Dynamics of infection with multiple transmission mechanisms in unmanaged/managed animal populations

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Abstract

Deterministic and stochastic models motivated by Salmonella transmission in unmanaged/managed populations are studied. The SIRS models incorporate three routes of transmission (direct, vertical and indirect via free-living infectious units in the environment). With deterministic models we are able to understand the effects of different routes of transmission and other epidemiological factors on infection dynamics. In particular, vertical transmission has little influence on this dynamics, whereas the higher the indirect (direct) transmission rate the greater the tendency to persistent oscillation (stable endemic states). We show that the sustained cycles are also prone to demographic effect, i.e., persistent oscillation becomes impossible in the managed case (in the sense of balanced recruitment and death rates) by comparing with results in unmanaged populations (exponential population dynamics). Further, approximations of quasi-stationary distributions are derived for stochastic versions of the proposed models based on a diffusion approximation to the infection process. The effect of transmission parameters on the ratio of mean to standard deviation of the approximating distribution, used to judge the validity of the approximations and the expected time until fade out of infection, is further discussed. We conclude that strengthening any route of transmission may or may not reduce the expected time to fade out of infection, depending on the population dynamics.

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1. Introduction

Investigating the mechanisms that lead to varying epidemiological patterns is important when different epidemiological patterns are observed in data. It is essential to identify the key parameters or key processes that could explain the differences in observed patterns. Studies of epidemiological dynamics have largely been confined to models with direct transmission between susceptible and infected hosts only (Hethcote, 2000; Anderson and May, 1992; Diekmann and Heesterbeek, 2000) and/or vertical transmission—the direct transfer of a disease from an infective parent to a newborn offspring (Busenberg and Cooke, 1993; Lipsitch et al., 1995). Some pathogens (microsporidian protozoan spores, viral polyhedra and bacteria such as Salmonella spp) can survive for long periods outside the host in suitable conditions. In such cases indirect transmission via free-living stages is an important route of transmission. Epidemic models with indirect transmission via free-living stages alone have been considered by Anderson and May (1981), Bowers et al. (1993) and Begon and Bowers (1995), but little attention has been paid so far to examining models with both direct and indirect transmission, and little is known about how inclusion of indirect transmission affects the dynamics.
Our purpose is to formulate models for diseases that can be transmitted in populations by a combination of direct, indirect and vertical routes, and to study their qualitative behaviour. The models are of SIRS (Susceptible \( \rightarrow \) Infected \( \rightarrow \) Recovered \( \rightarrow \) Susceptible) type, in which susceptibles become infectious, then recovered with temporary immunity, and then susceptible again when the disease-acquired immunity wears off. Mena-Lorca and Hethcote (1992) considered several SIRS models with direct transmission only, and found thresholds which determine whether the disease dies out or remains endemic and whether the population declines to zero, remains finite or grows exponentially. Based on exponential population dynamics we consider density-dependent transmission and formulate SIRS models with three routes of transmission. By thoroughly analyzing the proposed models we try to answer the following question. How does indirect/vertical transmission influence the dynamics of the system; and especially does it stabilize or destabilize the original system with direct transmission only? We then turn our attention to the role of the underlying population dynamics and introduce models in which a management strategy is used to keep the total population size constant by recruitment to balance deaths (which is often the case for livestock). The resulting models include the type of population dynamics which is considered as potential generator of oscillations in epidemiological models (Hethcote and Levin, 1989). The central question is how the epidemiological formulation and varying population dynamics influence the infection dynamics.

Since deterministic models do not accommodate the intrinsic variability present in most biological populations, which can be important during the early stages of an epidemic or more generally in small populations, stochastic models are of fundamental interest when attempting to understand related aspects of population dynamics. The corresponding stochastic versions of the proposed models are studied. It is important to observe that a qualitative difference exists between the deterministic and stochastic models that we study. We find that usually, above a threshold determined by the parameters of the model, the deterministic model predicts that the (proportion of) infected individuals will approach a positive endemic level as time approaches infinity. In the stochastic model there is nonzero probability that the epidemic will die out early in the process and a nonzero probability that the number of infecteds will increase to a long-lived quasi-stationary state the mean of which is close to the deterministic endemic level. Thus, it is interesting to investigate effects of epidemiological factors (transmission rates, recovery rate, the rate of loss of immunity, etc.) on persistence of infection.

Our analyses are motivated by attempting to understand the processes that lead to the varying epidemiological patterns of endemic and epidemic strains of Salmonella in livestock populations. Since in the specific case of Salmonella infection the latent period is short we consider a model of SIRS type. Given that a typical UK dairy farm does not contain large numbers of animals, it is reasonable to assume that the contact rate depends on the density of animals. Therefore, in both managed and unmanaged population models, we modelled direct transmission using density-dependent (i.e., \( \beta SI \)) transmission terms (Xiao et al., 2005; Turner et al., 2003). In UK there have been some epidemic strains of S. typhimurium (e.g., DT193, 204C and DT104) which have peaked and declined to low levels or disappeared completely but the temporal trends in other common zoonotic serotypes of Salmonella, such as S. dublin, reveal a fluctuating endemic state (VLA, 2002; MAFF, 1999, 2000). So it is interesting to know why salmonella strains display so much variation in their epidemiological patterns. We aim to improve our understanding of the mechanisms that drive the epidemic behaviour of strains of S. typhimurium and lead to the fluctuating endemic behaviour of other Salmonella serotypes. Such information will help to predict the nature of emerging strains and inform the development of control strategies. We address this question by considering the effect of a number of epidemiological parameters on the long-term dynamic behaviour of such pathogens.

2. SIRS model formulation

The model with three routes of transmission is formulated by elaborating the basic SIRS model examined by Mena-Lorca and Hethcote (1992). We suppose the recruitment is via a natural birth process in which the birth rate is proportional to the population size. Let \( \rho \) be the fraction of newborns who are infected by an infectious dam. The model is shown schematically in Fig. 1 and the system of differential equations is as follows:

\[
\begin{align*}
\dot{S}(t) &= b(S + R) + (1 - \rho)\beta I - \beta SI - \nu SW - dS + rR, \\
\dot{I}(t) &= \rho bI + \beta SI + \nu SW - (d + \alpha + \gamma)I, \\
\dot{R}(t) &= \gamma I - (d + r)R, \\
\dot{W}(t) &= \lambda I - (\mu + \nu(S + I + R))W,
\end{align*}
\]

\[\text{(2.1)}\]

![Fig. 1. Flow diagram representing transmission routes and other processes modelled by system (2.1).](image-url)
where \(S(t), I(t)\) and \(R(t)\) are the number of susceptible, infective and recovered individuals at time \(t\). \(W(t)\) is the number of infectious units in the environment at time \(t\). The parameters which we take throughout to be nonzero are defined in Table 1. We can easily show that the population size \(N(t) = S(t) + I(t) + R(t)\) declines to zero if \(b < d\) since \(N'(t) \leq (b - d)N(t)\). To avoid population extinction we assume \(b > d\) throughout this work. Then the extinction equilibrium \((0, 0, 0, 0)\) is unstable (US) with repulsion along the \(S\)-axis. The unique endemic equilibrium \((S^*, I^*, R^*, W^*)\) is feasible if \(\phi_{DV1} < 1\), where

\[
\phi_{DV1} = \frac{b - d}{x} \left(1 + \frac{\gamma}{d + r}\right),
\]

and

\[
S^* = \frac{x(1 - \phi_{DV1})}{b - d},
\]

\[
R^* = \frac{\gamma I^*}{d + r}, \quad W^* = \frac{\lambda(b - d)I^*}{\mu(b - d) + x\lambda I^*},
\]

with \(I^*\) being the unique positive root of the following quadratic equation:

\[
b\lambda x I^2 + I \left[(b\mu + \lambda\gamma)(b - d) - \frac{\gamma(b - d)(d + x + \gamma - \rho b)}{(1 - \phi_{DV1})}\right] - \frac{\lambda(b - d)^2(d + x + \gamma - \rho b)}{x(1 - \phi_{DV1})} = 0.
\]

The inequality \(\phi_{DV1} < 1\) corresponds to the pathogen-induced mortality being sufficiently large to overcome the natural population growth. Further, by checking the Jacobian matrix at the equilibrium we can easily show that the equilibrium \((S^*, I^*, R^*, W^*)\) is locally asymptotically stable (LAS) if condition (A.1.1) of Appendix A.1 is

true. If \(\phi_{DV1} > 1\) the disease-related death rate \(x\) is not sufficiently large to overcome the exponential growth, but it does reduce the growth rate constant from \(b - d\). We show that \((S, I, R, W) \rightarrow (S_\infty, \infty, \infty, W_\infty)\), where

\[
S_\infty = \frac{d + x + \gamma - \rho b + \xi}{b}, \quad W_\infty = \frac{\lambda(b - d - \xi)}{x\gamma},
\]

and \(\xi = (z(d + r)/(d + r + \gamma))(\phi_{DV1} - 1)\) (see details in Appendix A.1). Note that \(\phi_{DV1}\) given in (2.2) is defined as the net growth threshold of the host, which is different from the basic reproduction number \(R_0\) in epidemiology (see the survey paper by Hethcote, 2000). \(R_0\), which governs whether or not the disease can invade successfully, is defined to be the expected number of secondary cases produced, in a completely susceptible population, by a typical infected individual during its entire period of infectiousness. For this model the disease can always invade successfully as long as the direct transmission rate \(\beta\) is nonzero (Mena-Lorca and Hethcote, 1992).

Assuming direct transmission only (i.e., \(\rho = 0, \nu = 0\)), system (2.1) has been completely analyzed by Mena-Lorca and Hethcote (1992). Thresholds are found which determine whether the disease dies out or remains endemic and whether the population declines to zero, remains finite or grows exponentially. Specifically, for \(b > d\), an endemic state exists and remains stable if \(\phi_D(= \phi_{DV1}) \leq 1\), and the population grows exponentially if \(\phi_D > 1\). This implies that persistent oscillation is impossible. Assuming indirect transmission only and no recovered class (i.e., \(\beta = 0, \rho = 0\) and \(r \to \infty\)), system (2.1) is reduced to the model \(G\) of Anderson and May (1981). Long-term limit cycles were predicted in this host–pathogen model. It is therefore interesting to investigate the relative contribution of three routes transmission to the infection dynamics.

In the presence of vertical transmission, similar analysis reveals that the asymptotic behaviours of solution paths are the same as for the model with direct transmission only (Mena-Lorca and Hethcote, 1992). This shows that vertical transmission does not affect the qualitative properties of the system, and hence it cannot induce any persistent oscillations. Comparing model (2.1) with the model with direct transmission only we see that the presence of indirect transmission affects neither existence of the endemic state (due to \(\phi_D = \phi_{DV1}\)) nor the possibility of the population growing exponentially. However, it has a significant influence on stability of the endemic state. We shall show that persistent oscillations can arise by Hopf bifurcation from the endemic equilibrium as the equilibrium loses its stability. This is confirmed numerically. In theory there is a Hopf bifurcation if \(\Delta(\theta)\), defined by \(\Delta(\theta) = p_1 p_2 p_3 - p_1^2 p_4 - p_2^2\), changes sign as \(\theta\) passes through \(\theta_0\) and \(\Delta(\theta_0) = 0\), where \(p_i\) (\(i = 1, \ldots, 4\)) are given in Appendix A.1 and \(\theta\) denotes any underlying parameter. It is complex to check this transversality condition if we choose a parameter, say indirect transmission rate \(v\), as the bifurcation parameter \(\theta\), so we shall investigate how varying parameters affect stability of the endemic state numerically. We

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition (units)</th>
<th>Parameter estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N_0)</td>
<td>Expected total herd size (animals)</td>
<td>175</td>
</tr>
<tr>
<td>(b)</td>
<td>Recruitment rate</td>
<td>(b = 0.0085)</td>
</tr>
<tr>
<td>(\rho)</td>
<td>Vertical transmission parameter</td>
<td>Unknown, assume (\rho = 1)</td>
</tr>
<tr>
<td>(d)</td>
<td>Death rate (per day)</td>
<td>(d = 0.00055)</td>
</tr>
<tr>
<td>(\alpha)</td>
<td>Pathogen-induced mortality rate (per day)</td>
<td>see details in text</td>
</tr>
<tr>
<td>(\gamma)</td>
<td>Recovery rate (per day)</td>
<td>Unknown, assume (\gamma = 0.05)</td>
</tr>
<tr>
<td>(r)</td>
<td>Immunity-loss rate (per day)</td>
<td>see details in text</td>
</tr>
<tr>
<td>(\lambda)</td>
<td>Shedding rate (per day)</td>
<td>Unknown, assume (\lambda = 5.0 \times 10^7)</td>
</tr>
<tr>
<td>(\mu)</td>
<td>Death rate of organism (per day)</td>
<td>Unknown, assume (\mu = 0.9)</td>
</tr>
<tr>
<td>(\beta)</td>
<td>Direct transmission parameter (per animal per day)</td>
<td>Unknown, assume (\beta = 0.002) when not varying</td>
</tr>
<tr>
<td>(v)</td>
<td>Indirect transmission parameter (per infectious unit per day)</td>
<td>Unknown, assume (v = 3 \times 10^{-12}) when not varying</td>
</tr>
</tbody>
</table>
Perform numerical studies on system (2.1) using software XPPAUT (Ermentrout, 2001, 2002).

Parameter values used in the following investigation are listed in Table 1. We use the specific context of Salmonella in a dairy herd. Here we acknowledge that dairy herds are unlikely to be unmanaged populations but for comparative purpose the same parameters are used. Values for demographic parameters (b and d) are estimated and derived from the literature (Gardner et al., 1990; Tyler et al., 1999; Young et al., 1983; Turner et al., 2003). Estimates for some parameters which are related to epidemiology are not yet available. There are studies relating to epidemiological questions (Huston et al., 2002a,b and references therein; Troutt et al., 2001; Veling et al., 2002; Edrington et al., 2004; Wray and Sojka, 1978; Xiao et al., 2005, 2006) and some of these inform parameter values indirectly. The epidemiological parameters are chosen to provide epidemic behaviour and endemic levels consistent with observed patterns in livestock. In particular, transmission rates, recovery rate, shedding rate and death rate of organism are set to be means of the corresponding values for our previous multigroup model on Salmonella infection (Xiao et al., 2005, 2006). The estimates for pathogen-induced mortality rate a and the rate of loss of immunity r given below are such that when they are substituted into our models, the predicted equilibrium prevalence matches the corresponding mean estimate given by Davison et al. (2005).

In Fig. 2(a) dynamics of model (2.1) is qualitatively different in two different regions of the (b, v) plane. The endemic state is LAS in the left area but US in the right one. For a given b, the endemic state becomes US as the indirect transmission rate v increases and exceeds a special value v_b, and Hopf bifurcation occurs when v = v_b. This shows that sustained oscillations arise if indirect transmission outweighs direct transmission, which implies that indirect transmission has a destabilizing effect. In contrast, for a given v, the endemic state becomes stable as the direct transmission rate b increases. This and the fact that the threshold value v_b increases with b mean that direct transmission has a stabilizing effect. Therefore, some Salmonella strains with stronger indirect transmission may have more tendency to persistent cyclicity.

In Fig. 2(b) the (b, a) plane is divided into two separated regions: the top one is the stable region and the lower one is the cyclic one. Suppose first the indirect transmission rate v is fixed. For relatively large direct transmission rates b the endemic state is stable for all a. For intermediate values of b, the endemic state continuously goes through stable, US, stable states in order as the pathogen-induced mortality rate a increases. This implies that pathogen-induced mortality has both stabilizing and destabilizing effects on the endemic state for these particular values of b. For relatively small values of b, increasing a does not induce the endemic state to return back to be stable.

![Fig. 2. Let z and r be 0.5 (per day) and 0.3 (per day). (a) Regions in (b, v) space for which cycles are expected (to the right of the curve) for the model (2.1). (b) Regions in (b, a) space for which cycles are expected (below the curve) for different indirect transmission rates.](image-url)
Fig. 2(b) also shows how the inclusion of indirect transmission expands the region in \((\beta, v)\) parameter space where cyclic dynamics are expected. As \(v\) increases, we observe that cycles are expected in a large region of \((\beta, v)\) parameter space. Decreasing \(v\) increases the stable region and this region approaches all the \((\beta, v)\) plane predicted by Mena-Lorca and Hethcote (1992) in the limit as \(v \to 0\). Thus, we conclude that the inclusion of indirect transmission increases the likelihood of persistent cycles, which further confirms that indirect transmission has a destabilizing effect. It follows from Fig. 2(b) that for relatively small values of \(x (x<0.42)\), the endemic state remains stable for all \(v\). This fact shows that pathogen-induced mortality is an important factor in relation to the destabilizing effect of indirect transmission.

Note that the above results were obtained with vertical transmission rate \(\rho = 1\). Plotting graphs corresponding to Fig. 2 for other values of \(\rho\) (say \(\rho = 0.2\) and 0.6), we find that the plots (which are omitted) are almost the same as that with \(\rho = 1\). Hence vertical transmission has little effect on the qualitative behaviour of the system in which there is both direct and indirect transmission. Further, the replacement rate \(b\) comes from estimation for the model where group structure (e.g., unweaned, weaned, dry and lactating cows) is considered (Xiao et al., 2005, 2006). Ideally, cows are expected to calve once a year. Considering a 50% chance of delivering a female calf, a more realistic replacement rate for this model formulation would be \(1/(365 \times 2) = 0.0014\). Here we fix \(b = 0.0014, x = 0.05, r = 0.05\). Numerical studies show that the endemic state is stable for the ranges of \(\beta\) and \(v\) used in Fig. 2. This fact shows that for this set of parameters (especially smaller replacement rate and consequently lower pathogen-induced mortality rate) indirect transmission does not induce any persistent oscillation. Further numerical studies show that for this set of parameters, persistent cycles do not exist in the system in which there is indirect transmission only.

When no persistent cycles occur we wish to investigate how the system approaches the endemic state, and then identify key parameters to which decaying oscillations are sensitive. More detailed information about how the system tends to the endemic equilibrium can be obtained by considering eigenvalues of the system (Anderson and May, 1992)—see details in Appendix A.1. If not all eigenvalues are real (but all have negative real part), the endemic state is a stable spiral. The approach to the steady state will therefore be oscillatory. Thus, we are interested in how transmission rates affect the imaginary parts of eigenvalues, and consequently influence the possibility of damped oscillation. In Fig. 3, the imaginary parts of eigenvalues are nonzero in the top area of the \((\beta, v)\) plane, above the plotted line, and hence decaying oscillations are possible in this region, whereas no oscillation occurs at all in the bottom area, where the imaginary parts of all eigenvalues are zero. The figure shows that decaying oscillation is likely to occur as indirect (or direct) transmission increases. It also shows that for a sufficiently high direct (indirect) transmission rate, damped oscillation is always possible for any indirect (direct) transmission rate. This implies that in a case of smaller replacement rate and lower pathogen-induced mortality either stronger direct transmission or stronger indirect transmission leads to a greater tendency for damped oscillations. Further, varying vertical transmission rate \(\rho\) has little effect on Fig. 3.

### 3. The SIRS model with management

The asymptotic behaviour of solutions of an infectious disease transmission model depends not only on the epidemiological formulation, but also on the demographic processes incorporated into the model. In order to highlight fundamental epidemiological patterns (in particular, to investigate effects of different routes of transmission), in traditional models population dynamics is taken to be as simple as possible, i.e., stationary by assuming recruitment balancing death. Results for the simplest epidemiological models are given in Hethcote (1976, 1989). Surveys of results for models with constant size populations are given in Hethcote and Levin (1989). These models have been developed more extensively partly because they are easier to analyze than variable population size models and partly because they are often realistic for human and herd disease (Rohani et al., 2002; Turner et al., 2003; French et al., 1999). In particular, when modelling epidemics where disease spreads in managed farming system this assumption that the herd population is fixed is often a reasonable approximation in order to fill milk or beef quotas. In this section we consider fixed population size (say, \(N_0\)) by
assuming recruitment balancing death. So model (2.1) becomes
\[
\begin{align*}
\dot{I}(t) &= \rho I I + \beta(I - R) + \gamma(N - R) W \\
\dot{R}(t) &= \gamma I + \mu + N W \\
\dot{W}(t) &= \lambda I - (\mu + \nu N) W,
\end{align*}
\]  
(3.1)

where parameters are the same as before. In fact, model (3.1) can be obtained from model (2.1) by varying the net growth of the population \(b - d\) such that
\[
b - d = \frac{(d - a - b)I}{S + R}.
\]

Here the basic reproduction number \(R_0\) is given by
\[
R_0 = \left(\rho b + \beta N_0 + \frac{\lambda v N_0}{\mu + \nu N_0}\right) \frac{1}{d + a + \gamma}.
\]  
(3.2)

Note that \(R_0\) consists of three components corresponding to vertical, direct and indirect transmission via free-living infectious units in the environment, respectively (Lipsitch et al., 1995). If \(R_0 < 1\), the pathogen is unable to invade and the host population remains at its pathogen-free level (i.e., the pathogen-free equilibrium (0, 0, 0) is locally stable). Conversely, when \(R_0 > 1\), the pathogen does invade the host population: the pathogen-free equilibrium becomes US and a new coexistence equilibrium \(E_s = (I_s, R_s, W_s)\) is feasible if an additional inequality \(d + a + \gamma - \rho b > 0\) holds true. By checking standard Routh–Hurwitz stability conditions (see Appendix A.2) we show that \(E_s\) is locally stable if it is feasible. So no persistent oscillations occur near the endemic equilibrium in the managed system. Again, when no persistent oscillations occur we wish to investigate how the system approaches the endemic equilibrium by using the same method as that used in Section 2. Since the characteristic equation (A.2.1) cannot be explicitly solved, the best way to identify the key parameters to which damped oscillations are sensitive is to study the effect of parameters of interest on eigenvalues numerically.

In Fig. 4(a) the \((\beta, \nu)\) plane is divided into two separated regions: in the upper region, the imaginary parts of eigenvalues are nonzero, and hence damped oscillation is possible (i.e., the endemic state is a stable spiral); in the lower region, the imaginary parts of eigenvalues are zero, and consequently no oscillation occurs (i.e., the endemic state is a stable node). Fig. 4(a) shows that increasing either \(\beta\) or \(\nu\) can lead to damped oscillation. This implies that in a managed population relatively strong direct or indirect transmission is likely to induce decaying oscillation, although they cannot induce persistent (nondecaying) cycles. Further, varying the vertical transmission rate \(\rho\) and repeating the above plotting process we found that vertical transmission has little effect upon the region in which damped oscillations occur.

Fig. 4(b) shows how inclusion of indirect transmission expands the region in \((\beta, z)\) parameter space where decaying oscillations are found. For a given indirect transmission rate \(v\), we see that either stronger direct transmission rate \(\beta\) or higher pathogen-induced mortality \(z\) leads to a greater tendency for damped oscillations. Moreover, increasing the indirect transmission rate expands the region where decaying oscillations occur. This implies that stronger indirect transmission increases the tendency to damped oscillation. It follows from Figs. 3 and 4 that dynamics in a managed population is similar to that in an unmanaged population with small replacement rate and low pathogen-induced mortality. Comparing Fig. 2 with Fig. 4 we see that indirect transmission is responsible for persistent cyclic behaviour in an unmanaged population or damped cyclic behaviour in a managed population, and also that increasing the indirect transmission rate expands the area where oscillations occur. However, whether or not increasing direct transmission is likely to induce oscillatory behaviour is dependent upon demographic processes. So we can see that Salmonella strains with stronger indirect transmission may have a greater tendency to cyclicity (persistent or damped).

4. Stochastic models

In this section, the corresponding stochastic versions of the proposed models are studied. The rates shown in Fig. 1 are now interpreted as average transition rates in a random process. If the population at time \(t\) consists of \(S\) susceptible, \(I\) infected and \(R\) recovered individuals (cattle in our specific context), and the environment has \(W\) infectious units, then in the small time interval from \(t\) to \(t + \Delta t\), the probabilities of the various possible transitions are as shown in Table 2 (which corresponds to system (2.1)). Note that here \(S, I, R, W\) and \(W\) are random variable with discrete state space in the stochastic models, and continuous variables in the corresponding deterministic models.

If infection ever dies out, then the population will remain disease-free from then on, as our model has no mechanism for the external re-introduction of infection. For some stochastic infection models it can be shown that with probability 1 infection will die out within a finite time (see, for example, Clancy et al., 2001). Even when this is the case, however, the process can exhibit apparently stable behaviour for a very long time before eventual extinction occurs (see Nåsell, 1999). The long-term behaviour of the process prior to extinction can be described by its quasi-stationary distribution, being the equilibrium distribution of the state \((S, I, R, W)\) conditioned upon nonextinction. An explicit expression for the quasi-stationary distribution cannot be determined. A major goal of the analysis of the stochastic model is therefore to derive an approximation of the quasi-stationary distribution. This derivation is based on a diffusion approximation of the stochastic discrete state model (Kurtz, 1970, 1971). We are here interested in the effect of epidemiological parameters on the quasi-stationary distribution. Firstly, we consider the
stochastic version of system (2.1)—unmanaged population dynamics.

4.1. Stochastic model of unmanaged population dynamics

We use diffusion approximations for density-dependent Markov jump process. The relevant results are summarized in chapter 11 of Ethier and Kurtz (1986), and also see details in Appendix A.3. We can approximate the equilibrium distribution of the disease process \( S(t), I(t), R(t), W(t) \) by a four-variate normal distribution with mean \((S^*, I^*, R^*, W^*)\), variance matrix \( H \Sigma \) (see details for \( H \) and \( \Sigma \) in Appendix A.3). Thus, the standard deviation of the marginal distributions in quasi-stationarity of the number of infected individuals is given by \( \sigma_I = \sqrt{\Sigma_{22} H} \), where \( \Sigma_{22} \) is the entry in the 2nd row and 2nd column of the covariance matrix \( \Sigma \).

The number of infected individuals cannot be negative, and so the normal approximation can only be expected to be acceptable if it assigns negligible probability to negative values. That is, we require the coefficient of variation \( \frac{\sigma_I}{I^*} \) to be sufficiently small. Equivalently, defining

\[
\psi = \frac{I^*}{\sigma_I},
\]

we expect the normal distribution to provide a good approximation when \( \psi \) is large, but a poor approximation when \( \psi \) is small. Since 99% of the probability mass of a normal distribution lies within three standard deviations of the mean, we might hope for a useful approximation provided \( \psi \geq 3 \) (Näsell, 1999, 2002; Clancy and French, 2001). Further, this ratio provides some indication of the expected persistence time of the infection. In particular, infection is expected to fade out quickly if \( \psi \) is small, and the expected time to extinction increases as \( \psi \) increases.
An infection occurs from direct transmission

An infection occurs from indirect transmission

An infected dies or is culled (S, I, R, W) → (S, I − 1, R, W) $\gamma$I

An infected gives birth to a susceptible (S, I, R, W) → (S + 1, I, R, W) $(1 - \rho)bI$

An infected gives birth to a susceptible (S, I, R, W) → (S + 1, I, R, W) $bR$

An infected gives birth to an infected (S, I, R, W) → (S, I + 1, R, W) $\rho bI$

A susceptible dies or is culled (S, I, R, W) → (S − 1, I, R, W) $dS$

A recovered gives birth to a susceptible (S, I, R, W) → (S + 1, I, R, W) $bR$

A recovered gives birth to a susceptible (S, I, R, W) → (S + 1, I, R, W) $bR$

A recovered dies or is culled (S, I, R, W) → (S, I − 1, R, W) $(d + \gamma)I$

A recovered dies or is culled (S, I, R, W) → (S, I − 1, R, W) $dR$

A recovered gives birth to a recovered (S, I, R, W) → (S, I − 1, R + 1, W) $\gamma I$

A recovered returns back to a susceptible (S, I, R, W) → (S + 1, I, R − 1, W) $rR$

Shedding of an infectious unit to the environment (S, I, R, W) → (S, I, R, W + 1) $\lambda I$

Death of an infectious unit (S, I, R, W) → (S, I, R, W − 1) $\mu W$

Consumption by the infected and recovered (S, I, R, W) → (S, I, R, W − 1) $\nu(I + R)W$

<table>
<thead>
<tr>
<th>Event</th>
<th>State transition</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>A susceptible gives birth to a susceptible</td>
<td>$(S, I, R, W) \rightarrow (S + 1, I, R, W)$</td>
<td>$bS$</td>
</tr>
<tr>
<td>An infected gives birth to a susceptible</td>
<td>$(S, I, R, W) \rightarrow (S + 1, I, R, W)$</td>
<td>$(1 - \rho)bI$</td>
</tr>
<tr>
<td>An infected gives birth to a susceptible</td>
<td>$(S, I, R, W) \rightarrow (S + 1, I, R, W)$</td>
<td>$bR$</td>
</tr>
<tr>
<td>An infected gives birth to an infected</td>
<td>$(S, I, R, W) \rightarrow (S, I + 1, R, W)$</td>
<td>$\rho bI$</td>
</tr>
<tr>
<td>A susceptible dies or is culled</td>
<td>$(S, I, R, W) \rightarrow (S − 1, I, R, W)$</td>
<td>$dS$</td>
</tr>
<tr>
<td>An infected dies or is culled</td>
<td>$(S, I, R, W) \rightarrow (S, I − 1, R, W)$</td>
<td>$(d + \gamma)I$</td>
</tr>
<tr>
<td>A recovered gives birth to a susceptible</td>
<td>$(S, I, R, W) \rightarrow (S + 1, I, R, W)$</td>
<td>$bR$</td>
</tr>
<tr>
<td>A recovered gives birth to a susceptible</td>
<td>$(S, I, R, W) \rightarrow (S + 1, I, R, W)$</td>
<td>$bR$</td>
</tr>
<tr>
<td>An infected gives birth to a susceptible</td>
<td>$(S, I, R, W) \rightarrow (S + 1, I, R, W)$</td>
<td>$bR$</td>
</tr>
<tr>
<td>An infected gives birth to a susceptible</td>
<td>$(S, I, R, W) \rightarrow (S + 1, I, R, W)$</td>
<td>$bR$</td>
</tr>
<tr>
<td>A recovered gives birth to a recovered</td>
<td>$(S, I, R, W) \rightarrow (S, I − 1, R + 1, W)$</td>
<td>$\gamma I$</td>
</tr>
<tr>
<td>An infected returns back to a susceptible</td>
<td>$(S, I, R, W) \rightarrow (S + 1, I, R − 1, W)$</td>
<td>$rR$</td>
</tr>
<tr>
<td>Shedding of an infectious unit to the environment</td>
<td>$(S, I, R, W) \rightarrow (S, I, R, W + 1)$</td>
<td>$\lambda I$</td>
</tr>
<tr>
<td>Death of an infectious unit</td>
<td>$(S, I, R, W) \rightarrow (S, I, R, W − 1)$</td>
<td>$\mu W$</td>
</tr>
<tr>
<td>Consumption by the infected and recovered</td>
<td>$(S, I, R, W) \rightarrow (S, I, R, W − 1)$</td>
<td>$\nu(I + R)W$</td>
</tr>
</tbody>
</table>

In Fig. 5(a), the ratio $\psi$ is plotted against indirect transmission rate $\nu$. We note that here we choose $\alpha = 0.02$, $r = 0.1$ and other parameters are from Table 1 such that the endemic equilibrium is locally stable in the deterministic model (2.1). We can see the ratio $\psi$ decreases with increasing $\nu$, which implies that increasing indirect transmission rate decreases the expected time until fade out of infection occurs. This is because increasing indirect transmission rate leads to a decline in the number of infecteds present at the endemic level. In fact, we have

$$\frac{d\nu}{dt} = \frac{1}{2\nu^2 \alpha} \left\{ \mu(b - d) \left( 1 - \frac{B}{\sqrt{B^2 + 4\beta\nu c}} \right) \right. $$

$$ \left. - \frac{2\nu \alpha C}{\sqrt{B^2 + 4\beta\nu c}} \right\},$$

where

$$B = (\beta \mu + \lambda \nu)(b - d) - \frac{v(b - d)(d + \alpha + \gamma - \rho b)}{(1 - \phi_{DVI})},$$

$$C = \frac{\alpha(b - d)^2(d + \alpha + \gamma - \rho b)}{\alpha(1 - \phi_{DVI})}.$$
to slow down growth of the population to the extent that persistence is not possible.

The following simulation further confirms the fact that increasing the indirect transmission rate leads to the infection being likely to fade out more quickly. A modified Monte Carlo simulation was used. Note that we actually use a semi-stochastic model in which, because of the very different time scales, the dynamics of the free-living stages is treated deterministically to do simulation and the algorithm for the process is described in detail in Appendix A.4.

Fig. 6. The ratio $\psi$ is plotted against both direct transmission rate $\beta$ and the indirect transmission rate $\nu$: (a) for the stochastic version of model (2.1) and (b) for the stochastic model (3.1) with constant herd size.
The 500 simulations were carried out, each starting from the endemic state. For each simulation, we record the number infected at time $t = 600$ days, and then assemble a histogram of the probability distribution of the number of infected individuals. For simulations with $\nu$ set at a value of $3 \times 10^{-12}$ (see Fig. 7(a)) infection fades out before 600 days in 6 out of 500 simulations; for simulations with $\nu$ set at a value of $3 \times 10^{-11}$ (see Fig. 7(b)) infection fades out before 600 days in 56 out of 500 simulations. Therefore, the probability of fade out of infection within 600 days is increased by strengthening indirect transmission. These two graphs also show that the distributions of the number of infected individuals (except for the extinction case) are close to normal distributions. Note that the theoretical mean and S.D. values are quite similar to those from simulations. In particular, for Fig. 7(a) the theoretical mean and standard deviation are 28.12 and 9.35 while the simulated counterparts are 28.80 and 9.70; for Fig. 7(b) the theoretical mean and standard deviation are 16.62 and 7.16 while the simulated ones are 17.77 and 7.34.

### 4.2. Stochastic model of managed population dynamics

The natural next step is to carry out similar analysis for a stochastic version of model (3.1) and then to investigate how transmission rates affect the ratio $\psi$. Unfortunately, balancing recruitment and death rates does not result in constant population size in the stochastic setting. Numerical simulation shows that population size may vary significantly although the average number is almost constant. In order to keep the population size exactly constant, as the deterministic model (3.1) predicts, we modify things so that we instantaneously introduce a new animal whenever an animal is lost from the population due to natural death or pathogen-induced mortality. That is, we balance the individual births and deaths rather than merely balancing the rates of birth and death. Thus, we have $S(t) + I(t) + R(t) = N_0$ for all $t \geq 0$, the state of the system is completely determined by the three-dimensional process $(I(t), R(t), W(t))$. Whenever a birth occurs, an animal is instantaneously culled. The culled animal is chosen from the population randomly: a susceptible animal is culled with probability $dS(t)/(dN_0 + aI)$, an infected animal with probability $(d + a)I(t)/(dN_0 + zI)$ and an immune animal with probability $dR(t)/(dN_0 + zI)$. The resulting transition rates are shown in Table 3.

In the same approach as above, we can apply results from Chapter 11 of Ethier and Kurtz (1986) to approximate this process by a deterministic process. We look for a stable endemic state of the deterministic process, and approximate the behaviour of the stochastic process close to equilibrium using a three-dimensional Ornstein–Uhlenbeck process. It transpires that the appropriate

![Fig. 7. Probability distribution of number of infected individual at $t = 600$ days for the stochastic version of model (2.1). (a) $\nu = 3 \times 10^{-12}$ and (b) $\nu = 3 \times 10^{-11}$.](image-url)
Table 3
Transition rates for the disease model when herd size is held constant

<table>
<thead>
<tr>
<th>Event</th>
<th>State transition</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or culling of infected, replaced with susceptible</td>
<td>((I, R, W) \rightarrow (I - 1, R, W))</td>
<td>((dN_0 + (z - \rho)I) dN_0)</td>
</tr>
<tr>
<td>Death or culling of recovered, replaced with susceptible</td>
<td>((I, R, W) \rightarrow (I - 1, R, W))</td>
<td>((dN_0 + (z - \rho)I) dN_0)</td>
</tr>
<tr>
<td>Loss of immunity</td>
<td>((I, R, W) \rightarrow (I + 1, R, W))</td>
<td>(rR)</td>
</tr>
<tr>
<td>Direct transmission</td>
<td>((I, R, W) \rightarrow (I + 1, R, R))</td>
<td>(\beta I(N_0 - I - R))</td>
</tr>
<tr>
<td>Indirect transmission</td>
<td>((I, R, W) \rightarrow (I + 1, R, W - 1))</td>
<td>(\mu W)</td>
</tr>
<tr>
<td>Recovery of infected</td>
<td>((I, R, W) \rightarrow (I - 1, R + 1, W))</td>
<td>(\gamma I)</td>
</tr>
<tr>
<td>Death or culling of recovered, replaced with infected</td>
<td>((I, R, W) \rightarrow (I + 1, R - 1, W))</td>
<td>(\rho I dN_0 dN_0)</td>
</tr>
<tr>
<td>Shedding of an infectious unit to the environment</td>
<td>((I, R, W) \rightarrow (I, R, W + 1))</td>
<td>(\lambda I)</td>
</tr>
<tr>
<td>Death of an infectious unit</td>
<td>((I, R, W) \rightarrow (I, R, W - 1))</td>
<td>(\mu W)</td>
</tr>
<tr>
<td>Consumption by the infected and recovered</td>
<td>((I, R, W) \rightarrow (I, R, W - 1))</td>
<td>(\nu(I + R)W)</td>
</tr>
</tbody>
</table>

5. Conclusions and discussion

The deterministic and stochastic SIRS models discussed here are motivated by Salmonella infection in animals. The models incorporate three routes of transmission: direct, vertical and indirect transmission via free-living stages. Historically, considerably more work has been done on models with direct transmission (and/or vertical) only (Anderson and May, 1992; Hethcote, 2000; Xiao and Chen, 2001; Xiao and Van Den Bosch, 2003) although there is some work concerning indirect transmission alone (Anderson and May, 1981; Bowers et al., 1993). A key question in epidemiology concerns what happens if we consider all three routes of transmission, and examine the relative contribution of them to the infection dynamics.

In this article, we have shown how three routes of transmission affect epidemiological dynamics, which could explain the differences in observed epidemiological patterns. In particular, vertical transmission has little influence on this dynamics, whereas the higher the indirect (direct) transmission rate the more tendency to persistent oscillation (stable endemic states). We have also shown that the sustained cycles are prone to demographic effect. Under management (in the sense of balanced recruitment and death rates) persistent epidemiological oscillation becomes impossible, i.e., only decaying oscillation is possible. This observation may explain why decaying oscillations are usually observed in dairy herds in which farmers usually keep the herd near constant to fill milk quotas.

It is interesting to further investigate to which parameters decaying oscillations are sensitive when no persistent (nondecaying) cycles occur. In a managed or unmanaged population with small \(b\) and low \(z\), either strong direct transmission or indirect transmission is likely to induce damped oscillations. Further studies can be done to analyse effect of other epidemiological parameters on occurrence of oscillations. Our extensive numerical studies show that higher pathogen-induced mortality, shorter infectious period and stronger persistent immune responses...
result in a greater tendency for damped oscillation. These are in agreement with results for a related multigroup model (Xiao et al., 2005, 2006). These effects could explain some of the observed difference in dynamics between Salmonella serotypes. In order to estimate the relative contribution of these factors to the dynamics of infection within herds, a greater understanding of the variation between serotypes is required. For example, although many studies have been conducted on the survival of Salmonella serotypes under various conditions (e.g., Taylor and Burrows, 1971; Wray and Callow, 1974) none have provided quantifiable and consistent comparisons between serotypes.

It is now becoming increasingly evident that many ecological systems are qualitatively affected by demographic and environmental noise, to such an extent that deterministic models may be incapable of capturing or indeed explaining their dynamics (Bartlett, 1957; Cushing et al., 1998; McCarley et al., 1999). Differently from the corresponding deterministic counterpart, the stochastic model predicts that the infection becomes extinct frequently. We therefore investigated how epidemiological factors (especially transmission rates) affect the likely time until fade out of infection. A surprising result here is that increasing any transmission rate decreases expected time until fade out of infection in unmanaged system, whereas almost the opposite result is obtained in the managed case. In fact, strengthening any route of transmission fails to induce higher endemic level of the number infected in the unmanaged system due to the disease regulatory mechanism. However, in a management case, more infected individuals are induced despite the pathogen-induced mortality, and hence the expected time to fade out of infection is increased. Therefore, transmission rates play different roles in the time to fade out of infection, in a way which is strongly related to population dynamics (managed or unmanaged systems). This indicates that in nonlinear systems small differences in biological characteristics can have profound qualitative implications (Rohani et al., 2002). In general, this work explored the consequences of the interaction between different routes of transmission, population dynamics (management strategy) and stochasticity, with surprising results. We have addressed the very questions which emerged in Section 1 as the motivation for our work. Clearly our results relate to particular modelling assumptions and parameter values as described in Section 2 and we have to urge caution on these grounds. We have set a baseline from which further progress may be made.

Note that we consider two extreme cases: ignoring constraints on population size completely (exponential growth) and constraining population size to remain exactly constant. We note that the assumption that the population is constrained to lie within a certain (small) range is often a reasonable approximation of real farming systems (Clancy and French, 2001; French et al., 1999). We leave this for future work. Finally, we note that there is evidence that clinical episodes and shedding of S. typhimurium DT104 recur periodically, at intervals of several months, before disappearing from the farm environment (Hollinger et al., 1998; Davies, 1997). Although this may be attributable to the factors inducing cyclicity described in this study, seasonally varying parameters—another issue for the future—may also be implicated.

Acknowledgment

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Appendix A

A.1. Asymptotic stability of system (2.1)

If $\phi_{D11} < 1$, the unique endemic state $(S^*, I^*, R^*, W^*)$ exists. The characteristic equation for the endemic equilibrium is

$$A^4 + p_1 A^3 + p_2 A^2 + p_3 A + p_4 = 0,$$

where the coefficients $p_i, i = 1, \ldots, 4,$ are

$$p_1 = d + r + \mu + v N^* - (A + b - d),$$

$$p_2 = (d + r)(\mu + v N^* - (A + b - d)) + \alpha(\beta I^* + v W^*) + A(b - d) - (\mu + v N^*)(A + b - d) - \lambda_s S^* + \gamma(\beta I^* + v W^*),$$

$$p_3 = (d + r)(\alpha(\beta I^* + v W^*) + A(b - d) - (\mu + v N^*)(A + b - d) - \lambda_s S^*) + \alpha(\beta I^* + v W^*)(\mu + v N^*)$$

$$-\lambda v^2 W^* S^* + A(b - d)(\mu + v N^*) + \lambda v (b - d) S^* - \gamma(\beta I^* + v W^*)(b - d) - (\mu + v N^*),$$

$$p_4 = (d + r)(\alpha(\beta I^* + v W^*) + v N^*) - \lambda v^2 W^* S^* + A(b - d)(\mu + v N^*) + \lambda v (b - d) S^* - \gamma(\beta I^* + v W^*)(b - d) - (\mu + v N^*),$$

and $A = \rho b + \beta S^* - (\beta I^* + v W^*) - (d + \alpha + \gamma)$. The criteria for stability are

$$p_1 > 0, \quad p_4 > 0, \quad p_1 p_2 > p_3, \quad p_1 p_2 p_3 > p_3^2 + p_1^2 p_4.$$  \hspace{1cm} (A.1.1)
If $\phi_{DVI} > 1$ the disease-related death rate $\alpha$ is not sufficiently large to overcome the exponential growth, but it does reduce the growth rate constant from $b - d$. The population size behaves according to

$$
\dot{N}(t) = (b - d)N - \alpha I.
$$

When the population size grows or declines exponentially, it is convenient to analyze the fractions $x = S/N, y = I/N$ and $z = R/N$ of the population which are susceptible, infectious and recovered, respectively. System (2.1) becomes

$$
\begin{cases}
    \dot{x}(t) = (1 - \rho)b(1 - x) - \beta x y N - v x W + (r + \rho b)z + \alpha x y,
    \\
    \dot{y}(t) = \beta x y N - (\alpha + \gamma + (1 - \rho)b)y + \alpha y^2,
    \\
    \dot{z}(t) = \gamma y - (b + r)z + \alpha z y,
    \\
    \dot{W}(t) = \lambda y N - (\mu + vN)W,
    \\
    \dot{N}(t) = N(b - d - \alpha y).
\end{cases}
$$

(A.1.2)

Let the growth rate constant in the equation for $N'(t)$ be $\xi = b - d - \alpha y$, so

$$
y_* = \frac{b - d - \xi}{\alpha}, \quad z_* = \frac{\gamma y_*}{d + r + \xi}, \quad W_* = \frac{\lambda y_*}{v}, \quad x_* = 0.
$$

The $W_*$ expression follows by setting the right-hand side of the $W'(t)$ Eq. in (A.1.2) to zero and taking the limit as $N(t) \to \infty$. Also $x_* = 0$ since otherwise $x_*N$ would approach infinity so that $y(t)$ would approach infinity by the equation for $y'(t)$ in (A.1.2). The same equation implies

$$
S_* = \frac{\gamma + \alpha + d - \rho b + \xi}{\beta}.
$$

From $y_* + z_* = 1$, we find that

$$
\xi = \frac{\alpha}{1 + \gamma / (d + r)}(\phi_{DVI} - 1),
$$

which is the asymptotic growth rate constant when $\phi_{DVI} > 1$, so $N(t)$ has exponential growth asymptotically.

More detailed information about how the system tends to the endemic equilibrium can be obtained by solving the characteristic equation and finding eigenvalues (Anderson and May, 1992). If the endemic state $E_*$ is locally stable, all the eigenvalues have negative real parts. We then have two cases to consider. One is that all roots are real, which corresponds to $E_*$ being a stable node, with no damped oscillations near the endemic equilibrium. The other is that there is a pair of complex conjugate roots and a real root, which implies that $E_*$ is a stable spiral. The approach to the steady state will therefore be oscillatory. The eigenvalues also give us the (approximate) period of the decaying oscillations. With complex conjugate eigenvalues $\lambda = m \pm ni$, the solutions to the linearized equations are a linear combination of $e^{nt} \cos(nt)$ and $e^{nt} \sin(nt)$, thus having period $T = 2\pi/n$.

A.2. Local stability of equilibria in system (3.1)

There are two possible biologically relevant equilibria in model (3.1). One is the pathogen-free equilibrium $E_0 = (0, 0, 0)$ and the other is the coexistence equilibrium $E_* = (I_*, R_*, W_*)$, where

$$
I_* = \frac{(d + r)(d + \alpha + \gamma)}{d + r + \gamma} \frac{\mu + v N_0}{\beta (\mu + v N_0) + \lambda \gamma} (R_0 - 1), \quad R_* = \frac{\gamma}{d + r} I_*, \quad W_* = \frac{\lambda}{\mu + v N_0} I_*.
$$

Clearly, $I_* > 0$ if $R_0 > 1$, and we also require $d + \alpha + \gamma - \rho b > 0$ so that $I_* + R_* < N_0$. So, $E_*$ is feasible if $R_0 > 1$ and $d + \alpha + \gamma - \rho b > 0$. By checking the Jacobian matrix at $E_0$ we easily show that the pathogen-free equilibrium $(0, 0, 0)$ is LAS if $R_0 < 1$. The characteristic equation of the Jacobian matrix at $E_*$ is

$$
A^3 + q_1 A^2 + q_2 A + q_3 = 0,
$$

(A.2.1)
Clearly, we have considered a second-order approximation of the model to first-order, for large $A$. The multivariate normal with mean vector $0$ and covariance matrix $\Sigma$ approximates the quasi-stationary distribution of our original infection process. This approximation is four-dimensional in the area which the population occupies, so that the components of $q$ process. Consider the limit as $n \to \infty$ and $m \to \infty$. By verifying Routh–Hurwitz conditions we find that the endemic state $E_s$ is locally stable if and only if it is feasible.

**A.3. Matrices involved in Section 4**

Define a family of scaled processes indexed by $H$ by

$$V_H(t) = \frac{1}{H}(S_H(t), I_H(t), R_H(t), W_H(t))^\top,$$  \hspace{1cm} (A.3.1)

where the superscript $\top$ is used to denote transpose. The scaling parameter $H$ can, for example, be considered as the size of the area which the population occupies, so that the components of $V_H$ are population densities. Thus, the infection rates $\beta$ and $\nu$ will be inversely proportional to $H$. In this way the epidemic model can be regarded as being a density dependent process. Consider the limit as $H \to \infty$ of $V_H(t)$. Theorem 11.2.1 of Ethier and Kurtz (1986) tells us (roughly speaking) that to first-order, for large $H$, the process $V_H(t)$ can be approximated by the deterministic process defined by (2.1). Now we consider a second-order approximation of $(S(t), I(t), R(t), W(t))$. Letting $V^* = (1/H)(S^*, I^*, R^*, W^*)^\top$, where $S^*, I^*, R^*$, and $W^*$ are given by (2.3), then close to the stable equilibrium point $V^*$, the process $F_H(t) = \sqrt{H}(V_H(t) - V^*)$ may be approximated by a four-dimensional Ornstein–Uhlenbeck process (Ethier and Kurtz, 1986). The Ornstein–Uhlenbeck process has local drift matrix $A(V^*)$ and local covariance matrix $G(V^*)$ (see details below). Its stationary distribution approximates the quasi-stationary distribution of our original infection process. This approximation is four-dimensional multivariate normal with mean vector $0$ and covariance matrix $\Sigma$ determined from the matrices $A(V^*)$ and $G(V^*)$ through the equation

$$A(V^*)\Sigma + \Sigma A(V^*)^\top = -G(V^*).$$  \hspace{1cm} (A.3.2)

The matrix $A(V^*)$ and matrix $G(V^*)$ are

\[
A = \begin{pmatrix}
    b - \beta I^* - \nu W^* - d & (1 - \rho) b - \beta S^* & b + r & -\nu S^* \\
    \beta I^* + \nu W^* & \rho b + \beta S^* + (d + \gamma) & 0 & \nu S^* \\
    0 & \gamma & -(d + r) & 0 \\
    -\nu W^* & \lambda - \nu W^* & -\nu W^* & -(\mu + \nu(S^* + I^* + R^*))
\end{pmatrix},
\]

\[
G = \frac{1}{H} \begin{pmatrix}
    G_{11} & -(\beta S^* I^* + \nu S^* W^*) & -r R^* & \nu S^* W^* \\
    -r R^* & G_{22} & -\gamma I^* & -\nu S^* W^* \\
    \nu S^* W^* & -\nu S^* W^* & \gamma I^* + (d + r) R^* & 0 \\
    -r S^* & -r I^* & \lambda I^* + (\mu + \nu(S^* + I^* + R^*))W^*
\end{pmatrix},
\]

where

\[
G_{11} = b(S^* + R^*) + (1 - \rho) b I^* + \beta S^* I^* + \nu S^* W^* + d S^* + r R^*,
\]

\[
G_{22} = \rho b I^* + \beta S^* I^* + \nu S^* W^* + (d + \gamma) I^*.
\]
The matrix $A_c$ and matrix $G_c$ in the managed case are

$$A_c = \begin{pmatrix} \rho b + \beta (N_0 - 2I_s - R_s) - \gamma W_s - (d + \gamma + \lambda) & -\beta I_s - \nu W_s & \nu (N_0 - I_s - R_s) \\ \gamma & d + r & 0 \\ \lambda & 0 & -\mu - \nu N_0 \end{pmatrix},$$

$$G_c = \frac{1}{H} \begin{pmatrix} G_{c11} & -\gamma I_s - \frac{\rho bdI_s R_s}{dN_0 + \gamma I_s} & -\nu (N_0 - I_s - R_s)W_s \\ -\gamma I_s - \frac{\rho bdI_s R_s}{dN_0 + \gamma I_s} & \gamma I_s + (d + r)R_s & 0 \\ -\nu (N_0 - I_s - R_s)W_s & 0 & \lambda I_s + (\mu + \nu N_0)W_s \end{pmatrix},$$

where

$$G_{c11} = (\beta I_s + \nu W_s)(N_0 - I_s - R_s) + \gamma I_s + \frac{(dN_0 + (\mu - \rho b)I_s)(d + \gamma + \lambda)I_s + \rho bdI_s(N_0 - I_s)}{dN_0 + \gamma I_s}$$

and $(I_s, R_s, W_s)$ is the unique endemic state of the three-dimensional deterministic model determined by the transition rates in Table 3, which is actually system (3.1).

### A.4. Semi-stochastic simulation algorithm

The definition of the fully stochastic model is given in Table 2. In practice, we used a semi-stochastic approximation to this model. Since the number of the infectious units in the environment is enormous, comparative to the herd size, and shedding and pathogen death happen frequently, these events are modelled deterministically. The recipe for the model is as follows. We first estimate a time to the next event $T$ by calculating the sum of the frequencies of all possible events

$$T = \min \left\{ t : \int_0^t Tr(\theta) \, d\theta \geq -\ln(U_1) \right\},$$

where $U_1$ is a uniform deviate in $[0, 1]$. Next, we order all possible events as an increasing faction of $Tr$ and generate another uniform deviate $(U_2 \in [0, 1])$, to obtain the nature of the next event.

### References


