently, so the probability for this to happen is $(1 - \pi)^x$.

For our model, with constant birth/infection rate λ during a Gamma distributed infectious period with mean μ_I and coefficient of variation τ_I, the distribution of X, and hence also $E[(1 - \pi)^X]$, can be computed explicitly. By first conditioning on the length of the infectious period $I = y$ it is easy to show that X then is Poisson distributed with mean λy, and removing the conditioning makes X follow a negative binomial distribution. Using this it can be shown that Equation (3.1) simplifies to

$$1 - \pi = \Big(\frac{1}{1 + \pi R_0 \tau_I^2}\Big)^{\tau_I^{-2}}, \tag{3.2}$$

(this relation can also be found in Asikainen, 2006, p 28). If for example $\tau_I = 0$, implying that the length of the infectious period is non-random, π is the largest solution to $1-\pi = e^{-\pi R_0}$ which is obtained by taking limits of (3.2) when $\tau_I \to 0$. If $\tau_I = 1$, corresponding to an exponentially distributed infectious period, we have that $\pi = 1-1/R_0$ which is clearly different.

By studying the balance equation (3.2) it is possible to see how π, the probability of a major outbreak, depends on model parameters. The first conclusion is not very surprising: π is increasing in $R_0 = \lambda\mu_I$ and hence also in the contact rate λ and in the mean infectious period μ_I. A less obvious conclusion is that π is *decreasing* in τ_I (the coefficient of variation of the infectious period). In other words, the more random the length of the infectious period is, the less likely is a major outbreak. Finally, π is independent of μ_L and τ_L.

In Figure 1 we have plotted π as a function of τ_I in the range 0 (corresponding to a deterministic infectious period) to 3 (being a very random infectious period), for three choices of R_0. It is seen that τ_I is quite influential. For example, if $R_0 = 3$ and $\tau_I = 0$, then $\pi \approx 0.940$. If R_0 is reduced to 1.5 and τ_I is unchanged we get $\pi \approx 0.583$, whereas if we instead keep R_0 unchanged (at $R_0 = 3$) and increase τ_I to 1, then $\pi \approx 0.667$. It is hence seen that the variation in the infectious period is as important as R_0 for determining the probability of a major outbreak.

The probability π defined above was for the case that the epidemic starts with 1 initially infectious. More generally, we can define π_k as the probability of a major outbreak

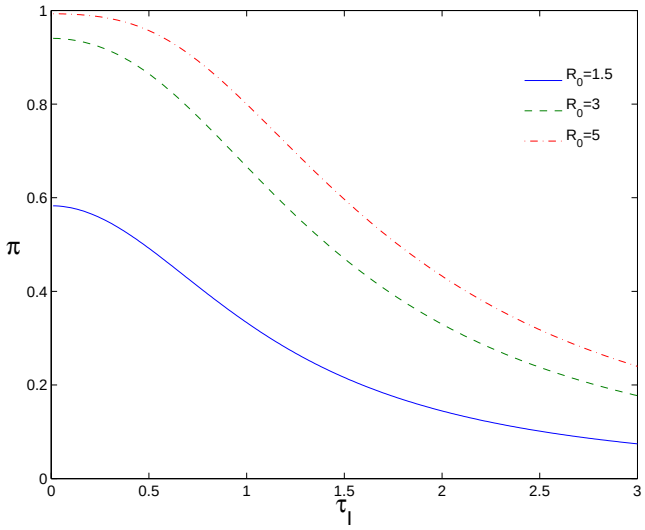

Figure 1: The probability of a large outbreak, π, as function of τ_I, the coefficient of variation of the infectious period.

starting with k initially infectious individuals (so $\pi_1 = \pi$). Since, for an epidemic *not* to take off, none of the initially infectives must initiate a major outbreak. As a consequence, π_k can be expressed in terms of $\pi_1 = \pi$ as

$$\pi_k = 1 - (1 - \pi)^k, \tag{3.3}$$

where π is the solution to (3.2). In Figure 2 π_k is plotted as a function of k for the cases $\pi = 0.25$ and $\pi = 0.5$. It is seen that π_k grows quickly up towards 1, implying that the outbreak probability is close to 1 when initiated by many individuals as long as $R_0 > 1$ and τ_I is not very large (meaning that infectious period is not extremely varying).

The distribution of the infectious period is hence mainly of interest when the epidemic is initiated by rather few individuals.

3.2 The initial growth rate of the epidemic

We now study another property which is heavily influenced by both the latent and infectious periods, their mean durations as well as their randomness: the initial growth rate of the epidemic. As before we assume that the community size n is large.

In Section 2 it was shown that an epidemic can only take off if $R_0 = \lambda\mu_I > 1$. Since we now focus on the growth rate of the epidemic we assume this to be the case. As mentioned before, the early stages of the epidemic in a large community can be approximated by a branching process. Since $R_0 > 1$ the branching process is said to be super-critical, and if the epidemic/branching process takes off branching process theory (e.g. Jagers, 1975) tells us that the epidemic will grow at an exponential rate during the initial phase. More precisely, in case of a major outbreak, the number of infectious individuals at t, $I(t)$, will

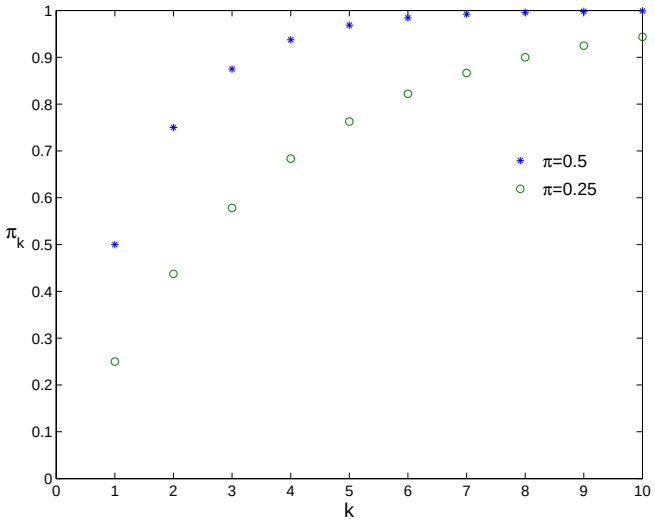

Figure 2: The probability π_k of an outbreak when k infectious individuals enters the population.

satisfy $I(t) \sim e^{\alpha t}$ for some α. The parameter α, denoted the Malthusian parameter, is known to solve

$$\int_0^\infty e^{-\alpha t} \lambda P(L < t < L + I) dt = 1, \tag{3.4}$$

where L and I are the (random) durations of the latent and infectious periods respectively. In the present paper L and I are assumed to be independent Gamma distributions with means μ_I and μ_L, and coefficients of variation τ_I and τ_L respectively. The solution α to (3.4) can then be shown to solve

$$\alpha = \frac{R_0}{\mu_I} \frac{1}{(1 + \alpha \tau_L^2 \mu_L)^{1/\tau_L^2}} \left(1 - \frac{1}{(1 + \alpha \tau_I^2 \mu_I)^{1/\tau_I^2}} \right) \tag{3.5}$$

(see the Appendix for details).

It can be shown that the exponential growth rate α (i.e. the solution to (3.5)) depends monotonically on all four parameters of the latent and infectious periods, μ_I, μ_L, τ_I and τ_L, keeping R_0 fixed. As for the mean infectious and latent periods, μ_I and μ_L, the growth is *decreasing*. This is not surprising: the longer the infectious period (keeping $R_0 = \lambda \mu_I$ fixed!) the slower the epidemic will grow, and the same applies to the situation where a latent period becomes longer on average. Perhaps more surprising is that α depends monotonically on the coefficients of variation τ_L and τ_I, and in different ways! It can be shown from (3.5) that the growth rate is *increasing* in τ_L but *decreasing* in τ_I. In other words, a more random latent period increases the growth rate whereas a more random infectious period decreases it.

A heuristic motivation for the different monotone dependence of the coefficients of variation goes as follows. Consider first two alternatives for the infectious period assuming,

for simplicity that there is no latency period: two infectious periods both being two time-units long (corresponding to small τ_I) and the other scenario having one infectious period of length 1 and the other of length 3, thus having the same mean μ_I but larger τ_I. During the first time-unit both scenarios will have two persons infecting but during the second time-unit the first scenario (small τ_I) will still have two persons infecting, but the second scenario only one person. During the third time-unit the second scenario will "catch up" in infecting new people by having one person infecting (as opposed to no one for the second scenario) but the first scenario will clearly infect new individuals at an *earlier state in time* thus resulting in higher growth rate α. This motivates why α is decreases in τ_I. The motivation for the growth rate being increasing in τ_L is similar. Suppose that we have two alternative scenarios similar to before: two latent periods of equal length two time-units, or one of length 1 and one of length 3, and assume for simplicity that all infectious periods last one time-unit in both scenarios. In the first scenario the two individuals will infect others between time 2 and 3 whereas in the second scenario one person will infect between time 1 and 2 and the other between 3 and 4. The second scenario (with higher τ_L) will have a higher growth rate because of the multiplicative effect the first person's infections will cause: these people will start new epidemic outbreaks at an earlier state.

In Figure 3 the exponential growth rate α is computed numerically for the case $R_0 = 2$, this being a common value for diseases like influenza (e.g. Mills et al., 2004). In each of the four sub-plots, one parameter is varied over an interval (1 to 14 days for the mean durations μ_L and μ_I and 0 to 3 for the coefficients of variation τ_L and τ_I) keeping the remaining parameters constant. The means are set to 7 days and the coefficients of variation to 3/7 (corresponding to a standard deviation of 3 days) when not varied.

From the figure it is clear that all four parameters μ_L, μ_I, τ_L and τ_I are quite influential for the initial growth rate of the epidemic. As mentioned above, the growth rate is decreasing in the two mean durations (recall that the expected accumulated infectivity $R_0 = \lambda\mu_I$ is kept fixed, so when μ_I changes, so does λ). As for the coefficients of variation, the growth rate α decreases with τ_I but increases with τ_L.

4 Practical relevance

4.1 Estimating R_0 from growth rate needs prior knowledge

Our first, and perhaps most important observation, lies in the consequences of knowing that the growth rate depends heavily on all of the parameters μ_L, μ_I, τ_L and τ_I, and not only R_0. This implies that it is harder to estimate R_0 from only observing the early stages of an epidemic as we now illustrate.

Recently, an important area in infectious disease epidemiology has been to analyse emerging infectious diseases, for example SARS (e.g. McLean et al., 2005) and the fear for a pandemic influenza (e.g. Ferguson et al., 2004). One important task when analysing emerging infectious diseases is to estimate R_0 using data from the initial phase of the epidemic. Such data sets typically consists of the number of diagnosed cases (per day or per week) over a certain observation period, typically weeks or months. One can argue that the number of diagnosed cases roughly corresponds to the number of recovered

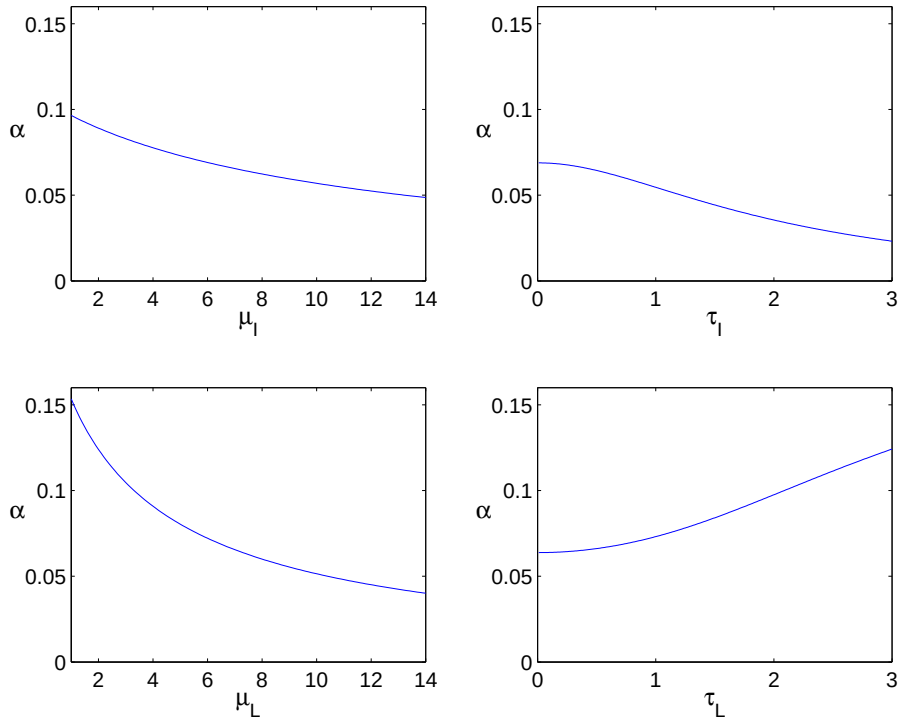

Figure 3: Plots of the initial exponential (per day) growth rate α as function of the model parameters. Parameters not varied are set to: $R_0 = 2$, $\mu_L = \mu_I = 7$ $\tau_L = \tau_I = \frac{3}{7}$.

individuals, and using branching process theory it can be shown that this number will have the same growth rate as the number of infectives. If we let $R(t)$ denote the accumulated number of removed individuals up to time t, it is known from branching process theory that

$$R(t) \approx We^{\alpha t}, \tag{4.1}$$

where W is random variable, the same for all t, and α is the Malthusian parameter treated in Section 3.2. If we look at the ratio of the number of removed individuals for two different observation times it follows that $R(t_1)/R(t_0) \approx e^{\alpha(t_1-t_0)}$ implying that we can estimate the growth rate α by

$$\hat{\alpha} = \frac{\log(R(t_1)) - \log(R(t_0))}{t_1 - t_0}. \tag{4.2}$$

The time-points $t_0 < t_1$ should be chosen such that the epidemic has really taken off at t_0 and not too many should have been infected by t_1.

The remaining problem lies in making conclusions about R_0 from the estimate $\hat{\alpha}$. Equation (3.5) gives a one-to-one correspondence between α and R_0 when the model parameters for the latent and infectious period are given. Rearranging Equation (3.5)

gives the following expression for R_0:

$$R_0 = \alpha\mu_I \frac{(1+\alpha\tau_L^2\mu_L)^{1/\tau_L^2}}{\left(1 - \frac{1}{(1+\alpha\tau_I^2\mu_I)^{1/\tau_I^2}}\right)} \tag{4.3}$$

However, for emerging infectious diseases the parameters of the infectious and latent periods are rarely known. The best one can hope for are some crude estimates. This will induce uncertainty in the estimate for R_0 no matter how precise the estimator $\hat{\alpha}$ is.

We now illustrate this using WHO data from the SARS outbreak (WHO webpage). Our model is of course unrealistic for this outbreak in several aspects as we are neglecting other community heterogeneities. However, the same qualitative conclusions would hold also for more realistic models. In Figure 4 part of a large outbreak of SARS in China is illustrated. It shows the incidence and accumulated number of diagnosed SARS cases by the day, between April and June in 2003.

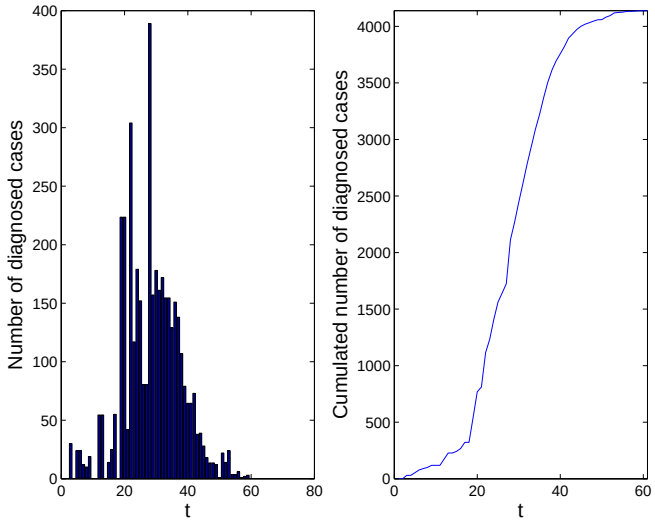

Figure 4: Sars outbreak in China 2003.04.02 - 2003.06.02. Data from WHO.

From this data we estimate the growth rate α using (4.2). Rather than estimating α from one time interval $(t_0,\ t_1)$ we take several, thus getting several α-estimates. We then take the mean of these estimates as our final estimate. More precisely we took the intervals (t_0, t_1)= (10,20), (10,25), and (15,25), all three representing the early stages of the epidemic neglecting the very first bit and stopping before the speed really starts dropping. The resulting α-estimates were $\hat{\alpha}_1 = 0.071$, $\hat{\alpha}_2 = 0.054$, and $\hat{\alpha}_3 = 0.034$. We take the mean of these values as our final estimate: $\hat{\alpha} = 0.0530$. (We will use the estimate to illustrate that a range R_0-values are consistent with this estimate, the exact value of $\hat{\alpha}$ is of secondary importance.)

Given the estimate ($\hat{\alpha} = 0.0530$) we now use Equation (3.5) to see what we can say about R_0. The disappointing answer is that, unless we assume some prior knowledge

about the latent and infectious periods, we can hardly say anything about R_0, except that $R_0 > 1$ since the epidemic is taking off. In order to say more about R_0 one needs either more detailed data or some other knowledge about the latent and infectious periods. If infections are contact-traced it is possible to make inference on the generation times. However estimating model parameters from such inference is far from simple (Svensson, 2007). If such information is not available, R_0 can be estimated by assuming interval ranges for each model parameter, ranges within which the true parameter values are believed to lie. To illustrate this from the SARS data we choose the following intervals: μ_I and μ_L is assumed to lie between 3 and 11 days (with 7 days as mid-point), and the coefficients of variation are assumed to lie between 0 and 4/7 (corresponding to 4 days for the mid-points above). In Table 1 the R_0 estimate, based on (3.5), $\hat{\alpha} = 0.053$ and current values of μ_L, μ_I, τ_L and τ_I, is listed for each of the 16 combinations interval end-points. The point estimate when each parameter takes on the mid-value ($\mu_L = \mu_I = 7$ and $\tau_L = \tau_I = 2/7$ and $\hat{\alpha} = 0.053$) equals $\hat{R}_0 = 1.747$.

μ_L	μ_I	τ_L	τ_I	$\hat{R}_0$
3	3	0	0	1.2903
3	3	0	4/7	1.2935
3	3	4/7	0	1.2897
3	3	4/7	4/7	1.2930
3	11	0	0	1.5528
3	11	0	4/7	1.6468
3	11	4/7	0	1.5521
3	11	4/7	4/7	1.6461
11	3	0	0	1.9674
11	3	0	4/7	1.9724
11	3	4/7	0	1.8834
11	3	4/7	4/7	1.8881
11	11	0	0	2.3677
11	11	0	4/7	2.5111
11	11	4/7	0	2.2666
11	11	4/7	4/7	2.4039

Table 1: Estimates of R_0 from SARS outbreak in China 2003.04.02 - 2003.06.02. within different assumptions of model parameters and $\hat{\alpha} = 0.053$. Data from WHO.

As can be seen from the table the estimate $\hat{R}_0$ depends quite a lot on our assumptions about the latent and infectious periods. The smallest estimate is $\hat{R}_0 = 1.2897$ obtained when μ_L, μ_I and τ_I are at their minimal possible point and where τ_L is at its maximal point. The largest estimate is $R_0 = 2.5111$ obtained for the "opposite" parameter choices. Within the range of "possible" parameter values for the latent and infectious periods, the R_0 estimate hence changes by a factor 2. It is hence hard to make precise estimates of R_0 without other sources of information regarding the latent and infectious periods.

This illustrates that an estimate of R_0 using data from the initial growth is quite

uncertain except in the rare case that the parameters of the latent and infectious periods are known with fairly high precision.

4.2 Estimating variability from final size data

In Section 3.1 it was shown that, for fixed R_0, the more random the infectious period is, the more unlikely is a large outbreak (the same conclusion holds when other factors, e.g. susceptibilities and/or infectivities, are varied, Andersson and Britton, 2000a and references therein). This observation can be used to say something about the randomness of the infectious period (and/or of individuals) from final size data, i.e. data lacking any time measurements. If we observe the final proportion infected $\tilde{\rho}$ in a large outbreak we estimate R_0 using Equation (2.1), which gives the estimate

$$\hat{R}_0 = \frac{-\ln(1-\tilde{\rho})}{\tilde{\rho}}. \tag{4.4}$$

The information about τ_I lies in the fact that a major outbreak took place, an event with small probability when τ_I is large. In the Bayesian framework this can be illustrated by comparing the prior distribution $p(\tau_I)$ with the posterior distribution $p(\tau_I|\tilde{\rho})$. Using Bayes formula we get

$$p(\tau_I|\tilde{\rho}) \propto p(\tilde{\rho}|\tau_I)p(\tau_I),$$

i.e. the posterior distribution equals the prior distribution multiplied by $p(\tilde{\rho}|\tau_I)$, the probability of a large outbreak, denoted π in Section 3.1. There it was shown that $\pi = p(\tilde{\rho}|\tau_I)$ was decreasing in τ_I, the coefficient of variation of the infectious period. So, any prior knowledge about τ_I is shifted towards smaller values in the posterior distribution. The same type of conclusion also applies to other individual heterogeneities: the fact that a major outbreak has occurred shifts any prior knowledge about individual variation towards less variation.

Of course, more detailed data containing time-measurements, or data from more than one outbreak is to be preferred. But, if no such data is available, any prior information about the randomness of the infectious period is shifted towards smaller values of τ_I when inference is based on final size data from one major outbreak. In Figure 5 we illustrate this for the case that τ_I has an exponential distribution with mean 0.5 as prior distribution, and where the posterior distribution is based on a major outbreak resulting in 50% getting infected.

It is seen that the posterior distribution is not more "concentrated" compared with the prior distribution, as is usually the case. Instead the posterior distribution is merely shifted towards smaller values implying that the belief after observing an epidemic with 50% getting infected results in that the posterior favors smaller values of τ_I (the coefficient of variation of the infectious period), as compared to prior beliefs. The posterior mean of τ_I is ??, The same qualitative conclusion, that a major outbreak results in higher posterior belief for small coefficient of variation of the infectious period, holds for any fraction getting infected and any prior distribution for τ_I.

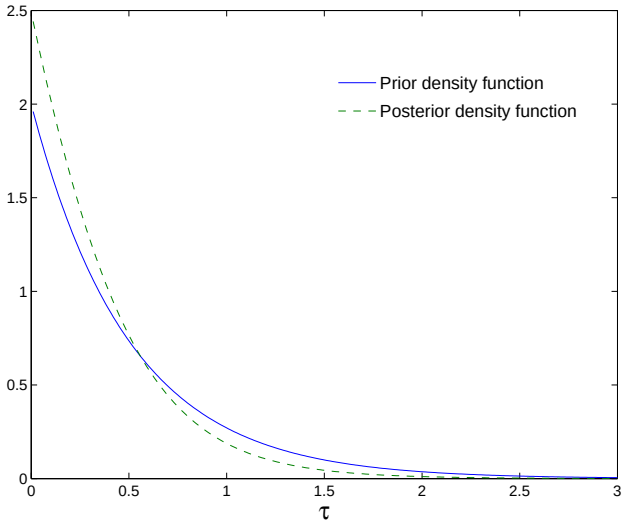

Figure 5: Exponential prior distribution function of τ_I with mean 0.5, and posterior distribution of τ_I after observing an outbreak resulting in 50% getting infected, with mean 0.384.

5 Discussion

In the present paper we have tried to motivate the use of stochastic models when studying certain features in epidemics. First it was illustrated that the *probability* for a major outbreak is greatly affected by the randomness of the infectious period, or more generally, the randomness of the "infectivity" exerted by an individual. The more variation the distribution of the infectious period contains, the less likely is a major outbreak. As a consequence, observed epidemics (major outbreaks) will tend to originate from diseases with infectious periods not having very skew/heavy-tailed distributions. It was also shown that the probability of a major outbreak is unaffected by a latency period of arbitrary length. The latter result relies on the assumption that individuals do not change behaviour as the epidemic progresses nor that preventive measures are put into place – then a latency period will have an effect.

The second feature studied was the initial exponential growth rate. This rate was shown to depend heavily on both the latent and infectious periods, there means as well as their randomness. From a practical perspective this implies that, unless additional information about the infectious period and latency period distributions is available, it is very hard to estimate the basic reproduction number R_0 (and effects of possible preventive measures) from the exponential growth rate of the initial outbreak phase.

There are also other features in epidemics affected by randomness and not only mean values. Common for most of these situations are that, for some type of event, only few random objects are influential. One such feature is the time to disease extinction of endemic diseases: before disease extinction only few are infectious. For example, Andersson

and Britton (2000b) show that not only the means but also the coefficients of variation of the latency period, infectious period and life-duration affect the time to extinction when starting at the endemic level.

Another feature affected by randomness is *vaccine response*. Two models for vaccine response are the *leaky* model and the *all-or-nothing* model (Halloran et al., 1992). The leaky model assumes that each person vaccinated has a susceptibility that is reduced by a factor e (for efficacy). The all-or-nothing model instead assumes that a proportion e are completely immune whereas the remaining proportion vaccinated are unaffected by the vaccine. Here too, e is called efficacy. In both cases, the relative risk that a vaccinated person gets infected by an infectious contact is $1-e$ (so the person avoids infection due to the vaccine with probability e). Even though the two models have the same "efficacy" their effect is different. In fact, a leaky vaccine always reduces the spread less than an all-or-nothing vaccine with the same efficacy – so the randomness in vaccine effect matters. A simple explanation to this is the following (Ball and Becker, 2006). Both vaccine models have the same probability of infection $(1-e)$ at the first contact with an individual. However, among the vaccinated people who escape infection upon the first contact, people vaccinated with a leaky vaccine still have relative susceptibility $1-e$ whereas those with the all-or-nothing vaccine escaping infection the first time all have the "all"-effect and are hence completely immune. As a consequence, the final size in case of a major outbreak will be smaller with an all-or-nothing vaccine as compared to a leaky vaccine having the same efficacy e $(0 \leq e \leq 1)$. Still, both vaccine responses have the same critical vaccination coverage $v_c = e^{-1}(1-1/R_0)$, meaning that the same fraction has to be vaccinated with either vaccine in order to obtain herd immunity.

As pointed out there are many other features less influenced by stochasticity, for example R_0. In the present paper we simply focus on aspects where stochasticity does matter.

Needless to say, the model we have studied is by no means fully realistic. Important extensions are for example to allow for different types of individuals having different susceptibility, infectivity and/or mixing patterns, e.g. households with higher contact rates within households (since households are small, stochasticity play a roll also here, cf. Ball et al., 1997). However, the features considered in the present paper are still valid under such more realistic models.

Appendix: The Malthusian parameter

The Malthusian parameter α is the solution to (3.4). To begin with,

$$\begin{aligned} \lambda P(L < t < L+I) &= \lambda \int_0^t f_L(s) \int_{t-s}^{\infty} f_I(r) dr ds \\ &= \lambda \int_0^t f_L(s)(1-F_I(t-s)) ds. \end{aligned}$$

Hence (3.4) equals

$$\lambda \int_0^\infty e^{-\alpha t} \int_0^t f_L(s)(1-F_I(t-s))dsdt = \lambda \int_0^\infty e^{-\alpha s} f_L(s) \int_s^\infty e^{-\alpha(t-s)}(1-F_I(t-s))dtds$$
$$= \lambda \varphi_L(\alpha)(1-\varphi_I(\alpha))\frac{1}{\alpha}. \quad (.1)$$

The second equality follows from partial integration and identifying the laplace transforms of the latent and infectious periods: $\varphi_L(\alpha) = E(e^{-\alpha L}) = \int_0^\infty e^{\alpha s} f_L(s)ds$, and similar for the infectious period. The infectious period I is gamma-distributed. Using first the more common parametrization $I \sim \Gamma(\alpha_I, \beta_I)$ we get

$$\varphi_I(\alpha) = \Big(\frac{\beta_I}{\beta_I + \alpha}\Big)^{\alpha_I}. \quad (.2)$$

Since also the latent period is gamma distributed we also have that $\varphi_L(\alpha) = \Big(\frac{\beta_L}{\beta_L+\alpha}\Big)^{\alpha_L}$. Thus, by (.1) and (.2), Equation (3.4) is simplified to

$$\alpha = \lambda\Big(\frac{\beta_L}{\beta_L + \alpha}\Big)^{\alpha_L}\Big(1 - \Big(\frac{\beta_I}{\beta_I + \alpha}\Big)^{\alpha_I}\Big). \quad (.3)$$

If we convert to the more interpretable parameters mean μ and coefficient of variation τ we have that $\mu_I = \alpha_I/\beta_I$ and $\tau_I = 1/\sqrt{\alpha_I}$, and similarly for the latent period. Equation (.3) can then, after some simple algebra and using that $R_0 = \lambda\mu_I$, be written as

$$\alpha = \frac{R_0}{\mu_I}\frac{1}{(1+\alpha\tau_L^2\mu_L)^{1/\tau_L^2}}\left(1 - \frac{1}{(1+\alpha\tau_I^2\mu_I)^{1/\tau_I^2}}\right).$$

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