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Understanding the dynamics of *Salmonella* infections in dairy herds: a modelling approach

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Abstract

There is evidence of variation in the infection dynamics of different *Salmonella* serotypes in cattle—ranging from transient epidemics to long term persistence and recurrence. We seek to identify possible causes of these differences. In this study we present mathematical models which describe both managed population dynamics and epidemiology and use these to investigate the effects of demographic and epidemiological factors on epidemic behaviour and threshold for invasion. In particular, when the system is perturbed by higher culling or pathogen-induced mortality we incorporate mechanisms to constrain the lactating herd size to remain constant in the absence of pathogen or to lie within a fairly small interval in the presence of pathogen. A combination of numerical and analytical techniques is used to analyse the models. We find that the epidemiologically dominating management group can change from the dry/lactating cycle to the weaned group with increasing culling rate. Pseudovertical transmission is found to have little effect on the invasion criteria, while indirect transmission has significant influence. Pathogen-induced mortality, recovery, immune response and pathogen removal are found to be factors inducing damped oscillations; variation in these factors between *Salmonella* serotypes may be responsible for some of the observed differences in within herd dynamics. Specifically, higher pathogen-induced mortality, shorter infectious period, more persistent immune response and more rapid removal of faeces result in a lower number of infectives and smaller epidemics but a greater tendency for damped oscillations.

Keywords: Demography; Epidemiology; Transmission; Infection; *Salmonella*

1. Introduction

Over the last two decades Great Britain experienced an epidemic of salmonellosis both in man and farm animals, mainly cattle, caused by a multiple antibiotic resistant strain of *Salmonella typhimurium* definitive type (DT) 104. Multi-resistant *S. typhimurium* DT104 first emerged as a human and animal pathogen in the 1980s (Hollinger et al., 1998). There were few reported cases per year in cattle until the early 1990s when the pattern changed dramatically; there was a sharp rise in cattle reports. This was followed by a steady decline in reports between 1995 and 2000 (Davies, 2001). A similar, but smaller pattern was seen in other livestock species including sheep, pigs and poultry (VLA, 2002). The reasons for the decline in reported cases are unclear. Some hypotheses for the decline in *S. typhimurium* DT104 include the development of herd immunity and the age-related demographic changes attributable to BSE slaughter control schemes (Gibbens, 1998; Davison et al., 2002). There have been other epidemic strains of *S. typhimurium* (e.g. DT193 and 204C) 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,

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1999, 2000). So far, it is still not known why DT104 was able to cause such a large epidemic in contrast to other *Salmonella* serotypes. This provides the motivation for this study.

There is little published information on the dynamics of *S. typhimurium* DT104 and other *Salmonella* serotypes within and between groups of animals. An understanding of why these strains emerge and decline could provide the key to predicting the long term behaviour of *Salmonella* infections in livestock and assist in the development of more effective control strategies. Although it is clear there are major differences in the transmission dynamics and epidemic behaviour of *Salmonella* serotypes at the herd level, relatively little is known about the dynamics within herds. There is some 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 and Evans, unpublished data). It is likely that within herd dynamics, in particular size of epidemic, persistence and recurrence, play an important role in determining the transmission and epidemic behaviour between herds. In this study we are primarily interested in the epidemiology of *Salmonella* infection within dairy cattle herds. We propose a modelling approach to identify the key processes and parameters that could explain differences in observed epidemiological patterns. Mathematical models which describe both management population dynamics and epidemiology are formulated. A combination of numerical and analytical techniques is used to analyse the models.

There is evidence of age, management group and seasonal variation in disease and shedding rates (Davies, 2001). The processes that give rise to host-specificity, such as the interaction between the pathogen and the host's immune response (Uzzau et al., 2001, 2000) and the development of persistent carriers (Wray et al., 1989; Giles et al., 1989), may also contribute to the variation in within-herd dynamics. Other parameters such as number of organisms shed in faeces, survival outside the host (Plym-Forshell and Ekesbo, 1996; McLaren and Wray, 1991) and pathogen-induced mortality and morbidity rates (including fetal loss) (Davies, 2001; Clegg et al., 1983) have also been shown to vary between *Salmonella* strains. We concentrate on two types of questions. First, what are the effects of demographic factors (e.g. culling rate) and epidemiological factors (such as pathogen-induced mortality, duration of infectiousness and off-host pathogen survival) on the invasion criterion for the pathogen, and especially, do these epidemiological factors in each group have the same effects? Second, what are the effects of pathogen-induced mortality, host immunity, persistence and off-host pathogen survival on the dynamics of infection within a dairy herd? Could variation in these parameters explain some of the apparent differences in behaviour of different *Salmonella* serotypes in cattle? We aim to use the contrasting epidemiology of different *Salmonella* serotypes to improve our understanding of the mechanisms that may drive the epidemic behaviour of strains of *S. typhimurium* and lead to the apparent fluctuating endemic behaviour of other *Salmonella* serotypes.

2. Model formulation

In a typical dairy herd there are multiple groups of animals (e.g., unweaned, weaned, bulling heifers, in-calf heifers, dry and lactating cows). Management practices vary; for this first model we choose one adopted for many herds in the UK in which weaned heifers are housed with mature dry cows for a short period before first calving as part of training prior to entering the milking herd (O'Connell et al., 1993)(typically 2 months given the parameter values in Table 1 below). We recognize that this is not the only possibility but we address it since it is employed and has the benefit of reducing the number of groups of animals to be considered. Thus we can effectively classify animals as unweaned, weaned, dry and lactating. An animal starts its life in the unweaned group (denoted by N_1), matures into the weaned group (denoted by N_2), and then matures again into the dry group (denoted by N_3). From here it enters the lactating group (denoted by N_4) and then the dry/lactating cycle.

In the absence of disease, the model proposed here is used to describe managed population dynamics. The mathematical model is

$$\begin{cases} \dot{N}_1(t) = B(N_3, N_4) - (d_1 + c_1)N_1, \\ \dot{N}_2(t) = c_1 N_1 - (d_2 + c_2)N_2, \\ \dot{N}_3(t) = c_2 N_2 - (d_3 + c_3)N_3 + c_4 N_4, \\ \dot{N}_4(t) = c_3 N_3 - (d_4 + c_4)N_4 - m(N_4), \end{cases} \tag{2.1}$$

where $B(N_3, N_4)$ is a recruitment function and $m(N_4)$ a culling rate function. In a typical dairy herd, dry cows may give birth to either dairy or beef-cross calves. Only the female dairy calves are eligible for recruitment into the dairy herd. Farmers may therefore increase recruitment by inseminating more cattle with dairy semen and/or selecting a greater proportion of female dairy calves for entry into the lactating herd. Recruitment is influenced by the total population of the lactating group. The recruitment function combines these management processes into a simple form and allows for unweaned calves to be sold in appropriate circumstances. Parameters are listed in Table 1. In the following we choose particular recruitment and culling functions. We take

$$B(N_3, N_4) = bN_3\left(1 - \frac{N_4}{K}\right), \quad m(N_4) = mN_4, \tag{2.2}$$

Table 1
Definitions of the parameters used in the model

Parameter	Definition (units)	Parameter estimate	References
b	Recruitment rate	$b = 0.0085$	—
m	Basic culling rate (per day)	$m = 0.0005$ when not varying	Young et al. (1983)
m_a	Additional culling (buying) rate (per day)	$m_a = 0.00027$	—
ρ	Pseudovertical transmission parameter	Unknown, assume $\rho = 1$	—
c	Maturation rate (per day)	$c_1 = 0.024$, $c_2 = 0.0015$	Blowey (1986)
	Rate of flow from dry (lactating) to lactating (dry) group (per day)	$c_3 = 0.017 (c_4 = 0.0032)$	Blowey (1986)
d	Death rate (per day)	$d_1 = 0.00014, d_2 = 0.000033$ $d_{3,4} = 0.000056$	Gardner et al. (1990) and Tyler et al. (1999)
K	Size of the lactating group above which recruitment ceases	$K = 100$	—
L_m	Desired size of the lactating group	$L_m = 100$	—
α	Pathogen-induced mortality	$\alpha_i = 0.001$ when not varying	—
γ	Recovery rate (per day)	Unknown, assume $\gamma_i = 0.1$ when not varying	—
r	Immunity-loss rate (per day)	Unknown, assume $r_i = 0.01$ when not varying	—
λ	Shedding rate (per day)	Unknown, assume $\lambda_1 = 4.0 \times 10^8$, $\lambda_2 = 5.0 \times 10^7$, $\lambda_{3,4} = 1.3 \times 10^8$	—
p	Pooling rate (per day)	Unknown, assume $p_{1,2} = 0.001$ $p_{3,4} = 0.0001$	Turner et al. (2003)
l	Death rate of organism (per day)	Some information in text, assume $l_i = 0.12$ for $i \in \{1, 2, 3, c\}$, $l_4 = 0.99$	Himathongkham et al. (1999)
β	Direct transmission parameter (per animal per day)	Unknown, assume $\beta_i = 0.006$	—
η	Group-specific indirect transmission parameter (per infectious unit per day)	Unknown, assume $\eta_i = 1.3 \times 10^{-11}$	—
δ	Ratio of general indirect transmission parameter to group-specific one	Unknown, assume $\delta_2 = 0.005$, $\delta_i = 0.01, i \in \{1, 3, 4\}$	Turner et al. (2003)

where K is the size of the lactating group above which positive recruitment would be replaced by selling. We note that $d_i (i = 1, \ldots, 4)$ is natural death rate in each group. $c_1(c_2)$ denotes the maturation rate (per day) from the unweaned (weaned) group to the weaned (dry) group. Furthermore, $c_3(c_4)$ denotes the rate of flow from the dry (lactating) to the lactating (dry) group. It is easy to show that if

$$b > \frac{(d_1 + c_1)(d_2 + c_2)}{c_1 c_2}\left(d_3 + c_3 - \frac{c_3 c_4}{d_4 + m + c_4}\right) \tag{2.3}$$

the system (2.1) has a positive equilibrium $(\bar{N}_1, \bar{N}_2, \bar{N}_3, \bar{N}_4)$, where

$$\bar{N}_1 = \frac{\bar{N}_2(d_2 + c_2)}{c_1},$$

$$\bar{N}_2 = \frac{\bar{N}_3}{c_2}\left(d_3 + c_3 - \frac{c_3 c_4}{d_4 + m + c_4}\right),$$

$$\bar{N}_4 = \frac{c_3 \bar{N}_3}{d_4 + m + c_4},$$

$$\bar{N}_3 = \frac{K(d_4 + m + c_4)}{b c_3}\left[b - \frac{(d_1 + c_1)(d_2 + c_2)}{c_1 c_2} \times \left(d_3 + c_3 - \frac{c_3 c_4}{d_4 + m + c_4}\right)\right]. \tag{2.4}$$

Simple calculation shows that $\bar{N}_4 < K$. Further, by checking the Jacobian matrix at the equilibrium we can easily show that the equilibrium $(\bar{N}_1, \bar{N}_2, \bar{N}_3, \bar{N}_4)$ is locally asymptotically stable if condition (A.1.1) of Appendix A.1 is true. In the following we assume (A.1.1) is true. Solutions of the system (2.1) are consequently positive provided the initial data are close to the equilibrium. In fact, parameters listed in Table 1 are such that (A.1.1) is satisfied.

In the presence of disease we assume that the total population of each group N_j $(j = 1, \ldots, 4)$ is composed of three population classes: susceptibles (denoted by S_j), infectives (I_j) and immunes (R_j). The infection-free group dynamics described above applies to these classes, but there is an overlay. Once infected, an individual may either die due to the disease, or, due to protective immune response, pass into the recovered class. In this study we consider a transient protective immune response of varying duration, with animals returning to the susceptible class.

Since the organism of *Salmonella* can survive for long periods outside the host in suitable conditions, the combination of these four groups and five environments (one specific to each group and one combined environment) containing free-living infective units results in many possible routes of transmission. The model incorporates direct host-to-host transmission, in which susceptible hosts become infected through direct faecal–oral or oral–oral transmission between animals. Additionally, infected individuals shed the pathogen into their local environment, which may be pooled into a combined environment via equipment or vehicles, and the model also includes transmission via encounters with free-living bacteria, which represents indirect faecal–oral transmission. The densities of free-living bacteria in the environment (denoted by $W_j, j=1,\ldots,4$ in the local environments and by W_c in the combined environment) are modelled, and the rate of infection of susceptibles is assumed to depend on susceptible density and free-living bacteria densities. Further, pseudovertical transmission, representing transmission from infected parent in the neonatal period, is also featured in this model. Fig. 1 shows the interactions of the four groups and five environments.

A system of non-linear ordinary differential equations is used to model the dynamics of host and pathogen. Suppressing time-dependence, t, for each variable, the seventeen model equations are

$$\begin{cases} \dot{S}_j = G_j^S - L_j^S - \Gamma_j^I, \\ \dot{I}_j = G_j^I - L_j^I + \Gamma_j^I, \\ \dot{R}_j = G_j^R - L_j^R, \\ \dot{W}_j = G_j^W - L_j^W - \mathscr{C}_j^W, \\ \dot{W}_c = G_c^W - L_c^W - \mathscr{C}_c^W, \end{cases} \tag{2.5}$$

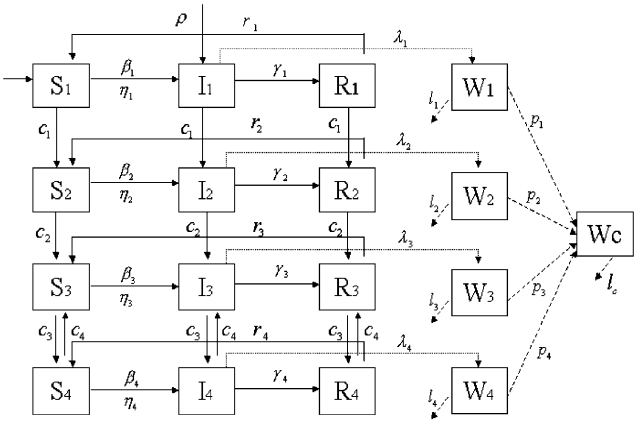

Fig. 1. Flow diagram representing transmission routes and other processes modelled by system (2.5). See the definition of parameters in Table 1.

where $j=1,\ldots,4$. Now we have $\dot{N}_j = \dot{S}_j + \dot{I}_j + \dot{R}_j$ so that our previous population model (2.1) is recaptured in the absence of infection. G_A^B and L_A^B denote the rates of gain and loss (other than by transmission) for animals or *Salmonella* of the compartment B in group or environment A. Γ_j^I represent the rate of appearance of new infections in group j; because of management practices they are only caused by infected individuals in group j and by infectious bacteria from environment j and the common environment c. $\mathscr{C}_j^W$ and $\mathscr{C}_c^W$ are the rates of consumption of infectious bacteria from environments j and c. In particular, the rates of transmission and consumption are

$$\begin{aligned} \Gamma_j^I &= \beta_j S_j I_j + \eta_j S_j W_j + \delta_j \eta_j S_j W_c, \\ \mathscr{C}_j^W &= \eta_j (S_j + I_j + R_j) W_j, \\ \mathscr{C}_c^W &= \sum_{j=1}^{4} \eta_j \delta_j (S_j + I_j + R_j) W_c \end{aligned} \tag{2.6}$$

and other rates for each group and environment are listed in Appendix A.2.

A combination of numerical and analytical techniques is used to analyse the model. The infection-free state is defined as $E_0\,(S_{10}, S_{20}, S_{30}, S_{40})$ and is feasible if inequality (2.3) holds true, since the value of S_{j0} is $\bar{N}_j$ $(j=1,\ldots,4)$, which is given in Eq. (2.4). In epidemiology, there is a criterion which governs whether or not the disease can invade successfully. The basic reproduction number R_0 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. In deterministic models, invasion is impossible (the disease-free equilibrium is locally asymptotically stable) when $R_0<1$, but if $R_0>1$, then the disease-free equilibrium is unstable and invasion is possible (see the survey paper by Hethcote, 2000).

For a heterogeneous population Diekmann et al. (1990, 2000) characterize R_0 as the spectral radius of the next generation matrix H. The elements (h_{ij}) of the matrix are the number of newly infected individuals of type i generated (via all possible routes) by an individual of type j in a totally susceptible population. To calculate h_{ij}, here we extend the method presented in terms of a general compartmental disease transmission model by Van den Driessche and Watmough (2002) to a system with free-living infectious organisms. Based on the methods of Van den Driessche and Watmough (2002), we write

$$\dot{I}_j = \mathscr{F}_{j1} + \mathscr{F}_{j2} + \mathscr{F}_{j3} - \mathscr{V}_j, \quad j=1,\ldots,4,$$

where $\mathscr{F}_{j1}$ $(\mathscr{F}_{j2}, \mathscr{F}_{j3})$ denotes the rate of appearance of new infections in compartment j via direct transmission (pseudovertical transmission, indirect transmission

through encounters with free-living bacteria). $\mathscr{V}_j = \mathscr{V}_j^- - \mathscr{V}_j^+$, where $\mathscr{V}_j^-$ ($\mathscr{V}_j^+$) is the rate of transfer of individuals out of (into) compartment j, both of these rates referring to means other than transmission. Maturing into one of the infectious compartments from another infectious compartment is not considered as a new infection. Denote $\mathscr{F}_i = (\mathscr{F}_{1i}, \mathscr{F}_{2i}, \mathscr{F}_{3i}, \mathscr{F}_{4i})^\top$ ($i = 1,2,3$) and $\mathscr{V} = (\mathscr{V}_1, \mathscr{V}_2, \mathscr{V}_3, \mathscr{V}_4)^\top$. Let

$$F_i \triangleq \left[\frac{\partial \mathscr{F}_i}{\partial I_j}(E_0)\right], \quad V \triangleq \left[\frac{\partial \mathscr{V}}{\partial I_j}(E_0)\right], \quad i = 1,2,\ j = 1,\ldots,4,$$

$$F_3 \triangleq \left[\frac{\partial \mathscr{F}_3}{\partial W_k}(E_0)\right], \quad k \in \{1,\ldots,4,c\}.$$

See details for $F_i (i = 1,2,3)$ and V in Appendix A.3. So the (i,j) entry of the product F_1V^{-1} (F_2V^{-1}) gives the expected number of new infections in compartment i produced by an infected individual originally introduced into compartment j due to direct transmission (pseudo-vertical transmission).

For the free-living bacteria, we consider the dynamics of the linearized system at uninfected equilibrium

$$\dot{W}(t) = \Lambda I - QW, \quad W = (W_1,\ldots,W_4,W_c)^\top,$$
$$I = (I_1,I_2,I_3,I_4)^\top,$$

where Λ and Q are defined in Appendix A.3. Similarly to the above, the matrix $Q^{-1}\Lambda$ gives the expected number of free-living bacteria produced by an infected individual during its infectious lifetime. So, the matrix $F_3Q^{-1}\Lambda V^{-1}$ gives the expected number of new infections produced by an infected individual during its lifetime due to indirect transmission. The next generation matrix for this model is the sum of the direct-transmission, pseudovertical transmission and indirect-transmission components, i.e.,

$$H = F_1V^{-1} + F_2V^{-1} + F_3Q^{-1}\Lambda V^{-1}. \tag{2.7}$$

Therefore, the basic reproduction number of model (2.5) is

$$R_0 = sp\ (H),$$

where $sp(H)$ denotes the spectral radius of the matrix H. Unfortunately, R_0 cannot be explicitly calculated for this general system. So the following section is devoted to investigating R_0 by plotting it against the parameters of central management or epidemiological interest, whilst keeping the remaining parameters fixed.

Parameter values used in the following investigation represent the demography and epidemiology as summarized below (see Table 1). Values for many demographic parameters are derived from the literature (Blowey, 1986; Gardner et al., 1990; Tyler et al., 1999; Young et al., 1983; Himathongkham et al., 1999; Turner et al., 2003). Estimates for some parameters which are related to epidemiology are not yet available. There are studies relating to epidemiological questions (Houston et al., 2002a,b and references therein; Troutt et al., 2001; Veling et al., 2002; Edrington et al., 2004; Wray and Sojka, 1978) and some of these inform parameter values indirectly. A range of values chosen to provide epidemic behaviour and endemic levels consistent with observed patterns in livestock is studied. The wide range of shedding behaviour observed in some of the above references is captured here via a distribution of infection/shedding periods with mean $1/\gamma$. This is indicated for a first study but could be revised for later work. For some parameters, whilst there is information, it is not precise for all compartments, for example, l_4 (the death rate of the pathogen for the lactating group) is set at 0.99 (per day), while other pathogen death rates are set at 0.12 (per day) to provide a decimal reduction time consistent with studies of survival in faecal material (Himathongkham et al., 1999). This is to reflect a situation in which the environment of the lactating animals is cleared of a high proportion of faeces regularly.

3. Effect of various parameters on the behaviour of the model

Numerical study and simulation of our mathematical model of *Salmonella* infection allow us to observe and quantify effects of demographic and epidemiological factors on the basic reproduction number R_0 and on the short-term behaviour of the proposed system. To illustrate these effects, we present numerical results in the following subsections.

3.1. Variation in R_0 with parameters

Variation in model parameters (due to uncertainty, differences between different *Salmonella* serotypes, etc.) will influence the value of R_0 and thus the prevalence of infection. We note that R_0, obtained in the previous section as the spectral radius of the next generation matrix, cannot be computed explicitly. To investigate changes in R_0 due to variation in parameters, we begin by investigating special cases of the model for which an explicit expression for R_0 is available (e.g. the model with direct transmission only). This allows us to distinguish the contribution made by other types of transmission. Further, it is possible to observe the effect of potential control strategies because some of these special cases correspond to intervention strategies. We then go on to numerically investigate corresponding questions for the full model.

First we consider a model with direct transmission only. In this case, all routes of transmission except direct host-to-host transmission are ignored (i.e., parameters $\eta_i, \delta_i, i = 1,\ldots,4$ and ρ are zero). This is unlikely to

occur, although it could in theory be achieved by optimal hygiene in the post-natal period and rapid removal of faeces from all environments. It nevertheless allows comparison with other transmission routes. The reduced next generation matrix simplifies to $H_1 = F_1 V^{-1}$ and the four eigenvalues can now be rendered algebraically:

$$\Lambda_1 = \frac{\beta_1 S_{10}}{D_1}, \quad \Lambda_2 = \frac{\beta_2 S_{20}}{D_2},$$

$$\Lambda_{3,4} = \frac{1}{2(D_3 D_4 - c_3 c_4)} \left(\beta_3 D_4 S_{30} + \beta_4 D_3 S_{40} \pm \sqrt{(\beta_3 D_4 S_{30} - \beta_4 D_3 S_{40})^2 + 4\beta_3 \beta_4 c_3 c_4 S_{30} S_{40}} \right). \tag{3.1}$$

The eigenvalue Λ_1 (Λ_2) denotes the number of newly infected animals produced in the unweaned (weaned) group by an infected animal whilst in the unweaned (weaned) group. It determines whether or not the pathogen can invade and then persist within the unweaned (weaned) group alone. The eigenvalue Λ_3 (we take $\Lambda_3 > \Lambda_4$), which determines whether or not the pathogen can invade the dry/lactating group, is more complicated due to the existence of this cycle. The cycle allows animals to be in the dry and lactating groups repeatedly, and hence makes the time that an infected animal spends in the dry or lactating groups more complicated.

The basic reproduction number R_0 is given by

$$R_0 = \max\{\Lambda_1, \Lambda_2, \Lambda_3\}.$$

Hence R_0 switches between three of the above four eigenvalues with varying parameters. In the following we will investigate how R_0 changes as the following parameters vary: culling rate m; pathogen-induced mortality α_i; recovery rate γ_i; and 'death' rate of the organism l_i.

R_0 is a function of the uninfected-equilibrium host population sizes, transmission rates and time spent in each group. We vary recovery rates to explore the effect on R_0 of varying infectious period $1/\gamma_i$ ($i = 1, \ldots, 4$). For simplicity, we keep all the γ_i equal, $\gamma_1 = \gamma_2 = \gamma_3 = \gamma_4$. We shall first give plots of the eigenvalues instead of plots of R_0 because these reveal information specific to each group. In Fig. 2(a) eigenvalues Λ_1, Λ_2 and Λ_3 are plotted against recovery rate γ_i. Eigenvalues Λ_1 and Λ_2 decrease monotonically with γ_j since $\partial \Lambda_j / \partial \gamma_j < 0$ ($j = 1, 2$) (although the decay is slow for Λ_1). Numerical studies show that Λ_3 also decreases with increasing γ_j ($j = 3, 4$). This is in accordance with the fact that faster recovery results in infected individuals remaining in

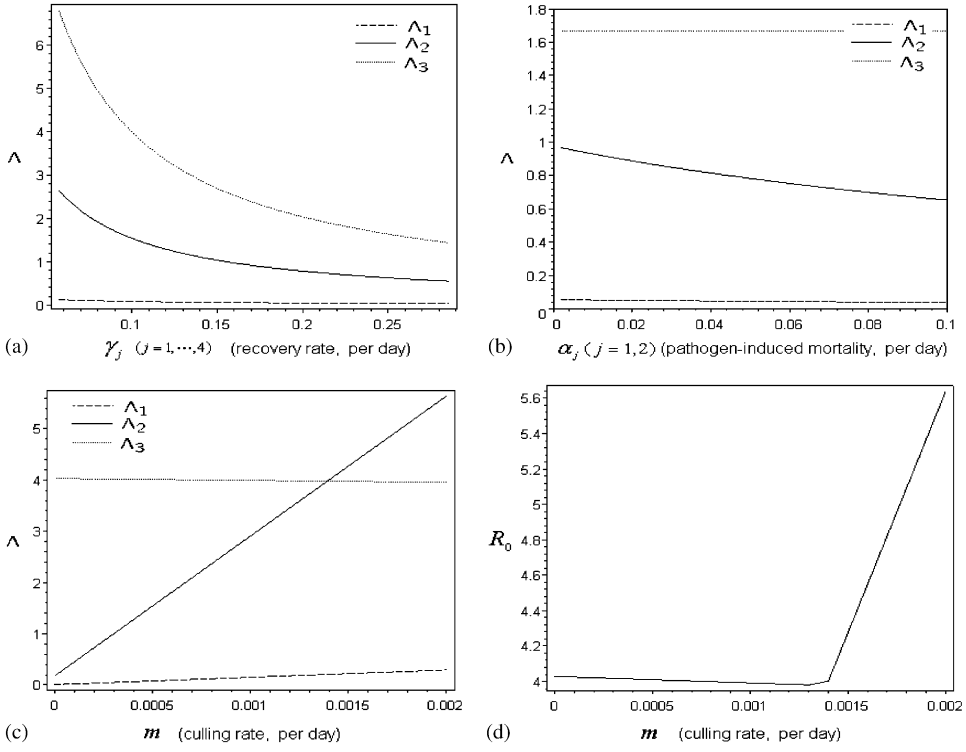

Fig. 2. Plots of eigenvalues Λ_1, Λ_2 and Λ_3 for the model (2.5) with direct transmission only (except for (d)). (a): Λ_1, Λ_2 and Λ_3 plotted against γ_j ($j = 1, \ldots, 4$). (b): Λ_1, Λ_2 and Λ_3 plotted against α_j ($j = 1, 2$). (c): Λ_1, Λ_2 and Λ_3 plotted against m. (d): R_0 plotted against m for the model with direct and pseudovertical transmission.

their compartment for a shorter period and hence the number of newly infected animals produced by an infected animal in its life time declines. Fig. 2(a) shows that the dry/lactating cycle always dominates. It also follows from Fig. 2(a) that for this particular set of parameter values R_0 $(=\Lambda_3)$ is always larger than unity whatever value the recovery rates γ_i take within the range considered, which means the pathogen can always invade successfully.

In Fig. 2(b) eigenvalues Λ_1, Λ_2 and Λ_3 are plotted against pathogen-induced mortality in the unweaned and weaned groups α_i $(i = 1, 2)$, keeping $\alpha_1 = \alpha_2$. We assume a higher level of mortality in young calves and negligible adult mortality (i.e., $\alpha_3 = \alpha_4 = 0$), although this is not the case for all *Salmonella* serotypes (Richardson, 1975). It follows from expressions (3.1) for Λ_i $(i = 1, 2, 3)$ that Λ_3 remains constant and Λ_1 and Λ_2 decrease as α_1 and α_2 increase (although again the decay is slow for Λ_1). This is because the infectious individuals remain in their compartments for a shorter period due to higher pathogen-induced mortality. This result is partly in accordance with the fact that pathogen-induced mortality is found to be stabilizing in the one-group models of Anderson and May (1980) and Brown (1984). Similarly, the dry/lactating group dominates for this set of particular parameter values.

Now we turn to consider the effect of varying the lifespan and turnover of lactating cows on the disease-free equilibrium, and hence on R_0. In particular, the nonlinearity introduced into the demography by the recruitment function allows this change to be complex. Simple calculation shows that the uninfected-equilibrium lactating population (S_{40}) always decreases with increasing culling rate m no matter how large the recruitment rate parameter b is (see Appendix A.4). The recruitment function given in (2.2) does imply that more young animals are recruited to the unweaned group when the number in the lactating group is low, but this still cannot prevent the lactating group from declining with increasing culling rate. Therefore, large culling unavoidably leads to a decline of the lactating group for this recruitment mechanism. However, this is not how most managed farming system should function. Dairy farmers typically want to keep the lactating group size near constant or within a small interval (e.g. to fill milk quotas). One realistic strategy is to adjust the recruitment rate parameter b when the lactating group suffers from high culling. It is reasonable to assume that b is a function $b(m)$ of culling rate m with $b'(m) > 0$. Here we choose the function $b(m)$ such that the lactating group size at the uninfected equilibrium is held constant, say $\bar{S}_{40}$. Further, $b(m)$ can be explicitly expressed (Appendix A.4) and is indeed an increasing function of m. The corresponding uninfected-equilibrium host populations $\bar{S}_{10}$, $\bar{S}_{20}$ and $\bar{S}_{30}$ are linearly increasing functions of m and their explicit expressions are given in Appendix A.4. Note that we use the varying recruitment rate parameter $b(m)$ whenever we vary the culling rate m, in Fig. 2(c),(d) and Fig. 3(a).

In Fig. 2(c), eigenvalues Λ_1, Λ_2 and Λ_3 are plotted against the culling rate m. We explore a wide range of culling rates from zero (representing the unlikely situation in which cows live for their full natural lifespan) to 0.002 (lactating cows survive on average for one and a half lactations). Here $\bar{S}_{40}$ is chosen as the value of the uninfected-equilibrium lactating population (i.e. $\bar{S}_{40} = S_{40} = 69.678$) when we use the usual culling rate $(m = 0.0005)$ and recruitment rate parameter $(b = 0.0085)$ given in Table 1. The eigenvalue Λ_3 decreases gradually, and Λ_1 and Λ_2 increase (due to positivity of $\partial\Lambda_1/\partial m$ and $\partial\Lambda_2/\partial m$) with increasing culling rate m. Fig. 2(c) shows that Λ_3 dominates for relatively small values of culling rate. However, for relatively large value of culling rate m, Λ_2 becomes dominant. This implies that the dominating group changes from the dry/lactating cycle to the weaned group as culling rate increases. Therefore, the curve which corresponds to R_0 is a composite curve composed of the 'dominant' parts of the three constituent curves. This figure also implies that large culling rates make the pathogen more likely to invade the host population.

Now we consider the model incorporating both direct transmission and pseudovertical transmission (but not indirect transmission, i.e., $\eta_i = 0$, $\delta_i = 0$, $i = 1, \ldots, 4$). In this case the expression for R_0 is complicated and cannot be interpreted biologically by inspection, and hence a graphical representation is given. Fig. 2(d) shows that as culling rate m increases, R_0 decreases first and then increases. Note that the curve in Fig. 2(d) is almost identical to the composite curve (of the maximum eigenvalue) equivalent to R_0 in Fig. 2(c) (for the model with direct transmission only). This implies that pseudovertical transmission contributes little to invasion for this particular set of parameter values, even with a high probability of pseudovertical transmission.

Consider the model with all routes of transmission (direct, pseudovertical and indirect). In Fig. 3(a), R_0 is plotted against the culling rate m. The values of R_0 lie much further above the line $R_0 = 1$ than in Fig. 2(c) and (d). This implies that invasion happens more quickly and easily when there is indirect transmission as an additional route of transmission. Therefore, invasion is more likely for the full model than for the model with direct transmission only. Moreover, for the model with all routes of transmission, numerical studies show that R_0 decreases monotonically as γ_j $(j = 1, \ldots, 4)$ or α_j $(j = 1, 2)$ increase. The relevant figures are qualitatively the same as the dominating curve in Fig. 2(a), and we omit them.

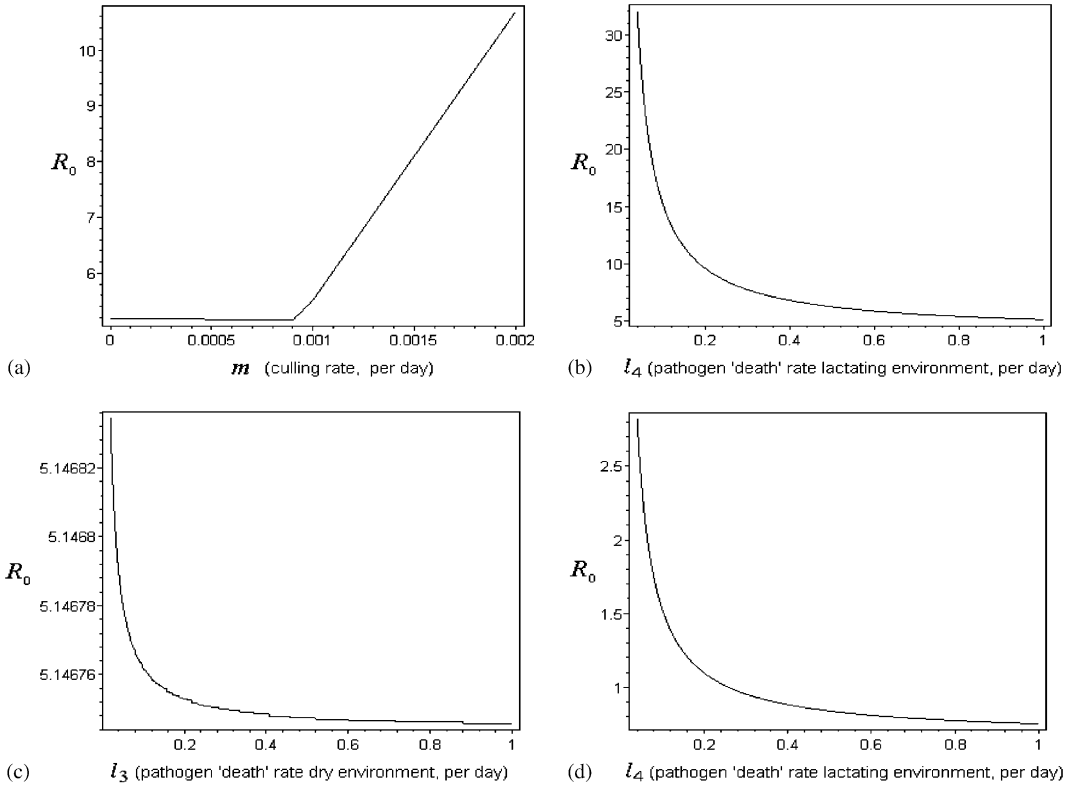

Fig. 3. Plots of R_0 for the model (2.5) with all routes of transmission. (a): R_0 plotted against m. (b): R_0 plotted against l_4. (c): R_0 plotted against l_3. (d): R_0 plotted against l_4 with small direct and indirect transmission rates ($\beta_i = 0.001$ (per day), $\eta_i = 1.0 \times 10^{-12}$ (per day), $i = 1, \ldots, 4$).

In addition, it is interesting to consider the effect of varying pathogen 'death' rates for the group-specific environments. Intuitively, the more frequently the animals' faeces are removed the fewer newly infected animals should appear, due to reduced indirect transmission via infectious bacteria in the environment. Firstly we consider the case of letting l_4 increase and other parameters l_j ($j \in \{1, 2, 3, c\}$) remain fixed. This is to reflect a situation in which the environment of the lactating animals is cleared of faeces frequently. In Fig. 3(b) we see that R_0 declines steeply as l_4 increases before levelling off at a value greater than 1. Next, we consider how other pathogen 'death' rates affect the basic reproduction ratio R_0. Extensive numerical studies show that increasing l_j ($j \in \{1, 2, 3, c\}$) has little effect on R_0. An example comes from Fig. 3(c) which shows quite slight variation in R_0 with l_3.

It follows from Figs. 2 and 3 that for the ranges of parameter values which we have considered the values of R_0 always lie above the line $R_0 = 1$, which is mostly due to the choice of transmission rates β_i and η_i (see Table 1). We therefore consider now the effect on the above numerical studies of choosing relatively low transmission rates. Here β_j ($j = 1, \ldots, 4$) is set at 0.001 (per day), and the indirect transmission rates are chosen as $\eta_j = 1.0 \times 10^{-12}$ (per day). We find the eigenvalues and R_0 (shown in Figs. 2 and 3) are lowered—lower transmission rates result in fewer newly infected animals due to reduced direct and indirect transmissions. For example, corresponding to Fig. 3(b), R_0 declines steeply and then levels out at a value below 1 with increasing l_4 (see Fig. 3(d)). This implies that for this set of parameter values, the condition $R_0 < 1$ can be satisfied by increasing l_4 only. Therefore, for this parameter set, we conclude that frequent and effective removal of animals faeces from the environment of the lactating group can make R_0 decline significantly, and hence effectively control the infection.

3.2. Variation in short term dynamics with epidemiological parameters

In this subsection we focus attention on the ability of a pathogen to invade a host population, addressing what happens in the short term immediately after the introduction of infection. Numerical simulations of the dynamical equations (2.5) show that persistence always follows invasion (as illustrated in Fig. 4). In the following simulations, we start from near the uninfected equilibrium and at time $t = 0$ introduce a single infective into the weaned group. In Fig. 4 prevalence of infection for each group is plotted against time (days). The capital letters U, W, D, L denote the unweaned, weaned, dry and lactating groups, respectively. With increasing

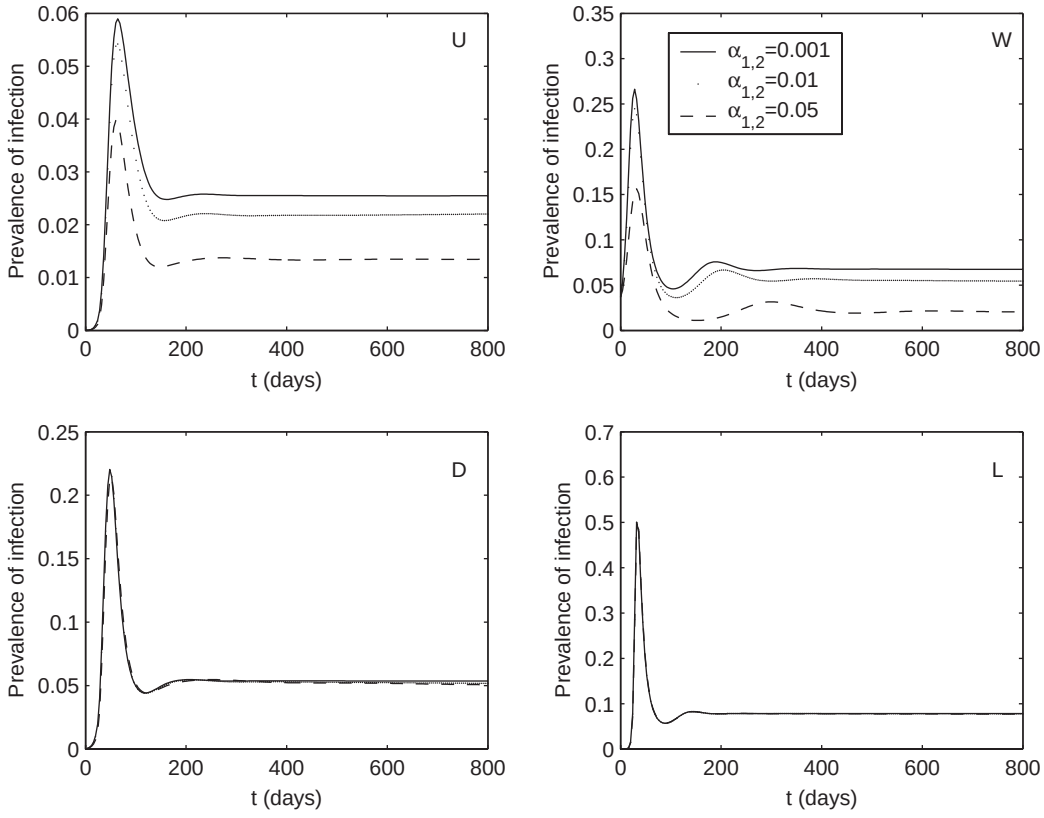

Fig. 4. The dynamic behaviour of the model equations (2.5) with varying levels of pathogen-induced mortality in the unweaned and weaned groups ($\alpha_1 = \alpha_2$).

pathogen-induced mortality in unweaned and weaned groups (keeping $\alpha_1 = \alpha_2$, $\alpha_3 = \alpha_4 = 0$), the different types of short-term model behaviour in each group are shown in Fig. 4. They all show that the pathogen can successfully invade the host population, since $R_0 > 1$. The initial epidemic peaks at about 30 days in the weaned group. It appears in other groups later than 30 days because of maturation and recruitment delays. For relatively small pathogen-induced mortality we can see a strong rapid peak in the epidemic, followed by a second peak (most noticeably in the weaned group) and a final endemic state. If pathogen induced mortality increases further we find the second epidemic in the weaned group is delayed. The higher the level of pathogen-induced mortality the lower the peak in the initial epidemic, the lower the endemic equilibrium, the more tendency to damped oscillation and the longer period between oscillations. Further, numerical simulation shows that the total population of the weaned group can reduce by up to 50% during the initial epidemic due to pathogen-induced mortality. We observe that the time at which the first epidemic peaks and the extent to which the weaned group population is reduced are significantly affected by the transmission rates and shedding rate. The population of the unweaned group goes up after the initial epidemic because the recruitment to this group increases following the decline in size of the lactating group. Thus although the number of infected individuals in the unweaned group increases after the initial epidemic for larger pathogen-induced mortality, there is no marked change in prevalence of infection, as shown in Fig. 4.

Fig. 5 shows changes in prevalence of infection in each group as the recovery rate γ_i $(i = 1, \ldots, 4)$ increases. (Similarly to the above, we keep all the γ_i equal to one another.) The disease rapidly approaches a stable equilibrium after initial fluctuation in the four groups for relatively small γ_i (as illustrated for $\gamma_i = 0.05$—infectious period of 20 days). For relatively large recovery rates γ_i and therefore shorter infectious periods, we see a rapid peak followed by decaying oscillations to the final endemic state. This implies that increasing recovery rate leads to decaying oscillations (most noticeably in the weaned group), as does increasing pathogen-induced mortality. Hence, we conclude that serotypes of shorter infectious period behave like more virulent serotypes.

Fig. 6 shows the effect of changing the pathogen loss/removal rates for the group-specific environments and the combined environment, with $l_1 = l_2 = l_3 = l_4 = l_c$. Naturally lower pathogen survival in the environment (e.g. due to differences between serotypes) or increased hygiene of equipment and personnel reduces the indirect transmission, and hence the number of infected

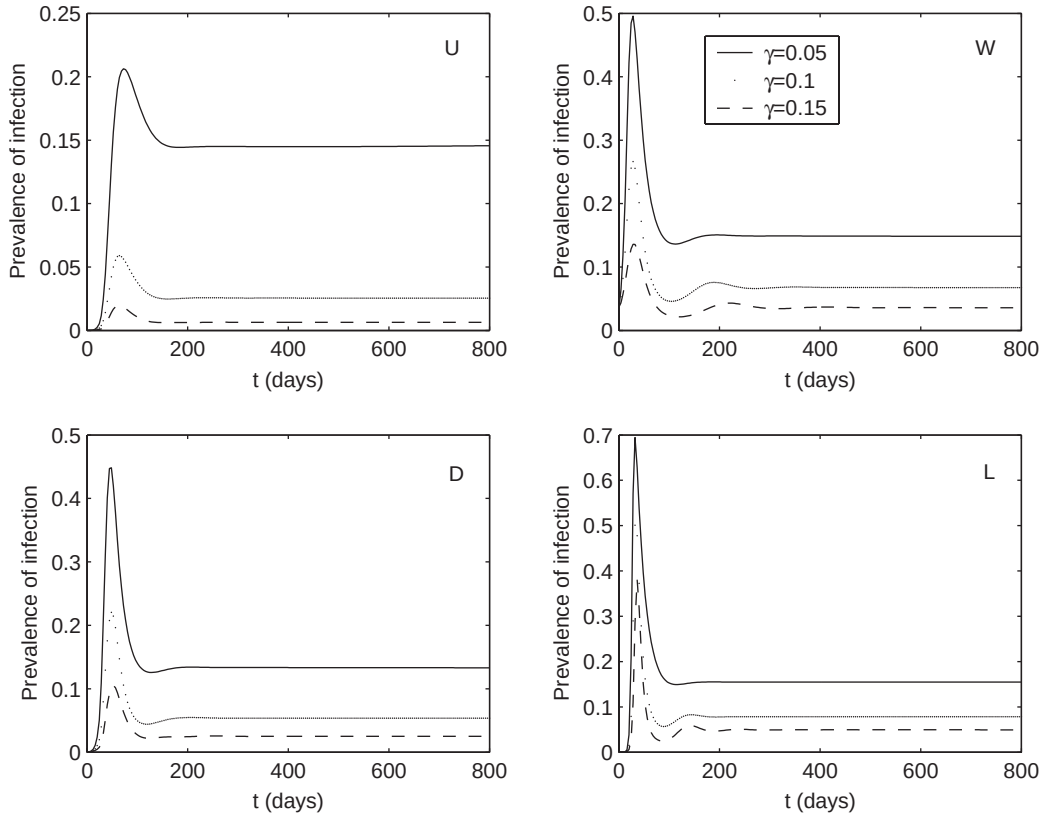

Fig. 5. The dynamic behaviour of the model equations (2.5) with varying levels of infectious period in each group ($1/\gamma_j$, $j = 1, \ldots, 4$).

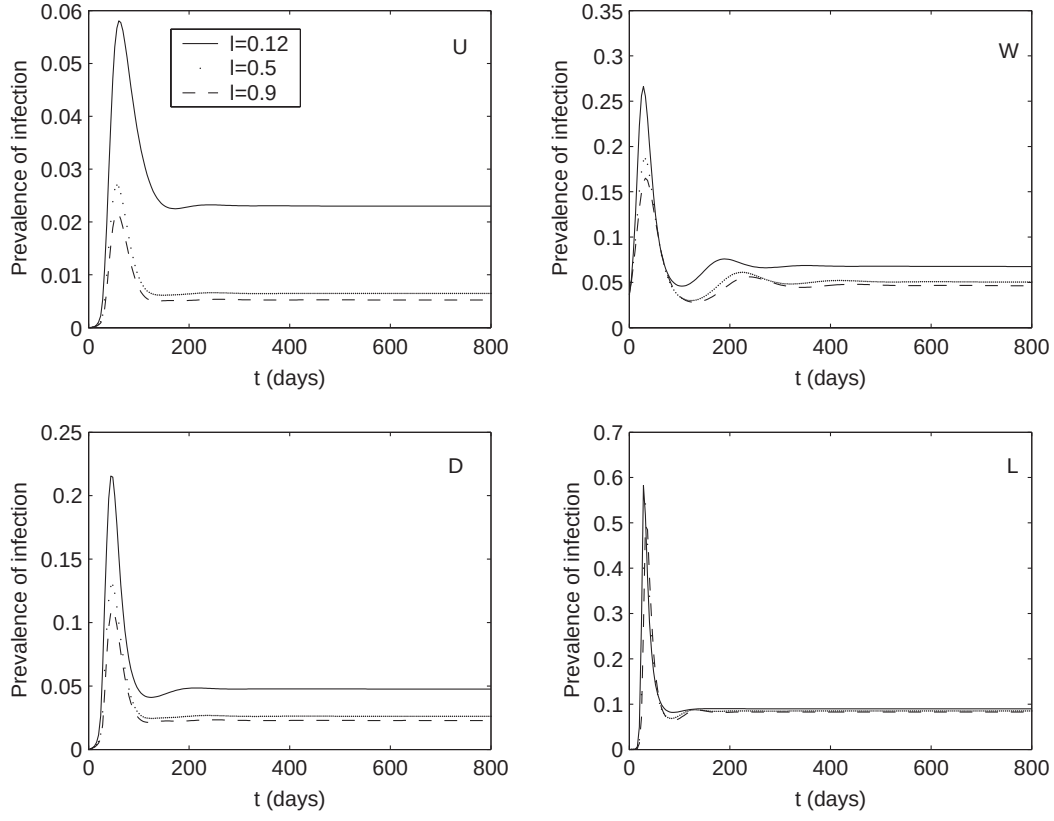

Fig. 6. The dynamic behaviour of the model equations (2.5) with varying levels of off-host pathogen survival in each group (l_j, $j \in \{1, \ldots, 4, c\}$).

individuals declines. In Fig. 6 we see that increasing these parameters reduces the endemic level and size of epidemic, and leads to longer periods between damped oscillations.

Recall that the next generation matrix H given by (2.7) does not involve the parameters r_i $(i = 1, \ldots, 4)$. Hence, R_0 is independent of the protective immunity-loss rates. However the dynamical behaviour of the system (2.5) is significantly influenced by them. The major effect of the loss of protective immunity is to contribute substantially to an increase in the numbers of susceptible individuals . In Fig. 7, we can see that as r_i $(i = 1, \ldots, 4)$ increase (with $r_1 = r_2 = r_3 = r_4$) there is a higher peak followed by decaying oscillation to a higher level endemic state. This implies that increasing immunity-loss rates strengthens disease infection and reduces damped oscillation. That is, a more persistent protective immune response results in lower prevalence of infection but a greater tendency for damped oscillation.

The work reported so far in this section involves introduction of an infected animal into the weaned group. Other introductions need to be studied. If we introduce an infected animal into the dry or lactating group we find similar shapes and possible oscillations of the epidemic. We observe the initial epidemic peaks earlier in the group in which the infected individual is introduced than other groups due to maturation or recruitment delay. If we introduce an infected individual into the unweaned group, we see that the prevalence of infection in the unweaned group decreases first and then the initial epidemic occurs; the dynamics in the other three groups is as before.

4. Managing the population structure through culling or recruitment in the lactating group

Model (2.5) has invariably assumed that culling actions occur no matter what the lactating herd size is, and more young animals are recruited to the unweaned group when the lactating group is low or suffers from high culling. Numerical simulations for model (2.5) show us that the total population of the lactating group can decrease for a period of time if pathogen-induced mortality is high. Even allowing a varying recruitment rate parameter $b(m)$ as described above cannot prevent the lactating group size from declining initially under higher culling. This would directly affect milk production and is therefore undesirable, particularly as it takes some time for the lactating group to return back to its original level, due to maturation delays. However, it is usually the case that dairy farmers keep the lactating group at least approximately constant or within a small

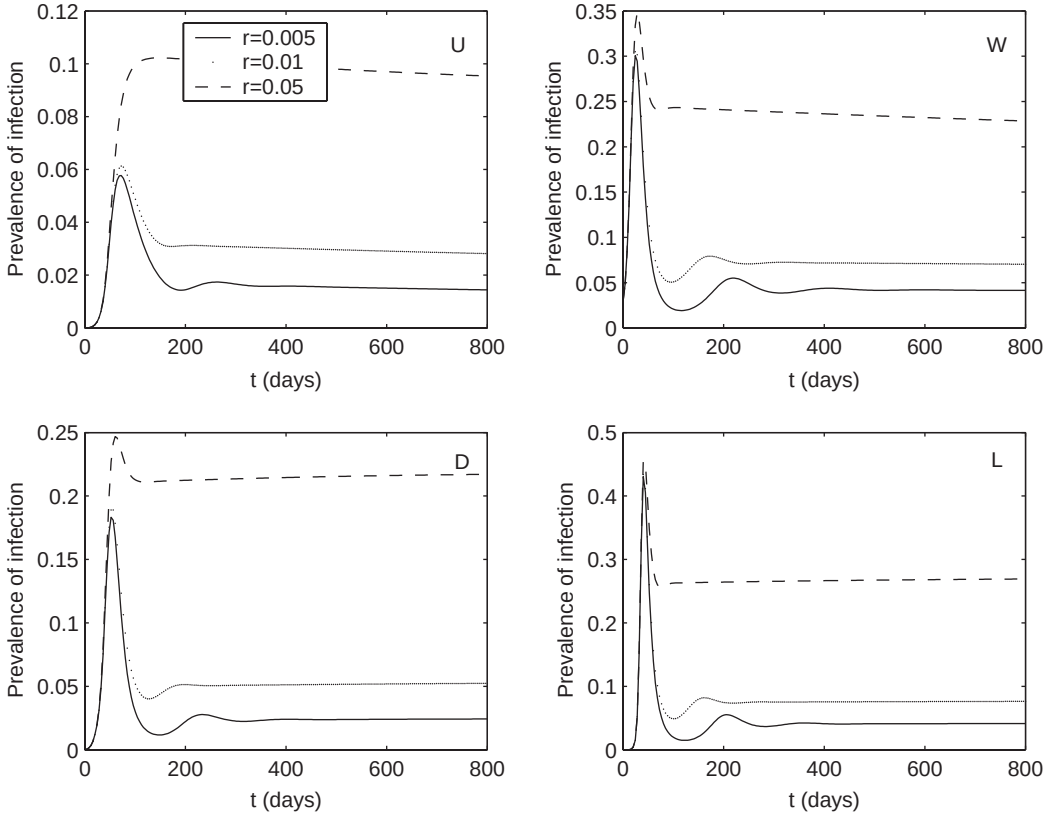

Fig. 7. The dynamic behaviour of the model equations (2.5) with varying rate of loss of protective immunity in each group (r_j, $j = 1, \ldots, 4$).

interval (e.g. to fill milk quotas) by buying, recruitment and/or culling within this group. Which action one chooses depends on the existing size of the lactating group. In particular, one combines recruitment of calves with culling in the lactating group unless the total population of this latter group reaches a critical lower level, when the option of buying directly into this group would be considered (e.g. through buying newly calved animals). A switching system as described below provides a natural description of such a mechanism.

In this section, we assume the recruitment function $B(N_3, N_4)$ depends linearly on the population N_3 of the dry group, $B(N_3, N_4) = bN_3$. We note that basic culling is still going on at a rate such that, in the absence of other effects, each animal will spend a total of around 5 years in the lactating group before being culled. We suppose that there is a desired level L_m of the lactating group size. Whenever the total population N_4 of the lactating group is lower than ξL_m $(0<\xi\leqslant 1)$, new animals are instantaneously bought into the susceptible compartment of the lactating group at rate $m_a N_4(L_m - N_4)$; otherwise animals are culled. These culled animals are chosen from the herd randomly with respect to infection status: susceptible animals in the lactating group are culled at total rate $mS_4 + m_a S_4(N_4 - L_m)$, infected animals at rate $mI_4 + m_a I_4(N_4 - L_m)$ and immune animals at rate $mR_4 + m_a R_4(N_4 - L_m)$. The system therefore evolves according to

$$\begin{cases} \dot{S}_j = G_j^S - L_j^S - \Gamma_j^I - \delta_{j4}[\delta(t)m_a S_j(N_j - L_m) \\ \qquad +(1-\delta(t))m_a N_j(N_j - L_m)], \\ \dot{I}_j = G_j^I - L_j^I + \Gamma_j^I - \delta_{j4}\delta(t)m_a I_j(N_j - L_m), \\ \dot{R}_j = G_j^R - L_j^R - \delta_{j4}\delta(t)m_a R_j(N_j - L_m), \\ \dot{W}_j = G_j^W - L_j^W - \mathscr{C}_j^W, \\ \dot{W}_c = G_c^W - L_c^W - \mathscr{C}_c^W, \end{cases} \tag{4.1}$$

where $j = 1, \ldots, 4$ and

$$\delta(t) = \begin{cases} 1 & \text{for } N_4 > \xi L_m, \\ 0 & \text{for } N_4 \leqslant \xi L_m. \end{cases} \tag{4.2}$$

G_A^B and L_A^B denote the rates of gain and loss (other than by transmission, or, in the lactating group, by buying in or by culling above the basic rate) for animals or infectious bacteria of the compartment B in group or environment A. Γ_j^I, $\mathscr{C}_j^W$ and $\mathscr{C}_c^W$ have the same definitions as in system (2.5). For details of these rates, see Appendix A.5. We note that buying in exactly balances culling in the lactating group when N_4 drops to ξL_m; that is, $d_4 + m + m_a(N_4 - L_m) = 0$ for $N_4 = \xi L_m$. Hence the additional culling (or buying) rate m_a should be chosen such that $m_a = (d_4 + m)/((1-\xi)L_m)$.

The infection-free equilibrium, denoted $(\hat{N}_1, \hat{N}_2, \hat{N}_3, \hat{N}_4)$, is feasible if inequality (A.5.3) holds true (see details in Appendix A.5). By using similar methods to those in Section 2, we can compute the basic reproduction ratio for the system with buying (denoted by R_{0b}) and for the system with culling (denoted by R_{0c}). Note that the size of the lactating group in disease-free equilibrium ($\hat{N}_4$) can be either greater than L_m or less than L_m. Parameter values used here ($L_m = 100$, $\xi = 0.98$, which implies $m_a = 0.00027$, and other parameter values as before) are such that $\hat{N}_4$ is greater than L_m (i.e., inequality (A.5.4) is satisfied). As before we introduce an infected individual into the weaned group and start from near the uninfected equilibrium. Numerical simulations show that solutions initiating near to the uninfected equilibrium immediately stabilize into a level above the switching point ($N_4 = \xi L_m = 98$). This means that the system with culling does not switch into the system with buying, for these parameter values. This is because the whole system has a stable endemic equilibrium (since $R_{0c} > 1$) in which the total population of the lactating group (with a level of $N_4 = 102.5$) is greater than the switching point.

Investigating what happens in the short-term immediately after introduction of an infected individual into the weaned group, we observe similar short-term dynamics to those obtained for system (2.5) with varying epidemiological factors. For example, as pathogen-induced mortality α_1 and α_2 increase ($\alpha_1 = \alpha_2$, $\alpha_3 = \alpha_4 = 0$), we observe similar results to those shown in Fig. 4. That is, higher pathogen-induced mortality results in a smaller epidemic but a greater tendency to damped oscillation. The first epidemic in the weaned group appears at about 30 days and the total population of this group reduces by up to fifty percent during the first epidemic due to larger pathogen-induced mortality. In this scenario, the system with culling only applies; there is never a switch to the system with buying. The important difference from system (2.5) is that the population of the lactating group shows no marked decrease (actually stabilizing at 102.5 from 109).

5. Conclusions and discussion

We have derived thresholds for pathogen invasion in differential equation models which describe the transmission of infectious organisms both directly and indirectly, via free-living bacteria, in a multi-group managed herd. We note that, for simplicity, the only indirect transmission route which we consider is via free-living bacteria, although wildlife (e.g., farm cats and wild birds) is also found to be a factor in the dissemination of *Salmonellae* (Evans and Davies, 1996). The models developed here provide a mathematical framework for our understanding of *Salmonella* infections in dairy herds, and could easily be adapted to other pathogens in other livestock systems. This understanding may help in identifying possible strategies for disease control, and assessing their possible results.

Compared to the work by Turner et al. (2003), a novelty of the work is the inclusion—vital for *Salmonella*, but not evident in their work on other food borne pathogens—of two new factors: pathogen-induced mortality and acquired immunity. These allow qualitatively different dynamical patterns. It is in differences in these and other parameters that we seek to understand the variation in the behaviour of outbreaks between *Salmonella* serotypes (and the study of serological variation is also not considered in Turner et al. (2003)).

The basic reproduction number R_0, the spectral radius of the next generation matrix, is often used to assess the effect of various control strategies on the persistence of infection. It is interesting to consider strategies which reduce R_0 below 1, because these are successful at eliminating disease in a deterministic setting. As we show above, R_0 is influenced by the uninfected equilibrium and by epidemiological factors. Variation in R_0 with demographic and epidemiological parameters is investigated, and our conclusions suggest possible strategies for disease control. We note that demographically we only varied the culling rate m (consequently $b(m)$ is varying) and assumed that natural death rate d_i and maturation (flow) rate c_i ($i = 1, \ldots, 4$) are constant. However, these latter quantities embody information about the mean time of conception postpartum, lactation length, etc. and consequently it is interesting to know whether or not varying d_i and c_i affects the model results. Clearly, varying d_i and c_i changes the uninfected equilibrium $(\bar{N}_1, \bar{N}_2, \bar{N}_3, \bar{N}_4)$, but numerical studies show that it remains locally stable if it is feasible (i.e., (A.1.1) holds true). It follows from the definition of R_0 that the value of R_0 would consequently vary with varying d_i and c_i. However, numerical studies show that the shapes of all the figures do not change indicating unchanged qualitative epidemic behaviour. Therefore, variation in d_i and c_i ($i = 1, \ldots, 4$) has little effect on the main results.

Faster recovery or increased pathogen-induced mortality (Fig. 2(a) and (b)) result in infected individuals remaining infected for a shorter period, and hence the number of newly infected animals produced by an infected animal in its life time declines. The basic reproduction number R_0 is consequently decreased. Numerical study shows that pseudovertical transmission has little influence on invasion criteria although it can lead to more groups being affected (Fig. 2(d)). Thus measures aimed at reducing pseudovertical transmission are unlikely to have a major effect on invasion and persistence. Indirect transmission via the group-specific environments, however, has a major influence on R_0 because it is likely to be an important cause of new infections (Fig. 3(a)).

Measures that increase the 'death' rate of the pathogen, and which consequently reduce indirect transmission, are likely to result in a substantial reduction in R_0 (Fig. 3(b)). In particular, the pathogen 'death' rates in the group specific environments are found to play differing roles in reducing R_0 (Fig. 3(b) and (c)). l_4 is the most sensitive parameter and increasing it can reduce R_0 significantly, while others ($l_j, j \in \{1, 2, 3, c\}$) are not as important. Consequently, measures aimed at reducing indirect transmission should be concentrated on the lactating group environment rather than all the environments. In fact, there are various intervention strategies (e.g., reducing the shedding rates of animals by vaccination and competitive exclusion) which aim to minimize the number of infectious bacteria in the environment. Competitive exclusion, in particular, has been used successfully to reduce infection and shedding of *Salmonella* Spp. (Rantala and Nurmi, 1973) and *Campylobacter jejuni* (Schoeni and Doyle, 1992) in poultry, although this would not be directly applicable to adult cattle.

Another focus of this paper is on what happens in the short term immediately after an infected individual is introduced into the host population (Figs. 4–7). We observe how variation in parameters affects the time at which the first epidemic peaks, and the extent to which the weaned group population is reduced during the first epidemic. When the pathogen-induced mortality is increased, higher direct transmission rate, indirect transmission rate or shedding rate lead to significant reduction in the weaned group population during the initial epidemic. Increasing pseudovertical transmission rate, however, does not lead to reduction. This is in line with the fact that pseudovertical transmission has little influence on persistence. Recovery rate, pathogen-induced mortality, immune response and pathogen removal rate are found to be factors inducing damped oscillations. In particular, higher pathogen-induced mortality, shorter infectious period, stronger persistent immune responses and more frequent removal of faeces from the environment result in lower prevalence of infection and epidemic size but a greater tendency for damped oscillations. 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. Plym-Forshell and Ekesbo, 1996; Himathongkham et al., 1999; Taylor and Burrows, 1971; Wray and Callow, 1974) none have provided quantifiable and consistent comparisons between serotypes. However, it follows from Figs. 4–7 that prevalence of infection in the lactating group is higher than that in other groups. This qualitatively agrees with the result found by Huston et al. (2002b) that prevalence of fecal *Salmonella* shedding

in mature cows was higher than that in calves at individual sample collection times.

When the system is perturbed by higher culling rate or pathogen-induced mortality, we incorporate the feature that the lactating herd size is constrained to have no marked change. Firstly, a varying recruitment rate parameter $b(m)$ is used to describe the management through recruitment of young animals to the unweaned group of a system perturbed by culling. This, in particular, aims to keep the lactating herd size constant in the absence of pathogen. Fig. 2(c) shows that a relatively large culling rate makes pathogen invasion of the herd more likely. In addition, even in the closed farming system the dominating group changes from the dry/lactating cycle to the weaned group as the culling rate is increased. We further propose a switching system to describe management of the system through culling and/or recruitment within the lactating group. The model was formulated to ensure that the lactating group size is maintained within a small interval. When introducing an infected individual into the weaned group we observe similar short-term dynamics to those obtained for the system (2.5) when varying epidemiological factors. The only difference between these two kinds of systems is that in the switching system the population of the lactating group does not exhibit marked changes in size even when pathogen-induced mortality is relatively large.

In general, this work has explored the long-term dynamics of infections in populations and identified the key processes and parameters that explain differences in observed epidemiological patterns by investigating the effects of culling rate and a number of epidemiological parameters on the basic reproduction number R_0 and the short-term dynamical behaviour of these pathogens. This modelling approach provided a framework for using the contrasting epidemiology of *Salmonella* serotypes to gain insight into the main driving forces behind the dynamics of endemic and epidemic strains. Thus 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. Issues which need further study include the role of seasonally varying parameters which may be related to the evidence, mentioned in the introduction, that clinical episodes and shedding of *S. typhimurium* DT104 recur periodically (Hollinger et al., 1998; Davies, 1997), and which unavoidably cause cyclicity. Heterogeneity between individual hosts (e.g., immune response and shedding (Huston et al., 2002b; Edrington et al., 2004; Richardson, 1975)) will need further investigation. Furthermore, in order to represent random variation within the system, the deterministic models will need to be extended to stochastic models. While rather less tractable, stochastic models can be used to examine features not well described by deterministic models.

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Appendix A

A.1. Local stability of the model equations (2.1)

The stability of the four-dimensional system (2.1) can be evaluated using Routh-Hurwitz criteria. The characteristic polynomial of the Jacobian matrix for system (2.1) is

$$\lambda^4 + q_1\lambda^3 + q_2\lambda^2 + q_3\lambda + q_4 = 0,$$

where

$$\begin{aligned}
q_1 &= \sum_{j=1}^{4}(d_j + c_j),\\
q_2 &= (d_4 + c_4)(d_1 + c_1 + d_2 + c_2 + d_4 + c_4)\\
&\quad + ((d_1 + c_1)(d_2 + c_2 + d_3 + c_3)\\
&\quad + (d_2 + c_2)(d_3 + c_3)) - c_3c_4,\\
q_3 &= (d_4 + c_4)((d_1 + c_1)(d_2 + c_2 + d_3 + c_3)\\
&\quad + (d_2 + c_2)(d_3 + c_3))\\
&\quad + \prod_{j=1}^{3}(d_j + c_j) - \frac{bc_1c_2(d_1 + c_1)\bar{N}_1}{\bar{N}_3}\\
&\quad - c_3c_4(d_1 + c_1 + d_2 + c_2),\\
q_4 &= (d_4 + c_4)\left(\prod_{j=1}^{3}(d_j + c_j) - \frac{bc_1c_2(d_1 + c_1)\bar{N}_1}{\bar{N}_3}\right)\\
&\quad - c_3c_4(d_1 + c_1)(d_2 + c_2) + \frac{bc_1c_2c_3\bar{N}_3}{K}.
\end{aligned}$$

The criteria for stability are

$$\begin{aligned}
&q_1 > 0, \quad q_4 > 0, \quad q_1q_2 > q_3,\\
&q_1q_2q_3 > q_3^2 + q_1^2q_4.
\end{aligned} \tag{A.1.1}$$

A.2. Rates of gain, loss and transmission in model (2.5)

All variables, parameters and symbols are defined in Table 1 and in the text. The rates of gain and loss

appearing in model (2.5) are

$$
\begin{aligned}
G_j^S &= \delta_{j1}\left[b(S_3+R_3)\left(1-\frac{N_4}{K}\right)+(1-\rho)bI_3\left(1-\frac{N_4}{K}\right)\right]\\
&\quad+\delta_{j2}c_1S_1+\delta_{j3}c_2S_2+\delta_{j4}c_3S_3+\delta_{j3}c_4S_4+r_jR_j,\\
L_j^S &= (d_j+c_j\delta_{j1}+c_j\delta_{j2}+c_j\delta_{j3}+(c_j+m)\delta_{j4})S_j,\\
G_j^I &= \delta_{j1}\rho bI_3\left(1-\frac{N_4}{K}\right)+\delta_{j2}c_1I_1+\delta_{j3}c_2I_2\\
&\quad+\delta_{j4}c_3I_3+\delta_{j3}c_4I_4,\\
L_j^I &= (d_j+\alpha_j+c_j\delta_{j1}+c_j\delta_{j2}+c_j\delta_{j3}\\
&\quad+(c_j+m)\delta_{j4}+\gamma_j)I_j,\\
G_j^R &= \gamma_jI_j+\delta_{j2}c_1I_1+\delta_{j3}c_2I_2+\delta_{j4}c_3I_3+\delta_{j3}c_4I_4,\\
L_j^R &= (d_j+c_j\delta_{j1}+c_j\delta_{j2}+c_j\delta_{j3}+(c_j+m)\delta_{j4}+r_j)R_j,\\
G_j^W &= \lambda_jI_j,\quad L_j^W=(p_j+l_j)W_j,\\
G_c^W &= \sum_{j=1}^{4}(p_jW_j),\quad L_c^W=l_cW_c,
\end{aligned}
\tag{A.2.1}
$$

where

$$
\delta_{ij}=\begin{cases}1 & \text{if } i=j,\\ 0 & \text{if } i\neq j.\end{cases}
\tag{A.2.2}
$$

A.3. Matrices contributing to the next generation matrix H

See Table 1 for definitions. Let $D_i=d_i+\alpha_i+\gamma_i+c_i$, $i=1,\ldots,4$. Then we get

$$
F_1=\begin{pmatrix}\beta_1S_{10}&0&0&0\\0&\beta_2S_{20}&0&0\\0&0&\beta_3S_{30}&0\\0&0&0&\beta_4S_{40}\end{pmatrix},
$$

$$
F_2=\begin{pmatrix}0&0&\rho b(1-\frac{S_{40}}{K})&0\\0&0&0&0\\0&0&0&0\\0&0&0&0\end{pmatrix},
$$

$$
F_3=\begin{pmatrix}\eta_1S_{10}&0&0&0&\eta_1\delta_1S_{10}\\0&\eta_2S_{20}&0&0&\eta_2\delta_2S_{20}\\0&0&\eta_3S_{30}&0&\eta_3\delta_3S_{30}\\0&0&0&\eta_4S_{40}&\eta_4\delta_4S_{20}\end{pmatrix},
$$

$$
V=\begin{pmatrix}D_1&0&0&0\\-c_1&D_2&0&0\\0&-c_2&D_3&-c_4\\0&0&-c_3&D_4+m\end{pmatrix}.
$$

So the matrix F_1V^{-1} (F_2V^{-1}) gives the next generation matrix for the model (2.5) with direct transmission (pseudovertical transmission) only. For indirect transmission, we have

$$
\Lambda=\begin{pmatrix}\lambda_1&0&0&0\\0&\lambda_2&0&0\\0&0&\lambda_3&0\\0&0&0&\lambda_4\\0&0&0&0\end{pmatrix},
$$

$$
Q=\begin{pmatrix}l_{11}&0&0&0&0\\0&l_{22}&0&0&0\\0&0&l_{33}&0&0\\0&0&0&l_{44}&0\\-p_1&-p_2&-p_3&-p_4&l_c+\sum_{i=1}^{4}\eta_i\delta_iS_{i0}\end{pmatrix},
$$

where $l_{ii}=l_i+p_i+\eta_iS_{i0}$, $i=1,\ldots,4$. So the matrix $F_3Q^{-1}\Lambda V^{-1}$ gives the next generation matrix for the model (2.5) with indirect transmission only.

A.4. Variation in the uninfected equilibrium with culling rate m

Case I. Recruitment rate parameter is a constant b.

As the culling rate m increases, it follows from (2.4) that the disease-free equilibrium level of the lactating group always decreases as

$$
\frac{\partial S_{40}}{\partial m}=-\frac{Kc_3c_4(d_1+c_1)(d_2+c_2)}{bc_1c_2(d_4+m+c_4)^2}<0.
\tag{A.4.1}
$$

Further, we have

$$
\frac{\partial S_{30}}{\partial m}=\frac{K}{bc_3}\left[b-\frac{(d_1+c_1)(d_2+c_2)(d_3+c_3)}{c_1c_2}\right],
$$

so increasing culling rate may increase or decrease the disease-free equilibrium level of the dry group, depending upon the parameter values.

Case II. Recruitment rate parameter is a function $b(m)$ of the culling rate m

Let $\bar{S}_{40}$ be the required disease-free equilibrium level of the lactating herd size. It follows from (2.4) that

$$
\begin{aligned}
b(m)&=\frac{K(d_1+c_1)(d_2+c_2)}{c_1c_2(K-\bar{S}_{40})}\\
&\quad\times\left(d_3+c_3-\frac{c_3c_4}{d_4+m+c_4}\right),
\end{aligned}
\tag{A.4.2}
$$

and

$$\bar{S}_{10}(m)=\frac{\bar{S}_{40}(d_2+c_2)}{c_1c_2c_3}\left((d_3+c_3)(d_4+m+c_4)-c_3c_4\right),$$
$$\bar{S}_{20}(m)=\frac{\bar{S}_{40}}{c_2c_3}\left((d_3+c_3)(d_4+m+c_4)-c_3c_4\right),$$
$$\bar{S}_{30}(m)=\frac{\bar{S}_{40}}{c_3}(d_4+m+c_4).$$

A.5. Rates of gain, loss and transmission in model (4.1)

The rates of gain and loss appearing in model (4.1) are

$$\begin{aligned}
G_j^S &= \delta_{j1}[bS_3+(1-\rho)bI_3]\\
&\quad+\delta_{j2}c_1S_1+\delta_{j3}c_2S_2+\delta_{j4}c_3S_3+\delta_{j3}c_4S_4+r_jR_j,\\
L_j^S &= (d_j+c_j\delta_{j1}+c_j\delta_{j2}+c_j\delta_{j3}+c_j\delta_{j4}+m\delta_{j4})S_j,\\
G_j^I &= \delta_{j1}\rho bI_3+\delta_{j2}c_1I_1+\delta_{j3}c_2I_2+\delta_{j4}c_3I_3+\delta_{j3}c_4I_4,\\
L_j^I &= (d_j+\alpha_j+c_j\delta_{j1}+c_j\delta_{j2}+c_j\delta_{j3}\\
&\quad+c_j\delta_{j4}+m\delta_{j4}+\gamma_j)I_j,\\
G_j^R &= \gamma_jI_j+\delta_{j2}c_1I_1+\delta_{j3}c_2I_2+\delta_{j4}c_3I_3+\delta_{j3}c_4I_4,\\
L_j^R &= (d_j+c_j\delta_{j1}+c_j\delta_{j2}+c_j\delta_{j3}+c_j\delta_{j4}+m\delta_{j4}+r_j)R_j,\\
G_j^W &= \lambda_jI_j,\quad L_j^W=(p_j+l_j)W_j,\\
G_c^W &= \sum_{j=1}^{4}(p_jW_j),\quad L_c^W=l_cW_c
\end{aligned}\tag{A.5.1}$$

and the rates of transmission and consumption are as given by Eq. (2.6).

In the absence of disease, the switching system (4.1) reduces to the following:

$$\begin{cases}
\dot{N}_1(t)=bN_3-(d_1+c_1)N_1,\\
\dot{N}_2(t)=c_1N_1-(d_2+c_2)N_2,\\
\dot{N}_3(t)=c_2N_2-(d_3+c_3)N_3+c_4N_4,\\
\dot{N}_4(t)=c_3N_3-(d_4+m+c_4)N_4\\
\qquad -m_aN_4(N_4-L_m).
\end{cases}\tag{A.5.2}$$

It is easy to show that if

$$d_4+m+c_4<m_aL_m+\frac{c_3c_4(d_1+c_1)(d_2+c_2)}{(d_1+c_1)(d_2+c_2)(d_3+c_3)-bc_1c_2},\tag{A.5.3}$$

then system (A.5.2) has a positive equilibrium $(\hat{N}_1,\hat{N}_2,\hat{N}_3,\hat{N}_4)$, where

$$\hat{N}_1=\frac{b\hat{N}_3}{d_1+c_1},\quad \hat{N}_2=\frac{c_1\hat{N}_1}{d_2+c_2},$$
$$\hat{N}_3=\frac{c_4(d_1+c_1)(d_2+c_2)\hat{N}_4}{(d_1+c_1)(d_2+c_2)(d_3+c_3)-bc_1c_2},$$
$$\hat{N}_4=\frac{1}{m_a}\left[-(d_4+m+c_4)+m_aL_m+\frac{c_3c_4(d_1+c_1)(d_2+c_2)}{(d_1+c_1)(d_2+c_2)(d_3+c_3)-bc_1c_2}\right].$$

Clearly, we have $\hat{N}_4\geqslant L_m$ if

$$d_4+m+c_4\leqslant\frac{c_3c_4(d_1+c_1)(d_2+c_2)}{(d_1+c_1)(d_2+c_2)(d_3+c_3)-bc_1c_2},\tag{A.5.4}$$

and $\hat{N}_4<L_m$ if the inequality (A.5.4) is reserved.

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