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A model appropriate to the transmission of a human food-borne pathogen in a multigroup managed herd

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Abstract

We describe a model of microparasite transmission within a multigroup managed farming system. The model was formulated to represent transmission of *Escherichia coli* O157 within a typical UK dairy herd and was used to suggest possible on-farm control strategies. The model includes birth, death, maturation, the dry/lactating cycle and various types of transmission (i.e. direct, pseudovertical (representing direct faecal–oral transmission between dam and calf within the first 48 h) and indirect (via free-living infectious units in the environment)). A combination of numerical and analytical techniques was used to analyse the model. We found that pseudovertical transmission and indirect transmission via infectious units in the 'general' environment can lead to more groups being affected, but otherwise have relatively little effect on the invasion criteria. To reduce infection within the herd, we suggest that efforts be directed at reducing the opportunity for group-specific indirect transmission—particularly within the weaned group.

Keywords: Mathematical model; Transmission; Infection; Food-borne pathogen; Herd; *Escherichia coli* O157

1. Introduction

The past 20 years have seen an increase in the incidence of food-borne infections and the emergence of new food-borne pathogens such as *Escherichia coli* O157:H7 (now

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responsible for approximately 4500 reported cases per year in the US (CDC, 2001) and approximately 1500 per year in the UK (Subcommittee of the PHLS Advisory Committee on Gastrointestinal Infections, 2000; MAFF, 1999)). Efforts have been made to improve practices within slaughterhouses and food processing plants to reduce the risk to humans. However, the feasibility and role of reducing infection in animals on the farms of origin must be assessed for preventing contamination further down the food chain.

In Britain, most cases of food-borne illness are caused by *Campylobacter. Salmonella* and *E. coli* O157 infections are rarer, but the severe complications (e.g. haemolytic-uraemic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP)) associated with *E. coli* O157 have prompted much work on ways to reduce the levels of all food-borne pathogens within the food chain. Many of the organisms are found in domestic and wild animals and in the environment (Porter et al., 1997; Shere et al., 1998; Hancock et al., 1998). It seems unlikely that these organisms could ever be eradicated permanently from commercial herds (and from our food supply). However, the model we have developed suggests ways of controlling the spread of infection within these herds and reducing the prevalence of infection within the food-producing groups (especially the lactating group).

We chose the dairy system because milk and milk products are sources of *E. coli* O157 (Chapman, 1993, 2000; Chapman et al., 1993; Morgan et al., 1993; Upton and Coia, 1994). Also, there have been several outbreaks attributed to the consumption of dairy produce (PHLS Communicable Disease Surveillance Centre, 1998a,b, 1999; Willshaw et al., 2001; Parry and Palmer, 2000; Mechie et al., 1997).

2. General model and results

In a typical dairy herd there are multiple groups of animals (e.g. unweaned, weaned, bulling heifers, in-calf heifers, dry and lactating cows). For an organism such as *E. coli* O157 (which can survive for long periods outside the host), the combination of these groups and the multiple environments containing free-living infectious units (equivalent to free-living infective stages (Anderson and May, 1981)) results in many possible routes of transmission. Our model contains four groups (unweaned, weaned, dry and lactating) and five environments (one specific to each group and one general one). The model incorporates direct host-to-host transmission, which here constitutes direct faecal–oral or oral–oral transmission between two animals. The model also includes transmission via infectious units. In the case of *E. coli* O157 in cattle, this represents indirect faecal–oral transmission that can occur when cattle ingest bacteria present on contaminated equipment, such as feed and water troughs, walls, floors and the contaminated hides of other animals. Pseudovertical transmission (representing direct faecal–oral transmission between dam and calf) is also featured in the model. Although calves in UK dairy herds are generally removed from the dam within 48 h, various studies have observed infection within unweaned groups (Mechie et al., 1997; Paiba, personal communication).

In this model, direct transmission is described using a density-dependent transmission term with constant area (Begon et al., 2002; McCallum et al., 2001). However, we also

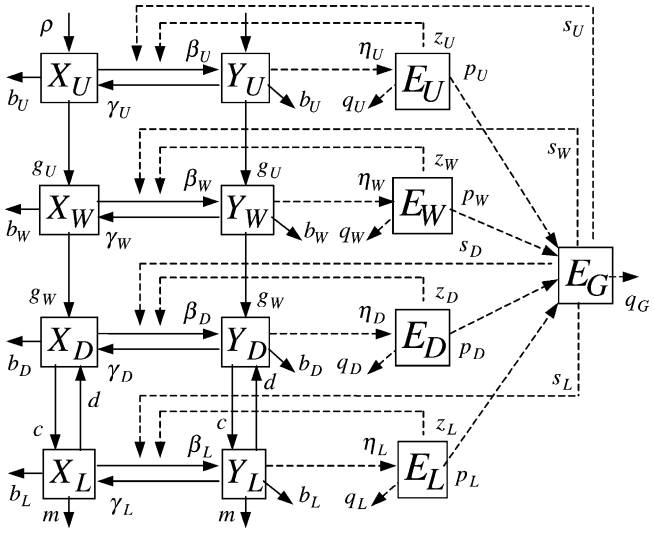

Fig. 1. Flow diagram showing the transmission routes and other processes described by the model given in Eq. (1). The model is designed to represent the transmission of a human food-borne pathogen within a typical UK dairy herd. The solid lines show the movement of animals. The dotted lines show the movement of infectious units and their contribution to transmission.

examined the corresponding model with a frequency-dependent term. In both the cases, the disease-free equilibrium is not affected by the disease dynamics. The total number of individuals in each group remains constant (at the disease-free equilibrium value) even when the population becomes infected. Under these circumstances, the two transmission terms are equivalent and differ only by a constant which scales the transmission parameter. For brevity, and because the results are similar, we only present the density-dependent model.

An animal starts its life in the unweaned group (denoted by subscript 'U'), matures into the weaned group (subscript 'W') and then matures again into the dry group (subscript 'D') (Fig. 1). From here it enters the dry/lactating cycle. For simplicity, all pregnant non-lactating animals in the last 2 months of pregnancy are classified as 'dry'. Individuals are classed as either susceptible (X) or infected (Y). Infected individuals shed the pathogen into their immediate environment (for example, in faeces) and are therefore a source of infection. In this model, the term 'infected' denotes that the pathogen is present, amplified within, and shed by the host. For simplicity, the rate at which the pathogen is shed by an infected animal is assumed to be the same for all infected animals within that group. At the end of the infectious period, infected animals become susceptible once more. We assumed that infection does not confer immunity because multiple re-infections with *E. coli* O157 have been observed in field (e.g. Mechie et al., 1997; Shere et al., 1998) and experimental studies (e.g. Johnson et al., 1996; Sanderson et al., 1999).

The 'general' environment poses a risk to all groups of animals. (It could represent personnel, equipment or vehicles that routinely move about the farm on a daily basis.) If precautions are taken to protect unweaned animals from external sources of infection, the

Table 1
Definitions of the variables used in the model for the transmission of a human food-borne pathogen in a multigroup managed herd

Variable	Definition
X	Number of susceptible animals
Y	Number of infected (and infectious) animals
E	Number of infectious units[a] in group-specific environment
E_G	Number of infectious units[a] in general environment

[a] Each infectious unit consists of 100 CFU (i.e. an infectious dose).

model can be modified to reflect that unweaned individuals are only at risk from infected animals within their own group and infectious units within their own environment. If the general environment were taken to represent slurry, then only grazing animals would be at risk (e.g. dry and lactating animals), and only during the summer months. To incorporate this seasonal risk, the model would have to be reformulated with a temporal discontinuity.

The variables of the model are defined in Table 1 and the parameters are defined in Table 2. Other symbols are defined in the text, close to the text to which they apply. The flow diagram (Fig. 1) describing the processes of the model is formalised as the dynamic equations:

$$\begin{aligned}
&\text{Susceptible}: \quad \frac{dX_i}{dt} = \Omega_i^X - \Gamma_i^X - \Psi_i^Y,\\
&\text{infected}: \quad \frac{dY_i}{dt} = \Omega_i^Y - \Gamma_i^Y + \Psi_i^Y,\\
&\text{environment (group-specific)}: \quad \frac{dE_i}{dt} = \Omega_i^E - \Gamma_i^E - \Phi_i^E,\\
&\text{environment (general)}: \quad \frac{dE_G}{dt} = \Omega_G^E - \Gamma_G^E - \Phi_G^E
\end{aligned} \tag{1}$$

where $i \in \{U, W, D, L\}$ and Ω_B^A and Γ_B^A represent the rates of gain and loss (other than by transmission), respectively, for animals or infectious units in group or environment B. Ψ_B^Y represents the rate of transmission caused by infected animals in group B and infectious units in environment B; Φ_B^E represents the rate of consumption of infectious units from environment B. All the rates for each group and environment are listed in Appendix A. The transmission and consumption rates are

$$\begin{aligned}
&\text{Transmission}: \quad \Psi_i^Y = \beta_i X_i Y_i + z_i X_i E_i + s_i X_i E_G,\\
&\text{consumption (from group-specific environemnt)}: \quad \Phi_i^E = z_i(X_i + Y_i)E_i,\\
&\text{consumption (from general environment)}: \quad \Phi_G^E = \sum_i (s_i(X_i + Y_i)E_G)
\end{aligned}$$

Wherever possible, a realistic parameter value, based on estimates derived from the literature, is given in Table 2. These values are used for illustrative purposes throughout this paper. Although the death rate of the organism (q) is estimated to be 0.118 (from data appearing in Bolton et al. (1999)), here the value for the lactating group is set at 0.99. This is to reflect a situation in which the environment of the lactating animals is cleared of faeces regularly (i.e. q_L is a combined death and removal rate). The value of p (the rate at which

Table 2
Definitions of the parameters used in the model for the transmission of a human food-borne pathogen in a multigroup managed herd[a]

Parameter	Definition (units)	Parameter estimate	References
N	Total herd size (animals)	175	Kossaibati and Esslemont (1995)
a	Replacement rate (per day) (maintains constant herd size)	$a = \sum_i b_i(X_i + Y_i) + m(X_L + Y_L)$ for $i \in \{U, W, D, L\}$	NA
ρ	Pseudovertical transmission parameter	$\rho = 1$, unless stated otherwise	None
g	Maturation rate (per day)	$g_U = 0.024$, $g_W = 0.0015$	Blowey (1986)
c	Rate of flow from dry to lactating group (per day)	$c = 0.017$	Blowey (1986)
d	Rate of flow from lactating to dry group (per day)	$d = 0.0032$	Blowey (1986)
γ	'Recovery' rate (per day)	$\gamma_U = 0.048$, $\gamma_i = 0.143$ for $i \in \{W, D, L\}$	Mechie et al. (1997)
b	Death rate (per day)	$b_U = 0.00014$, $b_W = 0.000033$, $b_D = 0.000056$, $b_L = 0.000056$	Gardner et al. (1990) and Tyler et al. (1999)
m	Culling rate (per day)	$m = 0.0008$	Young et al. (1983)
η	Shedding rate (per day)	$\eta_U = 4.0 \times 10^8$, $\eta_W = 5.0 \times 10^7$, $\eta_D = 1.3 \times 10^8$, $\eta_L = 1.3 \times 10^8$	Cray et al. (1998) and MacDiarmid and Watkin (1972)
p	Pooling rate (rate infectious units moved to general environment) (per day)	Unknown, have assumed $p_i = 0.001$ for $i \in \{U, W\}$, $p_j = 0.0001$ for $j \in \{D, L\}$ when not varying	None
q	'Death' rate of organism (per day)	$q_i = 0.118$ for $i \in \{U, W, D, G\}$, $q_L = 0.99$ when not varying	Bolton et al. (1999)
β	Direct transmission parameter (per animal per day)	Unknown, have assumed $\beta_U = 0.001$, $\beta_W = 0.002$, $\beta_D = 0.003$, $\beta_L = 0.001$ when not varying	None
z	Group-specific indirect transmission parameter (per animal per day)	Unknown, have assumed $z_U = 3.0 \times 10^{-12}$, $z_W = 2.0 \times 10^{-12}$, $z_D = 1.0 \times 10^{-12}$, $z_L = 1.0 \times 10^{-12}$ when not varying, unless stated otherwise	None
s	'General' indirect transmission parameter (per animal per day)	Unknown, have assumed $s_U = 0.01 z_U$, $s_W = 0.005 z_W$, $s_D = 0.01 z_D$, $s_L = 0.02 z_L$ when not varying, unless stated otherwise	None

[a] Also, parameter estimates for the transmission of *E. coli* O157 within a typical UK dairy herd. The parameter estimates are used in Figs. 2–7.

infectious units are moved to the general environment) is unknown and likely to be very variable. However, it is reasonable to assume that it will always be relatively small. Here, we have chosen values for the unweaned and weaned groups that are higher than those for the dry and lactating groups, to represent a situation whereby young animals are housed on deep-litter beds and faeces are allowed to accumulate. The transmission parameters β, z and s also are unknown. We have assumed various values, which are given in Table 2. In general, we have selected values for z which reflect a situation in which the unweaned and weaned animals display more oral behaviour than animals in the dry and lactating groups, and are therefore more likely to ingest faecally contaminated material present in their environment. Similarly, the values chosen for s represent the likely situation that unweaned and lactating animals are handled more frequently than those in other groups and are therefore at a greater risk of infection from personnel and equipment. Paiba (personal communication), Mechie et al. (1997) and Hancock et al. (1997) indicated that the highest prevalence of infection often is found in the weaned group. The fixed values of β, z and s that we used reproduce (in the general model) prevalences consistent with this pattern and with the constraint $\beta_U < \beta_W$. This constraint was imposed because unweaned animals often are housed individually or in small groups in adjoining pens and, therefore, have less direct contact with other animals in their group than those in the weaned group.

We used a combination of analytical and numerical techniques to analyse the model. The infection-free state (which is always feasible) is defined as $(X_U^*, X_W^*, X_D^*, X_L^*)$, where:

$$X_L^* = \frac{cg_U g_W N}{\{cg_U g_W + (g_U + b_W + g_W)[(b_D + c)(d + b_L + m) - dc] + g_U g_W (d + b_L + m)\}},$$

$$X_D^* = \left(\frac{d + b_L + m}{c}\right) X_L^*, \qquad X_W^* = \left[\frac{(b_D + c)(d + b_L + m) - dc}{cg_W}\right] X_L^*$$

and $X_U^* = N - X_W^* - X_D^* - X_L^*$, because herd size ($N$) is held constant (as in many managed herds). The herd remains in this state unless it is invaded by the pathogen. As the pathogen is eradicated, the herd settles back to this state.

The conditions for invasion of infection are particularly useful. By invasion, we mean a growing epidemic where the number of secondary infections exceeds the number of primary infections. The conditions can be expressed in terms of R_0 (the basic reproduction ratio of the pathogen): the average number of secondary infections produced during the infectious period by one primary infection in a totally susceptible population (Anderson and May, 1981, 1992; Diekmann et al., 1990; Diekmann and Heesterbeek, 2000). In deterministic models such as ours, invasion is impossible when $R_0 < 1$; when $R_0 > 1$, invasion occurs and persistence is possible.

The basic reproduction ratio (R_0) is the dominant eigenvalue of the next-generation matrix M (Diekmann and Heesterbeek, 2000). The elements (m_{ij}) of the matrix are the number of newly infected individuals of type i generated (via all routes) by an individual of type j in a totally susceptible population. To calculate m_{ij}, we needed to know the time spent in each group i by an individual that became infected whilst in group j. Here, i and j can be either U, W, D or L. Ordinarily, the times (T_{ij}) can be obtained by 'direct', 'intuitive' methods (e.g. Bowers and Turner, 1997). However, in this case, the dry/lactating cycle made such methods complicated. We found that it was better to use the general approach

involving the transition matrix (G) (Reade et al., 1998; Diekmann and Heesterbeek, 2000). The elements (G_{ij}) of this matrix are the net rates of increase in infected animals in group i per infected animal in group j in an otherwise totally susceptible herd (i.e. either minus the rate at which an infected animal leaves its own group or the rate at which it moves to a connected group). Here

$$G = \begin{pmatrix} -\theta_{\mathrm{U}} & 0 & 0 & 0 \\ g_{\mathrm{U}} & -\theta_{\mathrm{W}} & 0 & 0 \\ 0 & g_{\mathrm{W}} & -\theta_{\mathrm{D}} & d \\ 0 & 0 & c & -\theta_{\mathrm{L}} \end{pmatrix}$$

where

$$G_{\mathrm{UU}} = \theta_{\mathrm{U}} = b_{\mathrm{U}} + g_{\mathrm{U}} + \gamma_{\mathrm{U}}, \qquad G_{\mathrm{WW}} = \theta_{\mathrm{W}} = b_{\mathrm{W}} + g_{\mathrm{W}} + \gamma_{\mathrm{W}},$$
$$G_{\mathrm{DD}} = \theta_{\mathrm{D}} = b_{\mathrm{D}} + c + \gamma_{\mathrm{D}}, \qquad G_{\mathrm{LL}} = \theta_{\mathrm{L}} = b_{\mathrm{L}} + d + m + \gamma_{\mathrm{L}}$$

The symbol θ_i represents the average rate at which an infected animal in group i is lost from group i, where $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$. The times ($T_{ij}$) are identified as the elements of $-G^{-1}$ (Appendix B). The times spent in the dry and lactating groups depend heavily on the rates c and d because animals return to the dry group after lactation and then move into the lactating group again after calving (and so cycle between the two groups). If $d = 0$ (i.e. if there is no flow-back and hence no cycle), then the time spent in each group given that the animal became infected whilst in that group is just the inverse of the rate of loss (θ_i) from that group (i.e. $T_{ii} = 1/\theta_i$ where $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$) (Appendix B).

To calculate the number of newly infected animals of type i generated by an animal of type j via infectious units in the environment, we needed to find the time (T_{Eij}) spent in environment i by an infectious unit that was originally shed into environment j, where $i,j \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}, \mathrm{G}\}$. So, we constructed another transition matrix (H) for infectious units. The elements (H_{ij}) of this matrix are the net rates of increase in infectious units in environment i per infectious unit in environment j for a totally susceptible herd (i.e. either minus the rate at which an infectious unit leaves the environment into which it was shed or the rate at which an infectious unit moves to the general environment). Here

$$H = \begin{pmatrix} -\sigma_{\mathrm{U}} & 0 & 0 & 0 & 0 \\ 0 & -\sigma_{\mathrm{W}} & 0 & 0 & 0 \\ 0 & 0 & -\sigma_{\mathrm{D}} & 0 & 0 \\ 0 & 0 & 0 & -\sigma_{\mathrm{L}} & 0 \\ p_{\mathrm{U}} & p_{\mathrm{W}} & p_{\mathrm{D}} & p_{\mathrm{L}} & -\sigma_{\mathrm{G}} \end{pmatrix}$$

where

$$H_{\mathrm{UU}} = \sigma_{\mathrm{U}} = z_{\mathrm{U}} X^*_{\mathrm{U}} + p_{\mathrm{U}} + q_{\mathrm{U}}, \qquad H_{\mathrm{WW}} = \sigma_{\mathrm{W}} = z_{\mathrm{W}} X^*_{\mathrm{W}} + p_{\mathrm{W}} + q_{\mathrm{W}},$$
$$H_{\mathrm{DD}} = \sigma_{\mathrm{D}} = z_{\mathrm{D}} X^*_{\mathrm{D}} + p_{\mathrm{D}} + q_{\mathrm{D}}, \qquad H_{\mathrm{LL}} = \sigma_{\mathrm{L}} = z_{\mathrm{L}} X^*_{\mathrm{L}} + p_{\mathrm{L}} + q_{\mathrm{L}},$$
$$H_{\mathrm{GG}} = \sigma_{\mathrm{G}} = s_{\mathrm{U}} X^*_{\mathrm{U}} + s_{\mathrm{W}} X^*_{\mathrm{W}} + s_{\mathrm{D}} X^*_{\mathrm{D}} + s_{\mathrm{L}} X^*_{\mathrm{L}} + q_{\mathrm{G}}$$

The symbol σ_i represents the average rate at which an infectious unit in environment i is lost from environment i, where $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}, \mathrm{G}\}$. The times ($T_{Eij}$) are the elements of $-H^{-1}$ (Appendix B).

The elements of the next-generation matrix M are the total number of newly infected animals of type i generated by an individual animal of type j by all possible routes of transmission. Therefore, the next-generation matrix for this model is given by

$$M = K_\beta T + K_z T_E S T + K_a T$$

and consists of three components corresponding to direct transmission, transmission via infectious units in the environment and pseudovertical transmission, respectively. The matrices of times are $T = -G^{-1}$ and $T_E = -H^{-1}$. The transmission matrices are $K_\beta = (\beta_i \delta_{ij} X_i^*)$, $K_z = (z_i \delta_{ik} X_i^* + s_i \delta_{\mathrm{G}k} X_i^*)$ and $K_a = ([a/X_{\mathrm{D}}^*]\delta_{i\mathrm{U}} - [a/X_{\mathrm{D}}^*](1 - \delta_{\mathrm{D}j}))$, and the shedding matrix is $S = (\eta_k \delta_{kj})$, where $i, j \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$, $k \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}, \mathrm{G}\}$ and

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

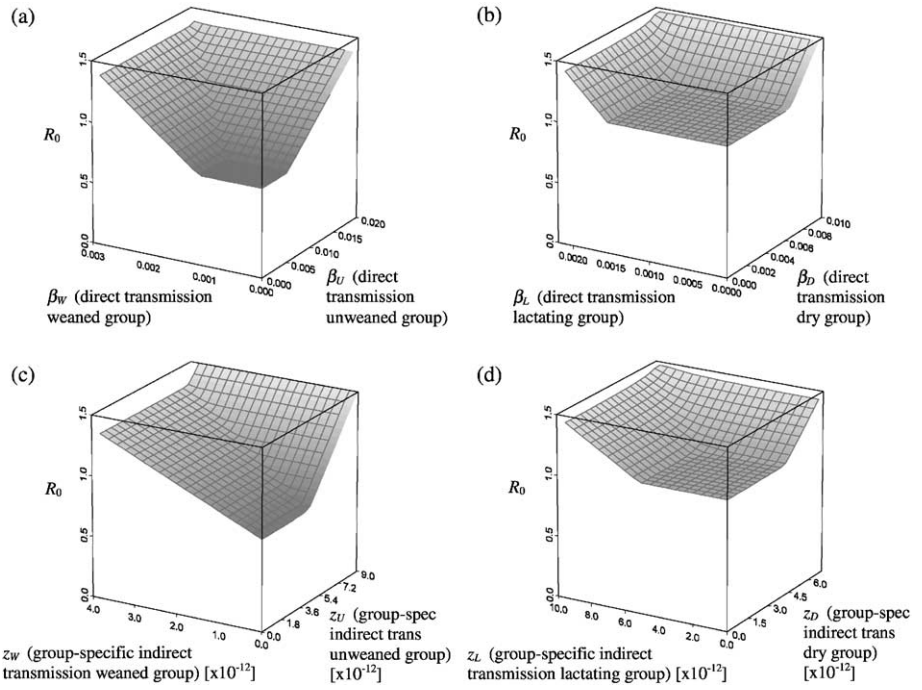

Fig. 2. Plots of R_0 for the general model, which has been parameterised for the transmission of *E. coli* O157 within a typical UK dairy herd. The model has direct, indirect (via the group-specific and general environments) and pseudovertical transmission ($\rho = 1$). In (c) and (d), the transmission parameters are given by the values on the horizontal axes multiplied by 10^{-12}: (a) R_0 plotted against β_U and β_W; (b) R_0 plotted against β_D and β_L; (c) R_0 plotted against z_U and z_W; (d) R_0 plotted against z_D and z_L.

R_0 (the dominant eigenvalue of M) is the largest solution of $\det(M - \lambda I) = 0$, where 'det' stands for determinant and I represents the identity matrix. The solutions of this equation are not simple in this general case. Hence, the expression for R_0 is large and complicated and cannot be interpreted biologically by inspection. We found that the best way to assess R_0 was to plot it against the parameters of interest (generally the transmission parameters, because these are unknown), while keeping the remaining parameters fixed.

Fig. 2(a) shows how R_0 changes with β_U and β_W (the direct transmission parameters for the unweaned and weaned groups, respectively). R_0 increases, seemingly monotonically, for large values of β_U and β_W. In contrast, for small values, R_0 remains relatively constant. The height of this 'plateau' is determined by the components of R_0 corresponding to the dry and lactating groups. (This is discussed in more detail for the special case in Section 3.1.) Changing β_U and β_W does not affect the size of R_0 in this region of parameter space. Therefore, we can conclude that, in this region (with our assumed inputs), transmission within the dry and lactating groups effectively determines whether or not invasion of the herd is possible. Fig. 2(b) shows a similar picture for the change in R_0 with respect to β_D and β_L.

When we plotted R_0 as a function of the indirect transmission parameters z_U and z_W (Fig. 2(c)) and z_D and z_L (Fig. 2(d)), we found that R_0 increased as each transmission parameter increased—but eventually levelled out. The level corresponds to the sum of the average number of newly infected animals produced by direct and pseudovertical transmission (by a single invader in a totally susceptible population) and the *maximum* number of newly infected animals produced by indirect transmission. The latter corresponds to the total number of infectious units produced by the invader during the infectious period. This is demonstrated for the simpler model in Section 3.3.1.

3. Special cases

By looking at special cases of this model, the contribution made by each type of transmission can be distinguished. Moreover, because some of these special cases correspond to intervention strategies, it is possible to observe the effect of potential control measures.

3.1. Direct transmission only

In this case, all the routes of transmission other than direct host-to-host transmission are closed (i.e. parameters z_i, s_i and ρ are zero for all $i \in \{U, W, D, L\}$). This could correspond to a system where calves are removed from their mother at birth (eliminating pseudovertical transmission) and all animals are housed, for example, on slats, so that contact (and contamination) with faecal matter is greatly reduced. Although in practice it would be impossible to eliminate all transmission via free-living infectious units, this special case demonstrates the most that could be achieved by using this strategy.

For this model, there is no single 'smooth formula' corresponding to the dominant eigenvalue R_0 of M. Instead, dominance switches (as illustrated in Fig. 3) between three of

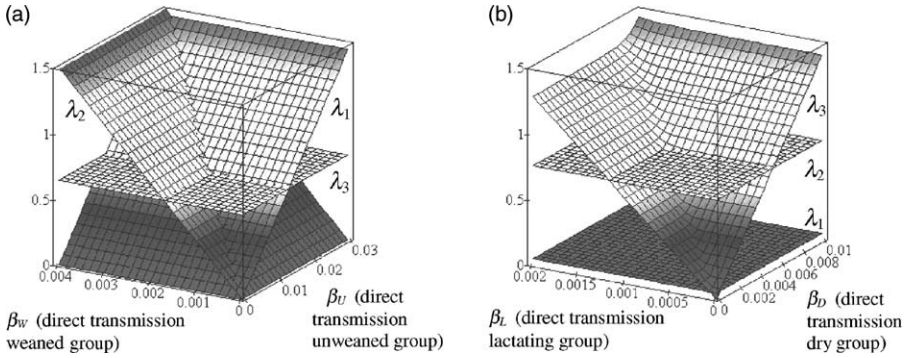

Fig. 3. Plots of eigenvalues λ_1, λ_2, λ_3 for the model with direct transmission only. This model corresponds to the general model (which describes transmission of *E. coli* O157 within a typical UK dairy herd) with $z_i = s_i = 0$ for $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$ and $\rho = 0$. R_0 corresponds to the highest (composite) surface: (a) λ_1, λ_2, λ_3 plotted against β_U and β_W; (b) λ_1, λ_2, λ_3 plotted against β_D and β_L.

the four eigenvalues of the next-generation matrix; we labelled these eigenvalues λ_1, λ_2 and λ_3. Here

$$\lambda_1 = m_{\mathrm{UU}}, \qquad \lambda_2 = m_{\mathrm{WW}} \tag{2}$$

and

$$\lambda_{3,4} = \frac{1}{2}\left\{(m_{\mathrm{DD}} + m_{\mathrm{LL}}) \pm \sqrt{(m_{\mathrm{DD}} + m_{\mathrm{LL}})^2 - 4m_{\mathrm{DD}}m_{\mathrm{LL}}\left(1 - \frac{T_{\mathrm{DL}}T_{\mathrm{LD}}}{T_{\mathrm{DD}}T_{\mathrm{LL}}}\right)}\right\} \tag{3}$$

with

$$m_{ii} = \beta_i X_i^* T_{ii} \quad \text{for } i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$$

The first eigenvalue (λ_1) is the number of newly infected animals produced in the unweaned group by an animal that became infected whilst in the unweaned group. λ_1 determines whether or not the pathogen can invade (and hence persist within) the unweaned group. The second eigenvalue (λ_2) has an equivalent interpretation for the weaned group. The third eigenvalue λ_3 (where $\lambda_3 > \lambda_4$) determines whether or not the pathogen can invade the dry and lactating groups. Information relating to these groups (i.e. m_{DD} and m_{LL}) is modified to take into account the dry/lactating cycle (via T_{DL} and T_{LD}). The cycle allows animals (including infected animals) to occupy repeatedly the dry and lactating groups. This causes the groups to be inextricably linked. The infection can persist only within both the groups or neither of them. However, if we imagine the extreme case where animals cannot flow back into the dry group (i.e. if $d = 0$ and hence $T_{\mathrm{DL}} = 0$), then Eq. (3) simplifies to give

$$\lambda_3 = m_{\mathrm{DD}} = \beta_\mathrm{D} X_\mathrm{D}^* T_{\mathrm{DD}}, \qquad \lambda_4 = m_{\mathrm{LL}} = \beta_\mathrm{L} X_\mathrm{L}^* T_{\mathrm{LL}}$$

and so dominance switches between all four eigenvalues of the next-generation matrix. The limited interaction between the groups leads to this disjointedness.

We give plots of the eigenvalues rather than just plots of R_0 because plots of the eigenvalues reveal information specific to each group (group-specific information is useful when designing intervention strategies). However, because R_0 corresponds to the dominant eigenvalue at any point, these plots include a plot of R_0 (albeit implicitly). In Fig. 3(a), eigenvalues λ_1, λ_2 and λ_3 are plotted against β_U and β_W. Eigenvalues λ_1 and λ_2 always increase monotonically with β_U and β_W, respectively, because $\partial\lambda_1/\partial\beta_U$ and $\partial\lambda_2/\partial\beta_W$ are both positive and independent of β_U and β_W. The eigenvalue λ_3 is independent of β_U and β_W and hence represented by a horizontal plane in Fig. 3(a). For relatively small values of β_U and β_W, λ_3 dominates. However, for relatively small values of β_U and large values of β_W, λ_2 dominates. For relatively small values of β_W and large values of β_U, λ_1 dominates. None of the three eigenvalues is dominant across the entire region of parameter space depicted in Fig. 3(a). Therefore, the surface corresponding to R_0 is a composite surface comprised of the 'dominant' parts of the three intersecting surfaces (i.e. the parts of each surface where that particular eigenvalue is dominant).

In Fig. 3(b), λ_1, λ_2 and λ_3 are plotted against β_D and β_L. The lower plane corresponds to λ_1, the upper plane corresponds to λ_2 and the sloping surface corresponds to λ_3. Note that, for this set of parameter values, when β_D and β_L are relatively small (i.e. when $\beta_D < 0.0054$ and $\beta_L < 0.0012$ approximately), λ_2 dominates and, because $\lambda_2 < 1$, the pathogen cannot invade. When β_D and β_L are relatively large, λ_3 dominates and, when $\lambda_3 > 1$, the pathogen can invade the dry and lactating groups.

3.1.1. Invasion and persistence

The line (or surface) corresponding to $R_0 = 1$ strictly marks the boundary of invasion. On one side invasion cannot occur; on the other invasion—and possibly also persistence—can occur. In deterministic models, the boundary of invasion and the boundary of persistence often coincide. However, invasion without persistence is possible. Pathogen-induced mortality and life-long protective immunity (when coupled with a high transmission rate and a low susceptible restocking rate) can lead to extinction of the pathogen after the initial invasion (Anderson and May, 1986; Dye, 1998; Diekmann and Heesterbeek, 2000). The models in this paper do not include pathogen-induced mortality or life-long immunity because *E. coli* O157 does not appear to cause disease or induce life-long immunity in cattle. Numerical results suggest that persistence always follows invasion (as illustrated in Fig. 4). Fig. 4 corresponds to the cross-section of Fig. 3(b) at the point where $\lambda = 1$. It shows the line corresponding to $R_0 = 1$ (i.e. in this case, $\lambda_3 = 1$) and points in parameter space where pathogen persistence (open square) or pathogen extinction (filled square) is the outcome. The points on either side of the boundary were selected using Latin Hypercube Sampling (Vose, 2000; Blower and Dowlatabadi, 1994). The outcome for each point was established using numerical integration. It is clear that the boundary of persistence (revealed by the change in behaviour) coincides with the boundary of invasion (given by $R_0 = 1$). Therefore, we can conclude that the conditions $R_0 > 1$ and $R_0 < 1$ determine whether or not invasion *and* persistence can occur.

When the infection pathways represent a small proportion of the possible transmission routes (i.e. there is a lack of connectivity), as in this special case, information about R_0 alone is not sufficient to determine whether or not invasion and persistence will occur. Details of the model structure, the initial site of infection and the size of the eigenvalues

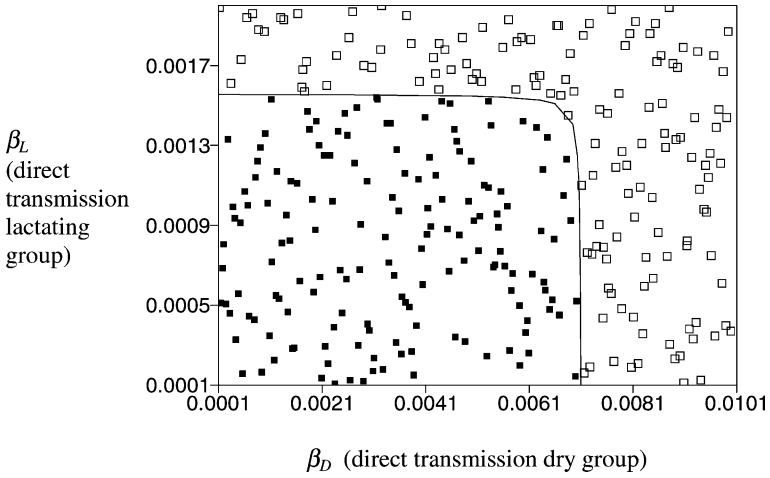

Fig. 4. Boundaries of invasion and persistence for the model with direct transmission only. This model corresponds to the general model (which describes transmission of *E. coli* O157 within a typical UK dairy herd) with $z_i = s_i = 0$ for $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$ and $\rho = 0$. The curve corresponds to $R_0 = 1$ (the boundary of invasion). The 'open' and 'filled' squares denote numerical examples of pathogen persistence and pathogen extinction respectively. The boundary of persistence coincides with the boundary of invasion.

(λ_1, λ_2 and λ_3) are required also. For example, when $\lambda_1 > 1$, $\lambda_2 < 1$ and $\lambda_3 < 1$, the pathogen can invade the unweaned group, but only if the pathogen is introduced directly into the unweaned group (because in this model, there are no routes of transmission to this group from the other groups). If the pathogen is introduced into the unweaned group, then the infection is maintained within this group. Numerical integration can be used to verify which groups contain infected animals when persistence does occur. For this example, infected animals were found in the unweaned group and also (in small numbers) in the other groups in the long term.

Alternatively, when $\lambda_3 > 1$ whilst $\lambda_1 < 1$ and $\lambda_2 < 1$, the pathogen can invade the dry and lactating groups but not the unweaned and weaned groups. Even if the pathogen were introduced into the unweaned group, infected animals would be found only in the dry and lactating groups in the long term (because, in this example, there are no transmission routes from the dry and lactating groups to the unweaned and weaned groups).

3.2. Direct and pseudovertical transmission

This model incorporates direct transmission and pseudovertical transmission (but not indirect transmission, i.e. parameters z_i and s_i are zero for all $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$). By comparing the results of this model with those of the previous special case, we were able to determine the contribution to transmission provided by the pseudovertical term. This allowed us to assess the impact of preventing transmission via this route (possibly by removing calves at birth to prevent them suckling potentially contaminated teats).

The pseudovertical term provides an additional source of interaction between the groups. Unfortunately, as for the full model, the expression for R_0 is complicated and cannot be

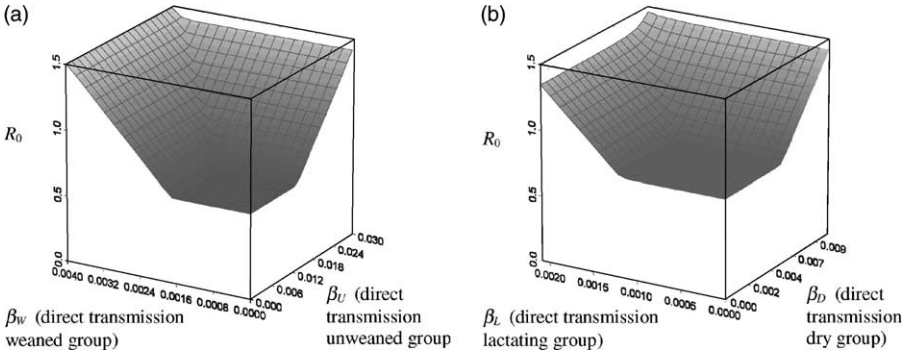

Fig. 5. Plots of R_0 for the model with direct and pseudovertical transmission. This model corresponds to the general model (which describes transmission of *E. coli* O157 within a typical UK dairy herd) with $z_i = s_i = 0$ for $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$ and $\rho = 1$: (a) R_0 plotted against β_U and β_W; (b) R_0 plotted against β_D and β_L.

interpreted biologically by inspection. Therefore, a graphical (rather than an algebraic) representation is given.

Fig. 5(a) shows that, in this example, R_0 increases as β_U and β_W increase beyond approximately 0.0125 and 0.0017, respectively. Similarly, Fig. 5(b) shows that R_0 increases as β_D and β_L increase beyond approximately 0.0056 and 0.0011, respectively. Note that the surfaces in Fig. 5 are almost identical to the composite surfaces equivalent to R_0 in Fig. 3 (for the model with direct transmission only). This suggests that, for this particular set of parameter values, direct transmission dominates the behaviour even when the probability of pseudovertical transmission is set to its maximum value of 1.0.

For this model, and the previous model with direct transmission only, R_0 decreases as the direct transmission parameters decrease until R_0 reaches a plateau determined by the fixed transmission parameters. When this plateau lies below 1 as it does in Fig. 5 (and Fig. 3), it is theoretically possible to prevent the pathogen invading the system by reducing one or more of the variable transmission parameters (which are β_U and β_W in Fig. 5(a) and β_D and β_L in Fig. 5(b)). For example, when $\beta_\mathrm{D} = 0.003$ and $\beta_\mathrm{L} = 0.001$ (as in Fig. 5(a)), $R_0 < 1$ only when $\beta_\mathrm{U} < 0.021$ and $\beta_\mathrm{W} < 0.0027$. To reduce a direct transmission parameter, we must reduce the probability of transmission per contact between a susceptible animal and an infected animal and/or reduce the number of contacts per susceptible animal per unit time in the group to which the parameter applies. In terms of the unweaned group, for example, the latter could be achieved by housing individual unweaned calves in solid-sided pens, which would prevent direct contact between these animals (and, hence, eliminate direct transmission within the unweaned group).

3.3. Direct and indirect transmission

The models discussed in this section incorporate direct transmission and indirect transmission via infectious units in the environment (but not pseudovertical transmission, i.e. $\rho = 0$). In the first model, animals are exposed only to infected animals within their own group and infectious units within their own environment (i.e. indirect transmission

occurs via the group-specific environment). This could be true for animals housed all year round. In the second model, there is also a general environment to which infectious units from all group-specific environments are added. This general environment permits between-group transmission and can be envisaged as a small amount of contaminated matter transported between the groups by personnel or equipment. In this example, only the dry and lactating animals are at risk from the general environment. This might be the case where calves are fed milk-replacer and extra hygiene precautions are taken when entering the unweaned and weaned pens (to minimise transmission to these potentially more-susceptible groups). If precautions were also taken when leaving the unweaned and weaned pens, then contributions to the general environment would only come from dry and lactating animals. Although a similar process can be observed with the movement of slurry and the subsequent exposure of grazing animals, this is not dealt with specifically in this paper (in which, for simplicity, we have assumed temporally continuous exposure to the general environment).

3.3.1. Without general environment

This model corresponds to the general model with $\rho = 0$ and $s_i = 0$ for all $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$. The results for this model are very similar to those for the model with direct transmission only, in that dominance switches between three eigenvalues (λ_1, λ_2 and λ_3). The expressions for the eigenvalues are equivalent to those given in Eqs. (2) and (3). However, the expressions for m_{ii} now consist of the sum of newly infected individuals produced by direct transmission and those produced via infectious units in the environment:

$$m_{ii} = \beta_i X_i^* T_{ii} + z_i X_i^* \eta_i T_{ii} T_{Eii} \quad \text{for } i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$$

The eigenvalues are illustrated in Fig. 6.

A comparison of Fig. 3(a) and (b) and Fig. 6(a) and (b) reveals how indirect transmission affects the behaviour in this case. As expected, in both examples invasion (and, hence, persistence) is more likely for the model with both direct and indirect transmission than for the model with direct transmission alone. In Fig. 6(a), a larger proportion of the 'R_0-surface' lies above the plane $\lambda = 1$ than in Fig. 3(a). This indicates that invasion is possible for smaller values of β_U and β_W when there is this additional route of transmission. In Fig. 6(b), the upper plane lies above 1 (i.e. $\lambda_2 > 1$ always). This indicates that, for this set of parameter values, the pathogen always can invade the weaned group. Numerical results confirm that, for this set of parameter values, the infection always persists within the weaned group (and, therefore, within the herd) regardless of the size of λ_3, provided that the infection is introduced into either the weaned group or the unweaned group (from where it passes into the weaned group). Otherwise, the infection only persists when $\lambda_3 > 1$ and then only within the dry and lactating groups, because there is no route of transmission from the dry and lactating groups to the unweaned or weaned group. A comparison of Figs. 3b and 6b illustrates how, for this set of parameter values, preventing indirect transmission within the weaned group can lead to elimination of the organism when $\beta_\mathrm{D} < 0.006$ and $\beta_\mathrm{L} < 0.0014$.

Fig. 6(c) and (d) shows how R_0 changes with the indirect transmission parameters. Fig. 6(c) reveals that R_0 increases as z_U and z_W increase. However, it does not show that R_0

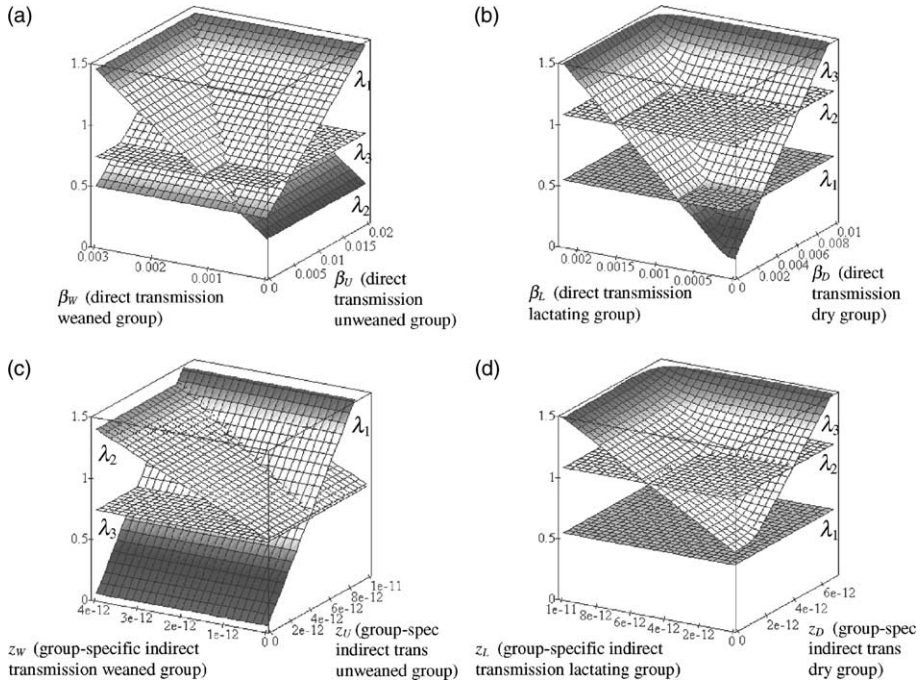

Fig. 6. Eigenvalues λ_1, λ_2, λ_3 for the model with direct and group-specific indirect transmission. This model corresponds to the general model (which describes transmission of *E. coli* O157 within a typical UK dairy herd) with $s_i = 0$ for $i \in \{\mathrm{U}, \mathrm{W}, \mathrm{D}, \mathrm{L}\}$ and $\rho = 0$. R_0 corresponds to the highest (composite) surface: (a) λ_1, λ_2, λ_3 plotted against β_U and β_W; (b) λ_1, λ_2, λ_3 plotted against β_D and β_L; (c) λ_1, λ_2, λ_3 plotted against z_U and z_W; (d) λ_1, λ_2, λ_3 plotted against z_D and z_L.

tends to a maximum value. When λ_1 dominates, the maximum value is $\beta_\mathrm{U} X^*_\mathrm{U} T_{\mathrm{UU}} + \eta_\mathrm{U} T_{\mathrm{UU}}$. The first term corresponds to the average number of newly infected animals produced by direct transmission by a single invader in a totally susceptible population. The second term is the maximum number of newly infected animals produced by indirect transmission by the same invader. This is equal to the total number of infectious units produced by the invader during the infectious period, because each E can only produce a single infected animal. Fig. 6(c) also shows that it is possible to make $R_0 < 1$ by reducing the number of host–pathogen encounters within the unweaned and weaned groups. This might be achieved by using raised feeding and water troughs, frequent removal of contaminated bedding or using a form of bedding that the animals are less likely to ingest (i.e. sawdust rather than straw). Fig. 6(d), on the other hand, indicates that just reducing z_D and z_L is not enough to prevent invasion.

3.3.2. With general environment

This model corresponds to the general model with $\rho = 0$ and $s_i = 0$ for all $i \in \{\mathrm{U}, \mathrm{W}\}$. Once again, dominance switches between three eigenvalues (λ_1, λ_2 and λ_3). Eigenvalues λ_1 and λ_2 are identical to those for the previous model because, in this example, the unweaned

and weaned groups are not affected by the general environment. However, λ_3 and λ_4 are more complicated. Each element m_{ij} is the sum of newly infected individuals produced by direct transmission and indirect transmission via the group-specific and general environments:

$$\lambda_{3,4} = \frac{1}{2}\left\{(m_{DD} + m_{LL}) \pm \sqrt{(m_{DD} + m_{LL})^2 - 4m_{DD}m_{LL}\left(1 - \frac{m_{DL}m_{LD}}{m_{DD}m_{LL}}\right)}\right\}$$

where

$$m_{ii} = \beta_i X_i^* T_{ii} + z_i X_i^* \eta_i T_{ii} T_{Eii} + s_i X_i^* \eta_i T_{ii} T_{EGi} + s_i X_i^* \eta_j T_{ji} T_{EGj}$$

and

$$m_{ij} = \beta_i X_i^* T_{ij} + z_i X_i^* \eta_i T_{ij} T_{Eii} + s_i X_i^* \eta_i T_{ij} T_{EGi} + s_i X_i^* \eta_j T_{jj} T_{EGj} \quad \text{for } i, j \in \{D, L : i \neq j\}$$

The effect of the general environment is governed largely by the rates at which infectious units enter and leave the general environment. Therefore, Fig. 7(a)–(e) shows R_0 plotted against parameters p_i and q_i for $i \in \{U, W, D, L\}$ and also q_G. Fig. 7(a) shows that λ_1 (lower plane) and λ_2 (upper plane) decrease as p_U and p_W increase, respectively. This reflects the fact that animals in the unweaned and weaned groups only encounter infectious units within their own group-specific environment. The faster the infectious units are moved from these group-specific environments to the general environment, the more slowly newly infected animals are produced within these groups. The same result is not observed for parameters p_D and p_L, because animals in the dry and lactating groups are exposed to the general environment. We assumed that animals are likely to encounter infectious units in the general environment less frequently than those within their own group-specific environment and, therefore, each transmission parameter s_i (for $E_G \rightarrow X_i$) was chosen to be a fraction of z_i (for $E_i \rightarrow X_i$) for $i \in \{D, L\}$. However, the number of infectious units in the general environment is the sum of those from the dry and lactating environments and those from the unweaned and weaned environments. Consequently, the lower transmission parameters are counteracted by the higher number of infectious units.

Fig. 7(c) and (d) shows the effect of changing the loss/removal rates for the group-specific environments. In Fig. 7(c), λ_1 and λ_2 decline steeply as q_U and q_W increase before levelling out at a value below 1. This indicates that (in this case) $R_0 < 1$ can be obtained by increasing q_U and q_W because $\lambda_3 < 1$ for this set of parameter values. Housing the unweaned and weaned animals on slatted floors or removing their faeces more frequently are possible ways to increase these parameter values. As demonstrated in Fig. 7(d), just increasing q_D and q_L is not sufficient to prevent invasion, because $\lambda_2 > 1$ always for this set of parameter values. For the same reason, just increasing q_G cannot prevent infection (as shown in Fig. 7(e)). This indicates that increased hygiene of equipment and personnel is not sufficient in itself to prevent the persistence of infection.

Note that (as in the previous special cases) if the pathogen is not introduced into the unweaned or weaned groups, then it can persist only within the dry and lactating groups. However, if all groups were at risk from the general environment, the infection could be transmitted to the unweaned and weaned groups. In this case, there would be a single 'smooth' surface corresponding to R_0.

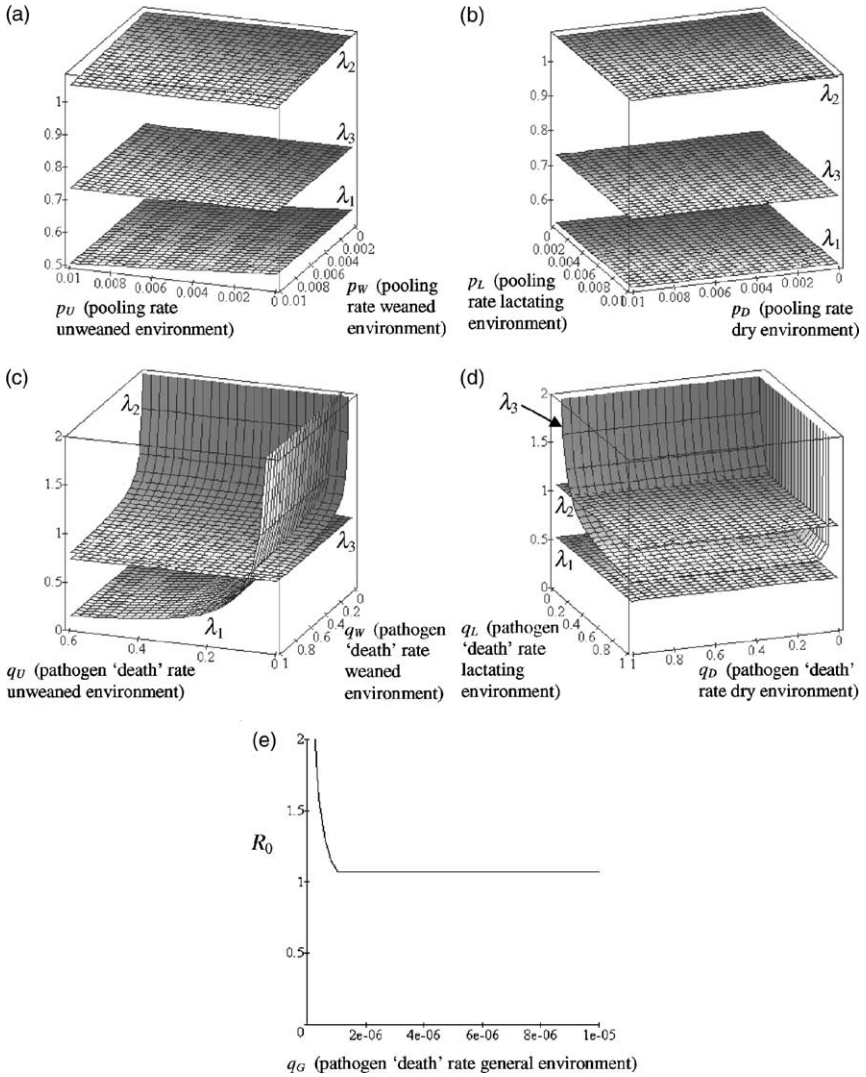

Fig. 7. Eigenvalues λ_1, λ_2, λ_3 for the model with direct and indirect (via the group-specific and general environments) transmission. This model corresponds to the general model (which describes transmission of *E. coli* O157 within a typical UK dairy herd) with $s_i = 0$ for $i \in \{U, W\}$, $\rho = 0$. R_0 corresponds to the highest (composite) surface: (a) λ_1, λ_2, λ_3 plotted against p_U and p_W; (b) λ_1, λ_2, λ_3 plotted against p_D and p_L; (c) λ_1, λ_2, λ_3 plotted against q_U and q_W; (d) λ_1, λ_2, λ_3 plotted against q_D and q_L; (e) R_0 plotted against q_G.

4. Discussion

Our aim was to develop and investigate a general differential equation model that describes the transmission of an infectious organism between the hosts and environment of a multigroup managed herd. The model was devised to represent the movement of the

human food-borne pathogen *E. coli* O157 within a typical UK dairy herd. However, the model could easily be adapted to other pathogens in other livestock systems—in some cases, just by setting some of the parameters in the general model to zero. In particular, we wished to evaluate the effect of some proposed on-farm control strategies.

The livestock-management system of a typical dairy farm creates a structured population with relatively little interaction between different groups of animals. Therefore, the models examined in this paper are unusual in that they contain fewer infection pathways than many other host–pathogen models. The very limited contact between some groups leads to a disjointedness that manifests itself in R_0 (the basic reproduction ratio). However, the disjointedness is reduced by the dry/lactating cycle. The 'flow-back' part of this cycle is a non-infection pathway that unites the dry and lactating groups. Although the models are designed to describe transmission within a dairy herd, they could easily be adapted to represent other livestock systems (such as suckler and fattening herds and also pig herds). In many ways, these other systems would be simpler to model because they contain fewer compartments and/or more pathways between compartments, both of which lead to a more united population. For example, a suckler herd might consist of only two groups of animals: weaned and 'other' (which contains unweaned, dry and lactating animals). In this system, there is more interaction between the unweaned and the dry and lactating animals than in a dairy herd. It is important to note, however, that our models describe the dynamics of a pathogen that does *not* invoke a protective immune response, because this seems to be the case with *E. coli* O157 (Sanderson et al., 1999) and other human food-borne pathogens.

The basic reproduction ratio (R_0) can be used to assess the effect of various control strategies on the persistence of infection. Strategies that make $R_0 < 1$ are of most interest because they are successful at preventing invasion in a deterministic setting. In some cases, the expressions for R_0 are so complicated that plots of R_0 over selected regions of parameter space are used to assess the effect of a particular strategy. In other cases, we can work directly with the expressions for R_0 and calculate the partial derivatives of R_0 with respect to various model parameters.

Whether or not the pathogen can invade the herd successfully depends on the size of R_0 (the dominant eigenvalue) and—in the case of the more 'disjointed' models—the sizes of the other eigenvalues, the possible transmission routes and the site of the initial infection. For example, in the models without a route of transmission between the dry and unweaned groups, the initial source of the infection determines which groups are affected when $R_0 > 1$. If infection is introduced into the unweaned group and $\lambda_1 > 1$, then all groups will contain infected individuals in the long term. In contrast, if infection is introduced into the dry group and $\lambda_3 > 1$, then only the dry and lactating groups will be affected.

Possible intervention strategies include: the use of raised feed and water troughs to prevent faecal contamination; regular removal of faeces to reduce indirect transmission; removal of calves at birth to prevent pseudovertical transmission; vaccination, dietary management and competitive exclusion to reduce shedding (Zhao et al., 1995); treatment of manure to reduce 'off-host' survival time (Lung et al., 2001; Kearney et al., 1993; Heinonen-Tanski et al., 1998); use of group-specific equipment such as automatic slurry scrapers and foot-baths to prevent between-group transmission. Comparisons of the models examined in this paper can reveal the effects of reducing direct, indirect (via infectious units in the environment) and pseudovertical transmission and reducing contact

between groups. Therefore, with this theoretical approach, we can investigate a wide range of control strategies from the simple and practical to the putative and novel (e.g. vaccination) without the constraints of cost and current availability. Future work will, of course, assess the economic implications of employing those strategies identified as potentially successful. However, it is important to begin by considering all possibilities.

The additional pathway between the unweaned and dry groups in the models with pseudovertical transmission, ensures that infection is found in all groups when it is present within the population. By closing this route of transmission (and other routes between the unweaned and dry and lactating groups, e.g. by ensuring that unweaned animals are not exposed to the general environment), we can limit the number of groups that become infected, but only when the infection is introduced initially into the dry or lactating group. Furthermore, if the pathogen cannot be maintained by the dry and lactating groups alone, then this strategy also will lead to elimination of the pathogen. However, if the infection is introduced into the weaned group, then the weaned, dry and lactating groups are all likely to be affected (i.e. in this case, preventing pseudovertical transmission only prevents the unweaned group becoming infected). This is because the pathogen can often be maintained by the weaned group when it can be maintained by the unweaned group, because β_W is constrained to be greater than β_U and so λ_2 is generally greater than λ_1 for realistic parameter values. Therefore, although pseudovertical transmission can result in more groups being affected, its impact on persistence appears to be minimal (as illustrated by comparing Figs. 3 and 5). Consequently, measures aimed at reducing pseudovertical transmission are unlikely to have a major impact on invasion and persistence.

Measures that reduce indirect transmission are likely to result in a substantial reduction in the prevalence of infection because indirect transmission via the group-specific environments is likely to be a leading cause of new infections. In terms of model parameters, the level of indirect transmission can be decreased by reducing the shedding rates (η_i), reducing the transmission parameters (z_i and s_i), increasing the 'off-host' death rates (q_i) and reducing the 'pooling' parameters (p_i). Each of these parameters can be targeted with a range of intervention strategies. For example, using raised troughs (to prevent faecal contamination of feed and water), avoiding floor feeding and using less-palatable bedding (such as shavings or sawdust) are ways to reduce contact with infectious units in the environment, and therefore reduce z_i and s_i.

Many intervention strategies aim to minimise the number of infectious units in the environment. They do this by either reducing the shedding rates of the animals or increasing the 'death' rates of the pathogen. Studies (Russell and Jarvis, 2001; Russell et al., 2000) have shown that shedding rates can be reduced by feeding straw or other high-fibre feeds that increase the pH of the colon. Zhao et al. (1995) suggested that vaccination and competitive exclusion could prevent colonisation, which would in turn prevent excessive prolonged shedding. Competitive exclusion, in particular, has been used successfully to reduce infection and shedding of *Salmonella* spp. (Rantala and Nurimi, 1973) and *Campylobacter jejuni* (Schoeni and Doyle, 1992) in poultry. Although the effects of strategies that reduce η_i have not been considered here, this model could be used to explore their effectiveness and indicate which group(s) should be targeted.

The 'death' rates (q_i) can be altered more directly. Increasing the frequency of bedding removal, using automated slurry scrapers and avoiding the use of deep-litter beds (e.g.

straw yards) are potential ways to reduce the number of infectious units in the environment. Fewer infectious units results in less contamination of hides and udders, which could lead not only to less indirect transmission on the farm but also to less contamination of carcasses at slaughter. Fig. 7(c) and (d) reveals that $\lambda_1 < 1$ and $\lambda_3 < 1$ even for relatively small values of q_U and of q_D and q_L, respectively, but $\lambda_2 > 1$ for similarly small values of q_W. This suggests that efforts to increase q would be best directed at the weaned group. A comparison of Figs. 3b and 6b illustrates how, for this set of parameter values, preventing indirect transmission within the weaned group can lead to elimination of the pathogen.

Another way to limit the spread of infection (and, hence, the number of animals affected) is to reduce the number of groups at risk from the infectious units in the general environment. One way to do this is to use hygiene barriers (e.g. foot-baths) between the different management groups (particularly when entering and leaving the unweaned and weaned pens) and use equipment that is specific to that area and that group of animals (e.g. automated slurry scrapers rather than tractor-towed ones). Although reducing the rate at which infectious units enter the general environment (i.e. reducing p_i) has a negligible effect on R_0 (as illustrated in Fig. 7(a) and (b)), reducing the number of groups at risk might lead to elimination of the pathogen (as with pseudovertical transmission).

Many food-borne pathogens can be found in domestic and wild animals and in the environment (Hancock et al., 1998; Shere et al., 1998; Porter et al., 1997). Rodents, birds and even flies could act as carriers—repeatedly re-infecting a particular herd or transmitting the infection to other herds. The role of such vectors and reservoirs will be the subject of future studies. The apparent seasonal fluctuations in the prevalence of infection will also be investigated using models that incorporate seasonally varying parameters.

Multigroup models are particularly useful for investigating complex systems because such models can incorporate important demographic processes and multiple infection pathways. One of the benefits of adopting a multigroup approach is that it allows key groups to be identified. By targeting these groups with specific control measures, the efficacy of the control strategy can be maximised. In addition, if results indicate that only the key groups need to be addressed, the cost of the control strategy can be minimised. The results for the models presented in this paper suggest that measures should be taken to reduce indirect transmission, particularly within the weaned group. Van Nes et al. (1998) obtained a similar result when they used a multigroup approach to assess the possibility of eradicating pseudorabies virus from pig herds in The Netherlands using vaccination. Their results suggested that, in addition to the current obligatory vaccination strategy, finishing and rearing herds should receive further vaccination to reduce indirect transmission between herds.

In summary, the results presented in this paper, for the transmission of *E. coli* O157 within a typical UK dairy herd, suggest that eliminating pseudovertical transmission would not contribute greatly to the elimination of infection and that efforts should be directed at reducing the opportunity for indirect transmission, particularly within the weaned group.

Acknowledgements

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Appendix A. Rates of gain, loss and transmission featured in the dynamic equations

All variables, parameters and symbols are defined in Tables 1 and 2 and in the text. The rates of gain and loss appearing in Eq. (1) are

$$\Omega_i^X = a\delta_{i\mathrm{U}}\left(1-\rho\frac{Y_\mathrm{D}}{X_\mathrm{D}+Y_\mathrm{D}}\right)+g_\mathrm{U}X_\mathrm{U}\delta_{i\mathrm{W}}+g_\mathrm{W}X_\mathrm{W}\delta_{i\mathrm{D}}+cX_\mathrm{D}\delta_{i\mathrm{L}}+dX_\mathrm{L}\delta_{i\mathrm{D}}+\gamma_iY_i,$$

$$\Gamma_i^X = (b_i+g_i\delta_{i\mathrm{U}}+g_i\delta_{i\mathrm{W}}+c\delta_{i\mathrm{D}}+(d+m)\delta_{i\mathrm{L}})X_i,$$

$$\Omega_i^Y = a\rho\delta_{i\mathrm{U}}\frac{Y_\mathrm{D}}{X_\mathrm{D}+Y_\mathrm{D}}+g_\mathrm{U}Y_\mathrm{U}\delta_{i\mathrm{W}}+g_\mathrm{W}Y_\mathrm{W}\delta_{i\mathrm{D}}+cY_\mathrm{D}\delta_{i\mathrm{L}}+dY_\mathrm{L}\delta_{i\mathrm{D}},$$

$$\Gamma_i^Y = (b_i+g_i\delta_{i\mathrm{U}}+g_i\delta_{i\mathrm{W}}+c\delta_{i\mathrm{D}}+(d+m)\delta_{i\mathrm{L}}+\gamma_i)Y_i, \qquad \Omega_i^E=\eta_iY_i,$$

$$\Gamma_i^E = (p_i+q_i)E_i, \qquad \Omega_\mathrm{G}^E=\sum_i(p_iE_i), \qquad \Gamma_\mathrm{G}^E=q_\mathrm{G}E_\mathrm{G}$$

and the rates of transmission and consumption are

$$\Psi_i^Y = \beta_iX_iY_i+z_iX_iE_i+s_iX_iE_\mathrm{G}, \qquad \Phi_i^E=z_i(X_i+Y_i)E_i,$$

$$\Phi_\mathrm{G}^E=\sum_i(s_i(X_i+Y_i)E_\mathrm{G})$$

where

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

The size of the host population is held constant (as in many managed herds), therefore:

$$a=\sum_i b_i(X_i+Y_i)+m(X_\mathrm{L}+Y_\mathrm{L})$$

Appendix B. Times spent infectious

All variables, parameters and symbols are defined in Tables 1 and 2 and in the text. The times spent in group i by an animal that became infected whilst in group j are given by

$$-G^{-1}=(T_{ij})=\begin{pmatrix}\frac{1}{\theta_\mathrm{U}} & 0 & 0 & 0\\ \frac{g_\mathrm{U}}{\theta_\mathrm{U}\theta_\mathrm{W}} & \frac{1}{\theta_\mathrm{W}} & 0 & 0\\ \frac{g_\mathrm{U}g_\mathrm{W}\theta_\mathrm{L}}{\theta_\mathrm{U}\theta_\mathrm{W}(\theta_\mathrm{D}\theta_\mathrm{L}-cd)} & \frac{g_\mathrm{W}\theta_\mathrm{L}}{\theta_\mathrm{W}(\theta_\mathrm{D}\theta_\mathrm{L}-cd)} & \frac{\theta_\mathrm{L}}{\theta_\mathrm{D}\theta_\mathrm{L}-cd} & \frac{d}{\theta_\mathrm{D}\theta_\mathrm{L}-cd}\\ \frac{g_\mathrm{U}g_\mathrm{W}c}{\theta_\mathrm{U}\theta_\mathrm{W}(\theta_\mathrm{D}\theta_\mathrm{L}-cd)} & \frac{g_\mathrm{W}c}{\theta_\mathrm{W}(\theta_\mathrm{D}\theta_\mathrm{L}-cd)} & \frac{c}{\theta_\mathrm{D}\theta_\mathrm{L}-cd} & \frac{\theta_\mathrm{D}}{\theta_\mathrm{D}\theta_\mathrm{L}-cd}\end{pmatrix}$$

The times spent in environment i by an infectious unit that was originally shed into environment j are given by

$$-H^{-1} = (T_{Eij}) = \begin{pmatrix} \frac{1}{\sigma_U} & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{\sigma_W} & 0 & 0 & 0 \\ 0 & 0 & \frac{1}{\sigma_D} & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{\sigma_L} & 0 \\ \frac{p_U}{\sigma_U\sigma_G} & \frac{p_W}{\sigma_W\sigma_G} & \frac{p_D}{\sigma_D\sigma_G} & \frac{p_L}{\sigma_L\sigma_G} & \frac{1}{\sigma_G} \end{pmatrix}$$

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