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Endemic persistence or disease extinction: The effect of separation into sub-communities

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Abstract

Consider an infectious disease which is endemic in a population divided into several large sub-communities that interact. Our aim is to understand how the time to extinction is affected by the level of interaction between communities.

We present two approximations of the expected time to extinction in a population consisting of a small number of large sub-communities. These approximations are described for an SIR epidemic model, with focus on diseases with short infectious period in relation to life length, such as childhood diseases. Both approximations are based on Markov jump processes.

Simulations indicate that the time to extinction is increasing in the degree of interaction between communities. This behaviour can also be seen in our approximations in relevant regions of the parameter space.

Keywords: Endemic diseases; SIR epidemic; Population heterogeneity; Expected time to extinction; Quasi-stationary distribution

1. Introduction

When modelling infectious diseases a simplifying assumption often made is that the social interaction within the population is homogeneous. This assumption becomes less credible as the population size increases, i.e. there is a need for including some kind of population heterogeneity. A way to include population heterogeneity is to divide the population into sub-communities. By doing so we can, in the easiest setting, allow two different levels of social interaction, one level within and one between sub-communities. Under these conditions it is natural to let the social interaction within sub-communities be homogeneous. In the present paper we study how this new level of social interaction affects the epidemic behaviour as an infectious disease is introduced into the population. This we do for the situation when there are k sub-communities each of size n, where typical values of k is $2,\ldots,5$ and n is 50,000 or larger. Throughout this report we will focus on infectious diseases which have a short infectious period in relation to life length and give rise to life long immunity, e.g. childhood diseases. When an outbreak of such a disease occurs in a community, we have three possible scenarios. The first being that only a few become infected and the time to extinction is short. The second one being that many become infected but the time to extinction is short. We are interested in diseases that behave as in the third scenario, namely when many individuals become infected and the time to extinction is long. When a disease behaves in this way it is called endemic. During the progression of an endemic disease there is only a rather small fraction of infectious individuals present in the population at each time point, but since the time until disease extinction is long, the accumulated number of infected individuals may still be large. Usually the fraction of infected individuals at each time point fluctuates around some specific level, the endemic level, until disease extinction.

Whether a disease becomes endemic or not depends on a number of factors, such as population size, the basic reproduction number, length of the latency and infectious period, seasonal effects, etc., see Anderson and May (1991, pp. 128–143). In the present paper we are primarily

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interested in the effect of a community being divided into sub-communities. For this reason we neglect most other heterogeneities, and the most important factors remaining are a sufficiently large population. The basic reproduction number, R_0, is defined as the expected number of individuals that a single infectious individual infects in a large susceptible population during its infectious period. One can show that the basic reproduction number works as a threshold which determines the dynamics of the disease and that it is dimensionless, see Anderson and May (1991, pp. 13–19). If $R_0 \leqslant 1$, the disease will go extinct rather quickly. On the other hand, if $R_0 > 1$, the disease has a positive probability to persist in the population over a long time period. Henceforth R_0 is assumed to be greater than one. The notion of 'sufficiently large population' which we have used above is not a trivial question, and this is something we discuss in Sections 5 and 6.

When the population is divided into sub-communities rather than being homogeneously mixing, the dynamics of the spread of disease becomes more intricate. Now, some sub-communities may be disease-free, while others contain infected individuals, and infectious contacts between individuals from different sub-communities may re-infect disease-free sub-communities. It seems reasonable to expect that the mean time to extinction of an endemic disease depends on the social activity between the different communities when keeping everything else fixed. This has been shown to be true by Hagenaars et al. (2004).

Endemic diseases can be modelled stochastically in several different ways. Depending on the model, different aspects of the qualitative behaviour of the dynamics of the disease can be studied. Our aim is to study the expected time to extinction of an endemic disease in the situation with a small number of large sub-communities, when each sub-community starts at the so-called endemic level. The model used is an SIR model for a population divided into sub-communities. This model will henceforth be denoted SIR-SC. For a homogeneously mixing population, from here on denoted SIR-HM, much work has been done, see for example van Herwaarden and Grasman (1995), Nåsell (1999, 2005), and Andersson and Britton (2000b). For more on epidemic models in general, see Anderson and May (1991), Andersson and Britton (2000a) and Diekmann and Heesterbeek (2000).

A short heuristic description of the SIR-HM model is that all individuals in the community are equally likely to meet, and that each individual may switch between being susceptible, infectious and recovered (and immune). Thus, switches occur according to $S \to I \to R$. Another important property is that susceptible individuals are born into the community and that individuals eventually die, i.e. demographic aspects. This will also give us a nonconstant community size. The version of this model which we use is from Nåsell (1999), and does not allow for birth of infectious individuals. Important results for the SIR-HM model that we will use are from Nåsell (1999, 2005). There approximations for the expected time to extinction when starting at the quasi-stationary level of infection are derived. Hagenaars et al. (2004) study the same expected time to extinction as Nåsell but for the case with a small number of sub-communities. They obtain an approximation of this expected time, but the approximation is derived under the assumption of low mixing between communities and that the infectious period is fairly long in relation to life length. Human childhood diseases, having infectious periods of 1–2 weeks out of life lengths of 70–80 years, fall outside of this domain. For more information on infectious periods of infectious diseases see Table 3.1 in Anderson and May (1991, p. 31).

In the present paper we study the SIR model for a population divided into sub-communities previously studied by Hagenaars et al. (2004) and Lloyd and May (1996) (who treat a more general model). Similar models can be found in the metapopulation literature (sometimes also referred to as patch models), see e.g. Keeling (2000a, b), Etienne and Heesterbeek (2000), van den Driessche and Watmough (2002), where they address related topics to those which we treat here. In a paper by Wonham et al. (2004) they also treat the situation when there are seasonal effects. Other versions of SIR models with heterogeneities are household models and models with several levels of mixing, where the population is divided into many small groups, see e.g. Ball and Lyne (2001), Ball et al. (1997) and Ball and Neal (2002).

In the present paper we have adopted ideas from both Nåsell (1999) and Hagenaars et al. (2004), trying to find better approximations for $\tau = E(T_Q)$, the expected time to extinction for a population divided into sub-communities given that all sub-communities are started at the endemic level, for diseases with short infectious period with respect to life length. We present two approximations of τ, the first one is based on similar arguments as in Hagenaars et al. (2004) and the second one is based on more heuristic arguments motivating the use of an exponential form. Further, we show that T_Q is exponentially distributed, and by approximating τ, we get that $T_Q \sim \text{Exp}(1/\tau)$. Simulations indicate that our approximations are more suitable for situations when there is low mixing between sub-communities and that the second, more heuristically motivated approximation, performs somewhat better.

In Section 2 we define the sub-community epidemic model and present results needed later on. In Sections 3 and 4 we describe our two approximations. Section 5 is devoted to a small simulation study and numerical evaluations of these approximations. A closing discussion and summary of our results is given in Section 6.

2. The SIR model for a population divided into sub-communities (SIR-SC)

We start with a brief look at the SIR model with homogeneous mixing (SIR-HM) defined in Nåsell (1999). We have a population which lack social structures and where individuals may switch between the states

susceptible, infectious and recovered (and immune) according to S → I → R. Once an individual becomes infected, this individual will stay so for an exponentially distributed time with mean $1/\nu$. During this time period the infected individual makes infectious contacts with a given susceptible individual according to a Poisson process with rate β/n. All infectious contacts are assumed to result in instantaneous infection. The demographic aspects of the model are as follows: susceptible individuals are 'born' according to a Poisson process with constant rate μn, and all individuals live for an exponentially distributed time with mean $1/\mu$. A consequence of the constant birth rate is that the population size will fluctuate around n, which is thought of as being large. This is deliberate to avoid that the dynamics of the disease depend on extensive population fluctuations. Once the population becomes disease-free, it will remain so forever on, since there is no birth or immigration of infectious individuals. Hence, the disease-free states are absorbing, and all other states are transient.

When the population is divided into sub-communities with higher mixing within, the dynamics of the disease becomes more involved. The simplest case is to let all sub-communities be equally large, having size n, and to let all individuals have the same within sub-community contact rates and the same between sub-community contact rates. We are interested in the situation when the number of sub-communities, k, is fixed and small in relation to n. With this model the population structure is symmetric and we only need to add one parameter, ε, which is the proportion of an individuals contacts that are with other sub-communities. This parameter, ε, is defined such that $\varepsilon = 0$ corresponds to having k isolated sub-communities, and $\varepsilon = 1$ corresponds to the case where all k sub-communities act as a single large community of size kn. (One can also think of ε as an inverse distance, where $\varepsilon = 0$ corresponds to that all sub-communities lie infinitely far apart and $\varepsilon = 1$ corresponds to the case when they coincide, and then ε works as a measure of spatial heterogeneity or spatial coupling, see e.g. Keeling, 2000a, b.)

A natural way to model the situation with sub-communities is to do so such that the overall infectious pressure in the entire population is kept constant regardless of the value of ε. This also has the advantage that we get the same basic reproduction number, R_0, as for the SIR-HM model and hence the two models become easier to compare. The basic reproduction number for the SIR-HM model is defined as the average number of individuals which a single infectious individual infects in an otherwise susceptible population during its infectious period. That is, a single infectious individual makes infectious contacts at rate β/n with any given individual of the surrounding n susceptible individuals, during an infectious period with mean $1/(\mu+\nu)$, since death can occur before recovery. Thus R_0 for the SIR-HM model becomes

$$R_0 = \frac{\beta}{\mu+\nu} = \frac{\beta}{\mu\alpha}, \tag{1}$$

where $\alpha = (\mu+\nu)/\mu$. For the case with sub-communities, an infected individual makes contacts with any given individual within its own sub-community at rate β'/n, and at rate $\varepsilon\beta'/n$ with a given individual in any of the $k-1$ surrounding sub-communities. This gives us that the probability that a contact is within the sub-community is

$$\frac{n\beta'/n}{n\beta'/n + (k-1)n\varepsilon\beta'/n} = \frac{1}{1+\varepsilon(k-1)}.$$

If we have a single infected individual in an otherwise susceptible population, this individual will infect a given individual within its own sub-community at rate β'/n during an exponentially distributed infectious period with mean $1/(\mu+\nu)$, and infect a given individual in any of the $k-1$ neighbouring sub-communities at rate $\varepsilon\beta'/n$, hence the basic reproduction number becomes

$$\begin{aligned} R_0 &= \frac{1}{\mu+\nu}(n\beta'/n + (k-1)n\varepsilon\beta'/n) \\ &= \frac{\beta'}{\mu+\nu}(1+\varepsilon(k-1)). \end{aligned}$$

Thus, if we let $\beta' = \beta/(1+\varepsilon(k-1))$ we see that we have found the proper scale in order to keep R_0 independent of ε. For this β' we have

$$R_0 = \frac{\beta}{\mu\alpha}.$$

The possible transitions and their rates for the SIR-SC model are specified in Table 1, which are the same as in Hagenaars et al. (2004).

We now derive the endemic level. In the stochastic model this corresponds to the mean in the quasi-stationary distribution. Let $(\mathbf{X}(t), \mathbf{Y}(t)), t \geqslant 0$, denote a $2k$ dimensional Markov jump process, where $X_j(t) = s_j$ and $Y_j(t) = i_j$ denote the number of susceptible and infectious individuals in sub-community j at time t, with random transition rates defined in Table 1. If we now look at the process of proportions $(\mathbf{X}(t)/n, \mathbf{Y}(t)/n)$, when n is large, this process can be approximated by the solution of a deterministic system of differential equations corresponding to the transition rates defined in Table 1. This system

Table 1
SIR model for a population divided into sub-communities rates for sub-community j

From	To	Rate
(s_j, i_j)	(s_j+1, i_j)	μn
(s_j, i_j)	(s_j-1, i_j)	μs_j
(s_j, i_j)	(s_j-1, i_j+1)	$\frac{\beta}{n}\frac{1}{n(1+\varepsilon(k-1))}s_j\left(i_j + \varepsilon\sum_{u\neq j} i_u\right)$
(s_j, i_j)	(s_j, i_j-1)	$(\mu+\nu)i_j$

is given by

$$\frac{dx_i}{dt} = \mu - \frac{\beta}{(1+\varepsilon(k-1))} x_i \left(y_i + \varepsilon \sum_{j \neq i} y_j \right) - \mu x_i,$$
$$\frac{dy_i}{dt} = \frac{\beta}{(1+\varepsilon(k-1))} x_i \left(y_i + \varepsilon \sum_{j \neq i} y_j \right) - (\mu + \nu) y_i. \quad (2)$$

Setting these equations equal to zero for $i = 1, \ldots, k$ gives us the stationary points, which turn out to be (1, 0), the disease-free state, and

$$(\hat{x}_i, \hat{y}_i) = (\hat{x}, \hat{y}) = \left(\frac{1}{R_0}, \frac{1}{\alpha} \left(1 - \frac{1}{R_0} \right) \right), \quad (3)$$

which corresponds to the endemic level, and which only exists if $R_0 > 1$. Equating the differential equations from (2) to 0 when $k = 1$, gives us the same endemic level as for the SIR-HM model.

A quasi-stationary distribution is defined as the distribution after a long time conditioned on that the process has not been absorbed. The endemic level can be thought of as the mean of this distribution, which the process fluctuates around. The quasi-stationary distribution is important when modelling endemic diseases, since we are interested in the behaviour of the epidemic until it goes extinct. But, quasi-stationary distributions give rise to many difficulties such as questions of uniqueness and existence, see Pollett and Roberts (1990), and the occurrence of quasi-cycles, Bartlett (1957) and Dushoff et al. (2004). A longer treatment of quasi-stationarity concerning birth and death process is given by van Doorn (1991).

Let $Q = \{q_{\mathbf{x},\mathbf{y}}\}$ denote the quasi-stationary distribution, where $q_{\mathbf{x},\mathbf{y}}$ is the probability that the process $(\mathbf{X}(t), \mathbf{Y}(t)) = (\mathbf{x}, \mathbf{y})$ as $t \to \infty$, conditioned on that the process has not been absorbed. Recalling that the lack of memory property implies an exponential distribution, we have

$$\begin{aligned} &P(T_Q > t + s \mid T_Q > t,\ (\mathbf{X}(0), \mathbf{Y}(0)) \sim Q) \\ &\quad = P(T_Q > t + s \mid T_Q > t,\ (\mathbf{X}(t), \mathbf{Y}(t)) \sim Q) \\ &\quad = P(T_Q > s \mid (\mathbf{X}(0), \mathbf{Y}(0)) \sim Q), \end{aligned}$$

which establishes that T_Q is exponentially distributed. The rate parameter for this exponential distribution is the intensity with which the process leaves the set of transient states. For the case with sub-communities the set of states from which the process can be absorbed is $(\mathbf{X}(t), \mathbf{Y}(t)) = \{(\mathbf{x}, \mathbf{y}); \mathbf{y} = \mathbf{e}_i, i = 1, \ldots, k\}$. We state the conclusions from above in the following proposition:

Proposition 1. *The time to extinction given that the process is started in the quasi-stationary distribution, T_Q, is exponentially distributed with mean*

$$\tau = \frac{1}{\mu \alpha q_{\cdot,1}}, \quad (4)$$

where

$$q_{\cdot,1} = \sum_{\mathbf{x}} \sum_{i=1}^{k} q_{\mathbf{x},\mathbf{e}_i} \quad (5)$$

and where $\mathbf{e}_i$ is the ith unit vector.

The reasoning here is the same as in the proof of Proposition 4.1 in Andersson and Britton (2000b), but this result was first derived for the homogeneous case by Nåsell (1999), and if we set $k = 1$ in Proposition 1 we obtain the result for a homogeneously mixing population. Another way of obtaining (4) and (5) from Proposition 1 is via the Kolmogorov forward equations for the process $(\mathbf{X}(t), \mathbf{Y}(t))$ conditioned on that it has not gone extinct by time t, and then use the identity $P(T_Q \leqslant s) = P(\mathbf{Y}(s) = 0)$.

To completely determine the distribution of T_Q, it remains to derive $q_{\cdot,1}$. One way to obtain an approximation for $q_{\cdot,1}$ is to use a diffusion approximation. Let $(\widetilde{X}_n(t), \widetilde{Y}_n(t))$ be the process defined by

$$(\widetilde{X}_n(t), \widetilde{Y}_n(t)) = \sqrt{n} \left(\frac{X(t)}{n} - \hat{x}, \frac{Y(t)}{n} - \hat{y} \right). \quad (6)$$

One can show that this process converges to an Ornstein–Uhlenbeck process, $(\widetilde{X}(t), \widetilde{Y}(t))$, as n tends to infinity, see e.g. in Ethier and Kurtz (1986, Chapter 11). From the theory of diffusion processes it is known that this process has a Gaussian *stationary* distribution with mean zero and computable covariance matrix, see e.g. Karatzas and Shreve (1991, p. 357). This together with (6) gives us that $Y(t) \approx \sqrt{n}\widetilde{Y}(t) + n\hat{y} = \sqrt{n}\widetilde{Y}(t) + \mu_Y$ for large n, so that $Y(t)$ is approximately $N(\mu_Y, \sigma_Y^2)$ when t is large. But, now the approximate marginal distribution of $Y(t)$ for large t is defined on $\mathbb{R}$, whereas the original process $Y(t)$ is integer valued and always greater or equal to zero (we cannot have a negative number of individuals). Thus, if we truncate the approximate marginal distribution for the number of infectious individuals at zero and use continuity correction we get an approximation of the underlying quasi-stationary distribution according to

$$q_{\cdot,1} = \frac{1}{\sigma_Y} \frac{\varphi((\mu_Y - 1)/\sigma_Y)}{\Phi((\mu_Y - 0.5)/\sigma_Y)}, \quad (7)$$

where $\Phi(\cdot)$ and $\varphi(\cdot)$ are the standard normal distribution function and density function, respectively, and

$$\sigma_Y = \mathrm{Sd}(\sqrt{n}\widetilde{Y} + n\hat{y}) = \frac{\sqrt{n}}{R_0} \sqrt{R_0 - 1 + R_0^2/\alpha},$$
$$\mu_Y = E(\sqrt{n}\widetilde{Y} + n\hat{y}) = n \frac{R_0 - 1}{\alpha R_0}. \quad (8)$$

Here σ_Y and μ_Y are the expectation and standard deviation of the marginal process of number of infected individuals, see Nåsell (1999, Eq. (2.10)), which are obtained with methods from Karatzas and Shreve (1991). Using (7) together with Proposition 1 gives us that T_Q is

exponentially distributed with approximate mean

$$\tau_n \approx \frac{\sigma_Y}{\mu\alpha}\frac{\Phi((\mu_Y-0.5)/\sigma_Y)}{\varphi((\mu_Y-1)/\sigma_Y)} \tag{9}$$

with σ_Y and μ_Y from Eq. (8), (cf. Nåsell, 1999, Eq. (2.13)). From here on τ_n refers to the case with a homogeneously mixing population of size n, and all other types of references to τ are for the case with sub-communities unless otherwise stated. Note that usually $\mu_Y \gg 1$ which gives us that $q_{\cdot,1}$ from (7) simplifies to

$$q_{\cdot,1} \approx \frac{1}{\sigma_Y}\frac{\varphi(\mu_Y/\sigma_Y)}{\Phi(\mu_Y/\sigma_Y)} \approx \frac{1}{\sigma_Y}\varphi(\mu_Y/\sigma_Y), \tag{10}$$

where the last approximation is good when $\mu_Y/\sigma_Y > 3$, since then $\Phi(\mu_Y/\sigma_Y) \approx 1$ holds. When $\alpha \gg R_0$, which is the case for childhood diseases, then $\sigma_Y \approx \sqrt{n(R_0-1)}/R_0$, and $q_{\cdot,1}$ from (10) becomes

$$\begin{aligned} q_{\cdot,1} &\approx \frac{1}{\sigma_Y}\varphi\left(\sqrt{n(R_0-1)}/\alpha\right) \\ &= \frac{R_0}{\sqrt{2\pi n(R_0-1)}}\exp\left(-n\frac{R_0-1}{2\alpha^2}\right) \end{aligned} \tag{11}$$

and τ_n from (9) simplifies to

$$\tau_n \approx \frac{\sqrt{2\pi n(R_0-1)}}{\mu\alpha R_0}\exp\left(n\frac{R_0-1}{2\alpha^2}\right). \tag{12}$$

When the average life length is long in relation to the average infectious period, Nåsell (2005) shows that (9) is a too crude approximation when n is only moderately large, e.g. $n \leqslant 2,000,000$ for a specific set of parameter values corresponding to measles, see Section 5 below. In Nåsell (2005) he instead proposes that the quasi-stationary distribution of the number of infected individuals could be approximated with a geometric distribution with $p = 1/\mu_Y$ where μ_Y is from (8). If $Y \sim \text{Geo}(p)$ then $E(Y) = 1/p = \mu_Y$ which together with Proposition 1 with $k = 1$ yields the following: When the quasi-stationary distribution of Y is approximated with a Geo$(1/\mu_Y)$ distribution with mean μ_Y from (8), then T_Q is exponentially distributed with approximate mean

$$\tau_n \approx n\frac{R_0-1}{\mu\alpha^2 R_0}, \tag{13}$$

c.f. Nåsell (2005, Eqs. (8.3) and (9.2)).

Returning to the case with sub-communities again, we would like to use the techniques described above, but due to symmetry the resulting Ornstein–Uhlenbeck diffusion process approximated at the endemic level is independent of ε, and hence not of much help. Due to this, the second approach will also give us an approximation of the quasi-stationary distribution which is independent of ε, since it was a geometric distribution with parameter $p = 1/\mu_y$, where μ_y is as (8), but with n replaced with kn. Despite of this, we can still say something about the expected time to extinction for the two extreme cases, $\varepsilon = 0$ and 1, using results from the SIR-HM model. Let $\tau(\varepsilon)$ be the expected time to extinction when all k sub-communities, each of size n, are started at the endemic level, when there is a proportion ε of contacts between sub-communities. (Note that $\tau(\varepsilon) = \tau(\varepsilon, n, k, \mu, \alpha, R_0)$.) When $\varepsilon = 0$ all k sub-communities are isolated and independent, and all k sub-communities start at the endemic level of infection, the expected time until one of the k infected sub-communities recovers is τ_n/k, due to independence and that the expected duration of an epidemic within a sub-community is exponentially distributed with mean τ_n, where τ_n is from one of Eqs. (9) or (13). Due to the Markov property and that a disease-free community never can be re-infected when $\varepsilon = 0$, the expected time until one of the $k-1$ remaining communities recovers is $\tau_n/(k-1)$. Repeating this argument gives us

$$\tau(0) = \tau_n \sum_{i=1}^{k}\frac{1}{i}, \tag{14}$$

where τ_n can be approximated using either of Eqs. (9) or (13). On the other hand, when $\varepsilon = 1$, all k communities behave as one large community of size kn, and we can again make use of (9) with n replaced by kn, i.e.

$$\tau(1) = \tau_{kn}. \tag{15}$$

If n is small we suggest to approximate $\tau(0)$ and $\tau(1)$ by using the geometric approximation of τ_n from Eq. (13), which gives us

$$\frac{\tau(0)}{\tau(1)} = \frac{\sum_{i=1}^{k} 1/i}{k} \tag{16}$$

which is smaller than one for $k > 1$, i.e.

$$\tau(0) < \tau(1). \tag{17}$$

If n is large we recommend to use the truncated normal approximation of τ_n from (9) instead. For n such that $\mu_Y/\sigma_Y > 3$ and when we are in the parameter region corresponding to childhood diseases we can approximate τ_n with (12). Inserting this into $\tau(0)$ and $\tau(1)$ from Eqs. (14) and (15) gives us that

$$\frac{\tau(0)}{\tau(1)} \approx \frac{\sum_{i=1}^{k} 1/i}{\sqrt{k}}\exp\left(-n\frac{R_0-1}{2\alpha^2}(k-1)\right) \tag{18}$$

which is smaller than 1 for sufficiently large n, i.e. $\tau(0) < \tau(1)$.

3. Approximation using a recovered (and immune) state

As we have seen, it is hard to find approximations of the quasi-stationary distribution which depend on ε. But, if we rely on Proposition 1, that T_Q is exponentially distributed, we can approximate $\tau = E(T_Q)$ directly, instead of going via approximations of the quasi-stationary distribution.

In Hagenaars et al. (2004) they look at the case when $0 < \varepsilon \ll 1$ and α is thought of as small, such as $\alpha = 2$ or 160. An example of a disease with small α is scrapie among sheep, see Hagenaars et al. (2004). For scrapie the average incubation period is a few years which is of the same order

of magnitude as the average life length of sheep. Hence, for diseases with small α one can assume that when an individual recovers from infection, this individual will likely be removed due to death within a relatively short time period. This motivates that we can look at the system from a sub-community view, classifying each sub-community as either endemic or susceptible. That a sub-community is endemic here means that the sub-community on average has a fraction of infected individuals corresponding to the endemic level $\hat{y}$. A sub-community that is susceptible only contains susceptible individuals. Further, switches between these two states are assumed to occur instantaneously. This is a reasonable approximation, since the time it takes from that a single individual becomes infected until the endemic level of infection is reached is short in relation to the time it takes for an endemic sub-community to become disease-free.

When defining the rate with which susceptible sub-communities becomes endemic, it is natural to think that this rate depends on the infectious pressure generated by the endemic sub-communities. But, we are only interested in those infectious contacts between sub-communities that result in a disease invasion and not those that fade out by chance, so we must take this fact into account. Thus, we need to derive the probability of this event. Suppose a sub-community with a fraction x susceptible and $1-x$ recovered (and immune) individuals has just been re-infected, i.e. a single susceptible individual has become infected. In the early stages of an epidemic it behaves approximately as a branching process. When there is only one infected individual in a population with a fraction x susceptible individuals, the effective reproduction number becomes xR_0. Since the infectious period is exponentially distributed, the number of children of this one infected individual, D, will be $\mathrm{Geo}(1/(1+xR_0))$, and we get that the probability that the epidemic started by this single infected individual will not fade out by chance, p, is the solution to the following equation:

$$1-p = E((1-p)^D), \tag{19}$$

see Andersson and Britton (2000a, pp. 22–25). Solving this gives us the solution

$$p = 1-\frac{1}{xR_0}. \tag{20}$$

From this we get that the probability that the introduced disease will not fade out by chance in a fully susceptible population is $1-1/R_0$. The more general result from (20) is needed later on.

One individual contacts a given individual from one of the surrounding sub-communities at rate $\varepsilon\beta'/n$, and hence contacts a fully susceptible sub-community at rate $\varepsilon\beta'$. Consequently, a sub-community at the endemic level, having $\hat{y}n$ infected individuals, infects a given susceptible sub-community at rate $\varepsilon\beta'\hat{y}n = \varepsilon\beta\hat{y}n/(1+\varepsilon(k-1))$, which is the same as the infectious pressure each endemic sub-community expose each susceptible sub-community to. This together with that each infectious contact has the probability $1-1/R_0$ that the introduced disease will become endemic, gives us the rate with which susceptible sub-communities become endemic.

If we again look at the rate with which sub-communities becomes disease-free, this is thought of occurring independently of everything else, i.e. the time to disease extinction in a sub-community is exponentially distributed with mean parameter τ. From this we can define a birth and death process of number of endemic sub-communities, with transition rates

$$\begin{cases} \zeta_j = (k-j)j\varepsilon n\dfrac{\mu R_0}{1+\varepsilon(k-1)}\left(1-\dfrac{1}{R_0}\right)^2, \\ \eta_j = j/\tau_n, \end{cases} \tag{21}$$

where ζ_j is the rate for a transition from j to $j+1$ endemic sub-communities, and η_j is the rate for a transition from j to $j-1$ endemic sub-communities.

Since ε is small, the probability of re-infection will also be small. Based on this fact Hagenaars et al. (2004) assume that the probability of more than one re-infection during the epidemic is negligible. Their approximation can be described as the expected time to absorption of a birth and death process for the number of endemic sub-communities, with rates as in (21), which only allow one birth, or more formally:

Approximation (*Hagenaars et al., 2004*). *The expected time to extinction given that the process is started at the endemic level can be approximated by*

$$\tau_{\mathrm{SI}}(\varepsilon) = \tau(0) + \varepsilon\left((k+1)\sum_{j=1}^{k}\frac{1}{j} - 2k\right) \times \tau_n^2\mu R_0\left(1-\frac{1}{R_0}\right)^2 + O(\varepsilon^2), \tag{22}$$

where $\tau(0)$ *is from* (14) *and* τ_n *is any approximation for a homogeneously mixing population of size* n, *e.g.* (9) or (13).

This corresponds to Eq. (6) in Hagenaars et al. (2004). Here SI in τ_{SI} is used to emphasise that they only use the two sub-community states, susceptible and infected, in their approximation.

When α is large the approach to approximate the expected time to extinction described above is not completely feasible. Because in this situation, the approximation that an endemic sub-community that becomes disease-free instantaneously becomes susceptible is not reasonable. One way to avoid this problem is to add a recovered (and immune) state to our approximating sub-community Markov process. A sub-community is defined as being recovered (and immune) when it is disease-free but not possible to infect. The difference between this state and the susceptible state is that, when a sub-community is recovered (and immune) there is on average a fraction $\hat{x}$ susceptible and $1-\hat{x}$ immune individuals, as opposed to

the susceptible state which only contain susceptible individuals.

By introducing this type of transitions for the sub-communities we have a communication between the states of sub-communities that can be described as $S \to I \to R \to S$, so what we need to define is the rate, ξ, with which a community makes a transition from R to S, since (21) can be used for the other transitions. A transition from $R \to S$ is similar to a $I \to S$ transition, so that one way of defining this rate is to assume that a sub-community stays immune for an exponentially distributed time with mean τ_R. We will return to the definition of τ_R later.

Let s be the number of susceptible sub-communities and i be the number of endemic sub-communities out of a total of k sub-communities, so that $k-(s+i)$ are recovered (and immune), then the transition rates become

$$\begin{cases} \zeta_{s,i} = si\varepsilon\dfrac{\mu n R_0}{1+\varepsilon(k-1)}\left(1-\dfrac{1}{R_0}\right)^2, \\ \eta_{s,i} = \dfrac{i}{\tau_n}, \\ \xi_{s,i} = \dfrac{k-(s+i)}{\tau_R}. \end{cases} \tag{23}$$

There are $k(k+1)/2+k$ possible states, and k of them are disease-free and hence an absorbing class of states. For a schematic graph of the dynamics of this process, see Fig. 1.

Based on the rates (23) we are able to set up a difference equation for $\tilde{t}_{s,i}$, the expected time to extinction when starting with i endemic and s susceptible sub-communities out of k possible, by conditioning on the first transition and using the process' lack of memory. We get the following relation:

$$\begin{aligned} \tilde{t}_{s,i} &= E(\{\text{time to extinction from } (s,i)\}) \\ &= E(\{\text{time spent in } (s,i)\}) \\ &\quad + P((s,i)\to(s-1,i+1)) \\ &\quad \times E(\{\text{time to extinction from } (s-1,i+1)\}) \\ &\quad + P((s,i)\to(s,i-1)) \\ &\quad \times E(\{\text{time to extinction from } (s,i-1)\}) \\ &\quad + P((s,i)\to(s+1,i)) \\ &\quad \times E(\{\text{time to extinction from } (s+1,i)\}) \end{aligned}$$

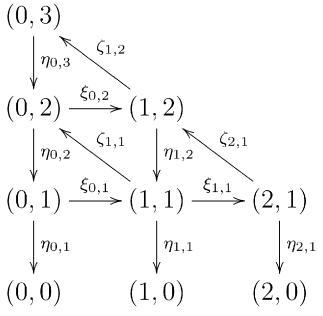

Fig. 1. Schematic graph of the dynamics in our approximating SIR Markov jump process for $k=3$ sub-communities, where each node is (no. of susceptible sub-communities, no. of endemic sub-communities) and the rates are from (23).

which gives us that

$$\begin{aligned} \tilde{t}_{s,i} = {} & \frac{1}{\zeta_{s,i}+\eta_{s,i}+\xi_{s,i}} + \frac{\zeta_{s,i}}{\zeta_{s,i}+\eta_{s,i}+\xi_{s,i}}\tilde{t}_{s-1,i+1} \\ & + \frac{\eta_{s,i}}{\zeta_{s,i}+\eta_{s,i}+\xi_{s,i}}\tilde{t}_{s,i-1} + \frac{\xi_{s,i}}{\zeta_{s,i}+\eta_{s,i}+\xi_{s,i}}\tilde{t}_{s+1,i}, \end{aligned} \tag{24}$$

see Karlin and Taylor (1975, pp. 148–150). In general this system has no closed form solution. Even so, by looking at the transition rates (23) and the relation (24), we see that we can write this as an equation system of the form

$$\tilde{\mathbf{t}} = \mathbf{v} + \mathbf{A}\tilde{\mathbf{t}}, \tag{25}$$

where $\tilde{\mathbf{t}} = (\tilde{t}_{0,k}, \tilde{t}_{0,k-1}, \ldots)'$, $\mathbf{v} = (v_{0,k}, v_{0,k-1}, \ldots), v_{s,i} = 1/(\zeta_{s,i}+\eta_{s,i}+\xi_{s,i})$, and $\mathbf{A}$ is the matrix with transition probabilities defined by the rates (23). A general solution to (25) is given by

$$\tilde{\mathbf{t}} = (\mathbf{I}-\mathbf{A})^{-1}\mathbf{v}, \tag{26}$$

which can be solved numerically, where $\mathbf{I}$ is the identity matrix of the same dimension as $\mathbf{A}$. As before, we are mainly interested in the expected time to extinction when all k sub-communities are initially endemic, i.e. $\tilde{t}_{0,k}$. This defines our first approximation of the expected time to extinction.

Approximation 1. *The expected time to extinction given that the process is started at the endemic level can be approximated by* $\tau_{SIR}(\varepsilon) = \tilde{t}_{0,k}$, *where* $\tilde{\mathbf{t}}$ *solves* (25).

If we look at τ_{SIR} for the case $k=2$, using the rates from (23), we get the following explicit expression:

$$\tau_{SIR}(\varepsilon) = \tau(0) + \frac{\varepsilon\mu n R_0(1-1/R_0)^2\tau_R\tau_n^3}{2(\varepsilon\mu n R_0(1-1/R_0)^2\tau_R\tau_n + \tau_R + \tau_n)}, \tag{27}$$

where $\tau(0)$ is from (14). From (27) one sees that τ_{SIR} is increasing in ε, and that if $\varepsilon = 0$ then $\tau_{SIR} = \tau_{SI}$. For larger values of k the calculations becomes more tedious, since the number of unknown equations increases rapidly.

We now return to the derivation of τ_R, the expected time which a sub-community stays recovered (and immune). When a sub-community becomes recovered (and immune), there is approximately a fraction $\hat{x} = 1/R_0$ susceptible individuals and a fraction $1-\hat{x}$ immune individuals. The problem now is that the probability that an introduced disease will be able to persist depends on the fraction of susceptible individuals in the sub-community.

If we look at the probability that the introduced disease will become endemic, (20), we see that this probability is zero when we have a proportion of susceptible corresponding to the endemic level, and we know that this probability is $1-1/R_0$ when a sub-community is fully susceptible. Thus, we can define the expected time which a sub-community stays recovered (and immune) in terms of the average time it takes until a fraction $\tilde{x} > \hat{x}$ becomes susceptible in a sub-community such that the introduced disease will persist in the population with a pre-specified probability. A natural, but somewhat arbitrary, choice of

this probability is $(1-1/R_0)/2$, i.e. half way between 0 and $1-1/R_0$. This gives us that the fraction of susceptible $\tilde{x}$ is the solution to

$$1-\frac{1}{\tilde{x}R_0}=\frac{1}{2}\left(1-\frac{1}{R_0}\right),$$

which is $\tilde{x}=2/(R_0+1)\approx 2\hat{x}$ when R_0 is fairly large.

While a sub-community is treated as recovered (and immune), no infectious contacts may occur, and the expected fraction of susceptible $x(t)$ at a certain time point t after becoming disease-free is given by the solution to the differential equation

$$\begin{cases}\dfrac{dx}{dt}=\mu(1-x),\\ x(0)=\hat{x}.\end{cases} \tag{28}$$

Solving this equation gives us the relation

$$x(t)=1-(1-\hat{x})\exp(-\mu t). \tag{29}$$

If we set $x(t)=\tilde{x}=2/(R_0+1)$ and solve (29) in terms of t, we get

$$t=\tau_{\mathrm{R}}=\frac{1}{\mu}\log\left(\frac{R_0+1}{R_0}\right). \tag{30}$$

Note that the longer we treat a sub-community as recovered (and immune), the harder it gets for the infection to persist in the rest of the population. If τ_{R} is close to zero, we lose the effect of the recovered (and immune) state and the approximation resembles that of Hagenaars et al. (2004), and if τ_{R} tend to infinity it is the same as removing a sub-community which becomes disease-free. Our suggestion of an approximation of τ_{R}, (30), will give relatively small values. But, as said before, it is hard to find a natural definition of this quantity.

4. Approximation using an exponential form

When we introduced the SIR model for a population divided into sub-communities, we derived the expected time to extinction both for the case when all communities are isolated and the case when they are mixing as one large homogeneous community, corresponding to $\varepsilon=0$ and 1, respectively. We have also mentioned that these two approximations cannot be improved along the present lines without improving the approximations for the SIR-HM model, Eqs. (9) and (13).

For $0<\varepsilon<1$ we now introduce a new approximation, $\tau_{\mathrm{Exp}}(\varepsilon)$, by simply fitting an exponential curve having $\tau(0)$ as starting point and approximately $\tau(1)$ as end point such that $\tau'_{\mathrm{Exp}}(0)=\tau'_{\mathrm{SIR}}(0)$, i.e. we make use of the behaviour of τ_{SIR} where we expect it to work satisfactory. These imposed restrictions on the exponential curve determines it completely, and we propose the following approximation:

Approximation 2. *The expected time to extinction given that the process is started in quasi-stationarity can be approximated by*

$$\tau_{\mathrm{Exp}}(\varepsilon)=\tau(1)-(\tau(1)-\tau(0))\exp\left(-\frac{\tau'_{\mathrm{SIR}}(0)}{\tau(1)-\tau(0)}\varepsilon\right), \tag{31}$$

where $\tau'_{\mathrm{SIR}}(\cdot)$ is the first derivative of (26) *with respect to* ε, *and* $\tau(0)$ *and* $\tau(1)$ *are from Eqs.* (14) *and* (15), *respectively.*

One can easily verify that $\tau_{\mathrm{Exp}}(0)=\tau_{\mathrm{SIR}}(0)$, $\tau'_{\mathrm{Exp}}(0)=\tau'_{\mathrm{SIR}}(0)$, and we see that when $\tau'_{\mathrm{SIR}}(0)\gg\tau(1)-\tau(0)$ then $\tau_{\mathrm{Exp}}(1)\approx\tau(1)$, as desired. To see that this is reasonable, look at the exponent of (31), $-\tau'_{\mathrm{SIR}}(0)\varepsilon/(\tau(1)-\tau(0))$, when $k=2$ and use τ_{SIR} from (27). We then get that $\tau'_{\mathrm{SIR}}(0)=\mu n(R_0-1)^2\tau_{\mathrm{R}}\tau_n^3/(2R_0(\tau_{\mathrm{R}}+\tau_n))$ and a first order expansion of τ_{R} around 1 gives us that $\tau_{\mathrm{R}}\approx 1/(\mu R_0)$ which together with the geometric approximation of τ_n from (13) yields

$$-\frac{\tau'_{\mathrm{SIR}}(0)}{\tau(1)-\tau(0)}\varepsilon\approx -n^3\frac{(R_0-1)^4}{R_0^3\mu\alpha^2(\alpha^2+n(R_0-1))}\varepsilon, \tag{32}$$

which is a very small number for reasonable parameter values and choices of n. We illustrate this with a numerical example: suppose that we have a population which is separated into two equally large sub-communities of size $n=50,000$. Suppose further that the average infectious period is 1 week and a typical individual lives for ca. 70 years, i.e. $\alpha\approx 3500$. This together with $R_0=14$ and $\varepsilon=1$ gives us that the exponent (32) is approximately -475, and $\exp(-475)\approx 0$, thus $\tau_{\mathrm{SIR}}(1)\approx\tau(1)$.

5. Examples and simulations

We now compare our two approximations with simulations for some different parameter values and number of sub-communities. For childhood diseases the average infectious period is typically 1–2 weeks, see Anderson and May (1991, pp. 81–86). This together with the assumption that the average life length among individuals in the population is 70 years, gives us α-values between 1800 and 3500. Usually, these kind of diseases have values of R_0 around 10 or higher, see Table 4.1 in Anderson and May (1991, p. 70). We have chosen to set R_0 to 14 in compliance with Nåsell (2005). These are the parameter values which we will use. As for the number of sub-communities we have chosen to concentrate on $k=3$ and 5.

All simulations have been done using Monte Carlo simulation and the routines are written in the C-programming language. For graphical presentation MATLAB has been used. The expected time to extinction when starting in quasi-stationarity is estimated from the simulations as follows: initially, 500 epidemics were started at the endemic level, which is the mean in the limiting quasi-stationary distribution. Then the epidemics were simulated long enough for 100 of them to go extinct, and at this time point, the clock for the remaining 400 simulations was started. These starting points will be approximately from the quasi-stationary distribution since the epidemics have

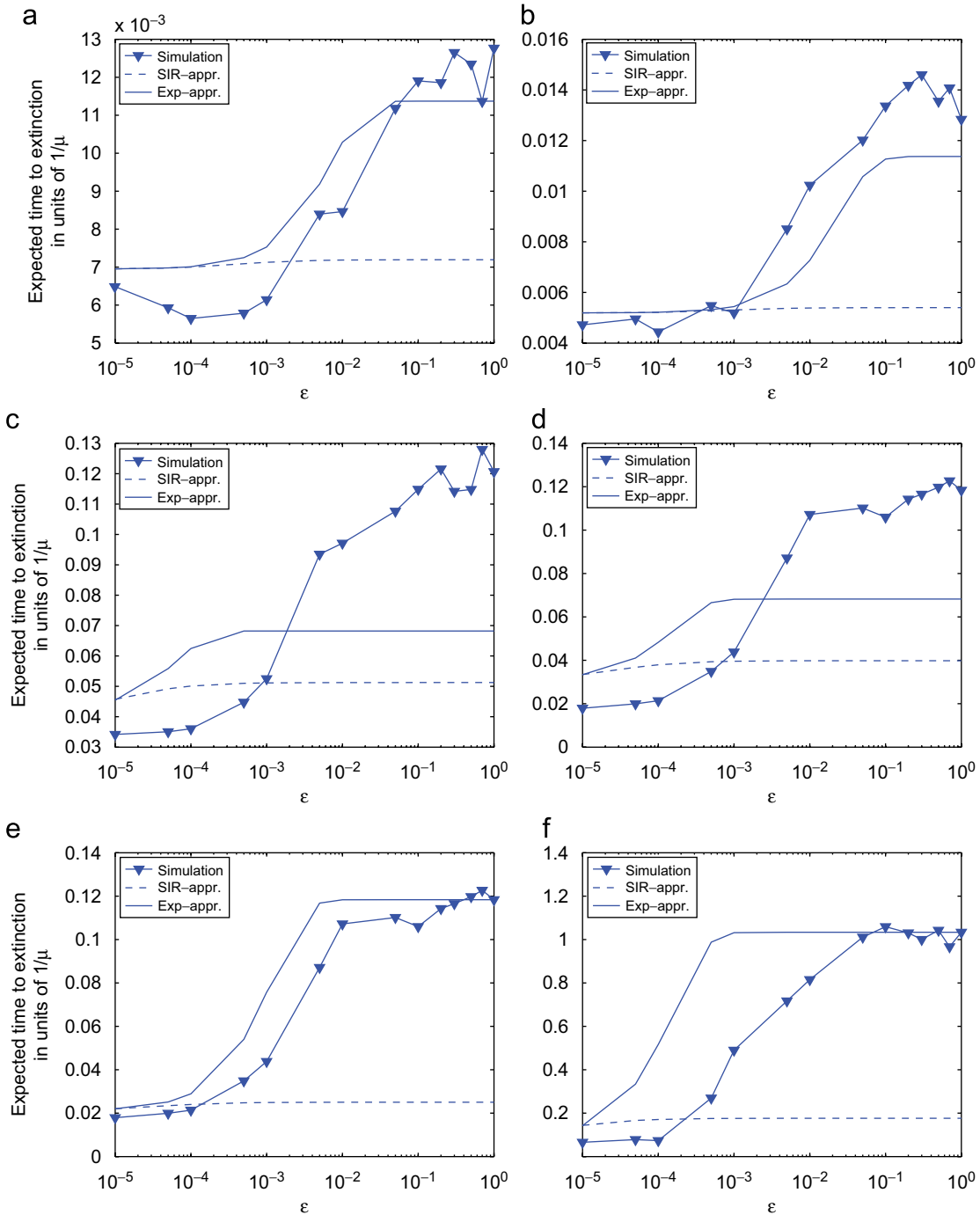

Fig. 2. In (a)–(f) we have used $\alpha = 3500$ and $R_0 = 14$, and time is measured in units of life lengths. In (a) and (b) we have a total population size of $n_{tot} = 150,000$, but in (a) there are $k = 3$ sub-communities where as in (b) $k = 5$. In (c) and (d) $n_{tot} = 900,000$ and $k = 3$ and 5, respectively. Further, (e) is same as (d), but here $\tau(0)$ and $\tau(1)$ are approximated with the values corresponding to $\varepsilon = 0$ and 1 from the simulation, and τ_n can be obtained from $\tau(0)$. In (f) $n_{tot} = 2,500,000$ and $k = 5$.

been started at the endemic level together with the fact that they had not gone extinct for some time.

Depending on the parameter values we have alternated between using the truncated normal and geometric approximation of the quasi-stationary distribution. For more on the appropriate choice of approximation in different parts of the parameter region see Nåsell (1999, Fig. 3). Roughly one can say that for the present parameter values, the geometric approximation, Eq. (13), is to prefer if n is smaller than ca. 500,000 to 600,000 and when n is greater than ca. 2,000,000 one should use the truncated normal approximation, Eq. (9). For values of n in between, neither of the approximations work well. In Fig. 2a we have a total population size of $n_{tot} = 150,000$ and $k = 3$, i.e. $n = 50,000$, and in this parameter region we use the geometric approximation of the quasi-stationary distribution.

By studying the graphs we see that both approximations work well for small values of ε, but that τ_{Exp} also works satisfactory for intermediate values of ε. Notice, however, that the expected time to extinction is too short to say that the disease is endemic, since the average time to extinction is ≈ 0.01 life lengths, i.e. less than a year. Still, the simulations indicate that the expected time to extinction is increasing in the degree of social interaction between sub-communities, and that already for small values of ε the expected time to extinction is close to the case when the population is mixing homogeneously. In Fig. 2b we have used the same parameter values as in Fig. 2a, but now with $k = 5$. Note that since we keep n_{tot} fixed the sub-community size is smaller. We again see that τ_{Exp} performs better than τ_{SIR}.

In Figs. 2c and d we have increased the total population size, n_{tot}, to 900,000. Now we are in a situation where neither of the approximations of the quasi-stationary distribution, Eqs. (9) and (13), work satisfactory, but we have chosen to use the geometric approximation, Eq. (13). In Figs. 2c and d it is seen that neither of τ_{SIR} and τ_{Exp} work that well unless ε is very small, i.e. $\varepsilon \sim 10^{-5}-10^{-4}$, and both $\tau_{\text{Exp}}(0)$ and $\tau_{\text{Exp}}(1)$ are quite far away from the corresponding simulated values. Values of $\varepsilon \sim 10^{-5}-10^{-4}$ are, however, probably not very realistic. A rough more realistic 'small' value of ε is for example if individuals visit other sub-communities one day per year, then an estimate of ε is $\frac{1}{365}$. Instead of using the analytical approximations of $\tau_n, \tau(0)$ and $\tau(1)$, we can use the corresponding 'true' values obtained from the simulations. If we do so our approximations perform better and this is illustrated in Fig. 2e for the same parameter values as before when $n_{tot} = 900,000$ and $k = 3$. The behaviour of τ_{SIR} and τ_{Exp} is very similar to that in Figs. 2a and b. That is, τ_{Exp} seems to perform better and the functional form of τ_{Exp} gives a rather good description of the expected time to extinction. The improvement in the behaviour of τ_{SIR} and τ_{Exp} between Figs. 2c and d, and Fig. 2e is an indication of that both our approximations are sensitive to the initial approximations of τ_n, $\tau(0)$ and $\tau(1)$.

In Fig. 2f we have five sub-communities and a total population size of 2,500,000, and in this situation we use the truncated normal approximation of the quasi-stationary distribution of $\tau(1)$, and the geometric approximation for τ_n and $\tau(0)$. Once again the behaviour of our approximations is similar to what we have seen before, but τ_{Exp} does not work particularly well for intermediate values of ε.

6. Discussion

In the present paper we have been concerned with approximations of τ, the expected time to extinction for an SIR model for a population divided into sub-communities, when each sub-community is started at the endemic level of infection. Our aim has been to understand the effect of the level of population subdivision on the time to extinction. We have mainly focused on endemic diseases which have a short average infectious period in relation to average life length, such as childhood diseases.

Our first approximation, τ_{SIR} (Approximation 1), extends a method presented in a paper by Hagenaars et al. (2004). In Hagenaars et al. (2004) they are mainly interested in diseases with long infectious period (small α), such as scrapie among sheep, in situations where the social activity between sub-communities is low, i.e. $0 < \varepsilon \ll 1$. Under these circumstances they argue that the underlying SIR model can be analysed from a sub-community view, where each sub-community is classified as either fully susceptible or endemic, and they approximate the dynamics in the population with a birth and death process for the number of endemic sub-communities, which only allow for one re-infection. The expected time to extinction for this process, τ_{SI} from Eq. (22), is then a reasonable approximation of τ. Here we are mainly interested in childhood diseases. Based on similar arguments as those made in Hagenaars et al. (2004), we argue that it is necessary to introduce a recovered (and immune) state when classifying sub-communities in order to avoid over-estimation of τ. For this extended model we approximate the underlying SIR model with a Markov jump process for the number of endemic sub-communities, see Fig. 1, and estimate τ with the corresponding expected time to extinction τ_{SIR}. We present a general solution form for an arbitrary number of k sub-communities in Eq. (26), which can be solved numerically, and we present an explicit expression for the case when $k = 2$ in (27).

Simulations indicate that the expected time to extinction is increasing in the degree of social interaction between sub-communities, which also can be seen in τ_{SIR}. Further, τ_{SIR} is more suitable to use when the degree of social activity between sub-communities is very low. One crucial part with this approximation is that it is difficult to find a natural way of defining the time which we let a sub-community stay recovered (and immune). If one could improve this part of the approximation, it is possible that τ_{SIR} could work better when the degree of social activity between sub-communities is somewhat higher. Furthermore τ_{SIR} is rather sensitive to the initial approximations of τ_n, $\tau(0)$ and $\tau(1)$. Depending on the parameter values we use either the truncated normal or geometric distribution respectively.

Our second approximation, τ_{Exp} (Approximation 2), is motivated in a slightly different way. At the end of Section 2 the time to extinction for the two extreme cases where derived, i.e. $\tau(0)$ and $\tau(1)$. These two approximations only rely on results for the SIR-HM model, and cannot be improved without improving results for that model. The idea behind τ_{Exp} is to approximate the expected time to extinction with an exponential curve starting at $\tau(0)$ and which has $\tau(1)$ as approximate end point and having $\tau'_{\text{Exp}}(0) = \tau'_{\text{SIR}}(0)$, since τ_{SIR} is reasonable to use when the social activity between sub-communities is very low. When comparing τ_{Exp} with simulations the same behaviour as for τ_{SIR} is seen. It works satisfactory when the degree of social

activity is low, and it is increasing in the degree of social activity.

To conclude, τ_{SIR} is only suitable to use for small values of ε and τ_{Exp} is suitable to use for intermediate as well as small values of ε. Thus, τ_{Exp} is the best approximation of the two. Note, however, that the use of these approximations is not recommended unless we are in the parts of the parameter region where either of the SIR-HM approximations of the quasi-stationary distribution is good. To our knowledge these approximations are the only ones at hand which deal with the expected time to extinction when α is large.

In the present paper it was also shown that T_Q, the time to extinction given that the epidemic process is started in the quasi-stationary distribution, is exponentially distributed, see Proposition 1. This result is important when talking about other quantities of interest such as critical community size.

Some possible improvements of the present results has been commented above, but as always it would be tractable to leave the assumption of exponential infectious periods which in most situations is not realistic. This would be interesting to do for both the SIR-HM and the SIR-SC model. Another, perhaps easier, generalisation of the model would be to allow for differently sized subcommunities. At least for the latter situation, the framework provided in the present paper could possibly be used.

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