

CONTROLLING THE TRANSMISSION OF MASTITIS-CAUSING PATHOGENS ACROSS HETEROGENEOUS DAIRY HERDS

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Abstract: Using a mathematical model for the transmission of mastitis-causing pathogens in a dairy herd and parameter estimation, control strategies are derived for a number of different herds. In addition, a single common strategy is derived for control of all of the herds. A key feature of all of the control strategies is that they minimise the combined costs associated with infection and treatment. Only a small decrease in performance results from developing a common strategy.
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1. INTRODUCTION

Mastitis (inflammation of the mammary gland) is an infection of the udder of dairy cows caused by bacteria entering any of the four secretory glands (termed *quarters*) through the teat end. Clinical mastitis is an infection that results in visible changes to the quarter and the milk it produces, and an infection that does not exhibit any visible changes is sub-clinical mastitis. Both classes of mastitis result in a decrease in milk production and a reduction in milk quality.

The pathogens that cause mastitis can be divided into two classes. *Major pathogens* are defined as those pathogens that are most likely to precipitate clinical disease or strong inflammatory responses (high somatic cell counts in milk). *Minor pathogens* are defined as those pathogens that infect the mammary gland, causing moderately elevated somatic cell counts, but infection by them

does not, in general, cause clinical mastitis (White *et al.*, 2001a).

Previous mathematical modelling of the transmission of mastitis-causing pathogens in dairy cows has been undertaken in order to improve understanding of the transmission dynamics and to guide design of effective strategies to control clinical mastitis (Lam *et al.*, 1996; White *et al.*, 2001a; White *et al.*, 2001b; White *et al.*, 2004). Cronin *et al.* (2004) considered the problem of controlling the transmission of mastitis in a single dairy herd. By observing that the control measures are modelled by the inclusion of additional parameters in the model, and defining the control problem in terms of a root-mean square (RMS) error, they reduced the problem to one of parameter estimation.

In this paper the method used by Cronin *et al.* (2004) is applied across the seven different herds

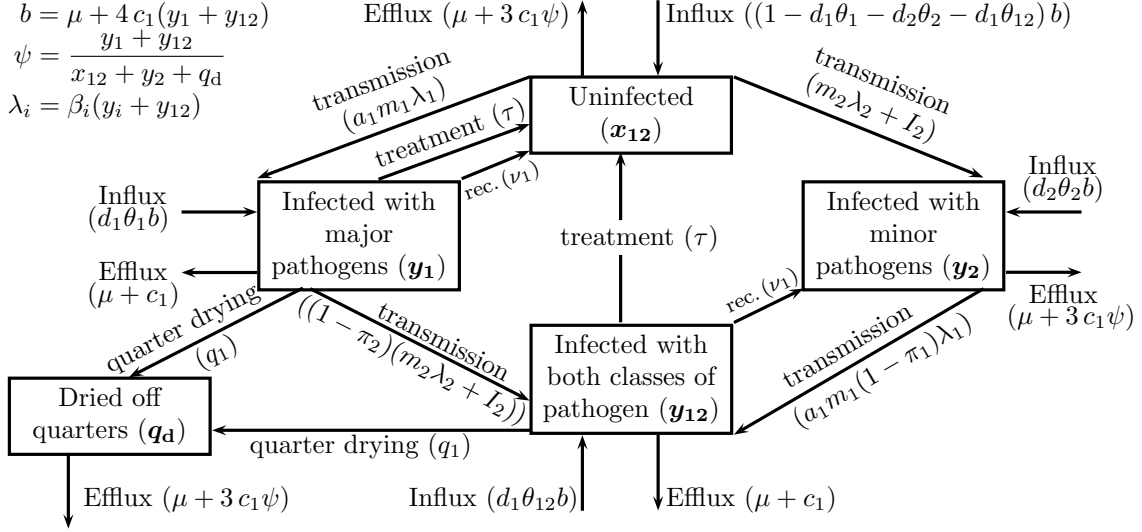


Fig. 1. Multispecies model for the transmission of mastitis in a dairy herd (White *et al.*, 2004).

used in the study by Lam *et al.* (1996) to consider the effects of inter-herd heterogeneity. To better reflect the practical situation, certain control parameters have discrete values that correspond to the control measure being applied or not.

2. MATHEMATICAL MODEL FOR MASTITIS TRANSMISSION IN A DAIRY HERD

A schematic of the multispecies model for the transmission and control of mastitis in a dairy herd proposed by White *et al.* (2004), with the addition of dry-cow therapy for minor pathogen infected quarters, is shown in Figure 1. This additional control measure was suggested by Evans *et al.* (2005) as being necessary when it is desired to reduce the equilibrium proportion of quarters infected with minor pathogens.

The model variables correspond to the proportions of quarters that are uninfected (denoted x_{12}), infected with major pathogens only (y_1), infected with minor pathogens only (y_2), infected with both classes of pathogens (y_{12}) and the proportion in a dried-off state (q_d), respectively. The latter variable is included to allow the modelling of quarter-drying as a control measure. The system of ordinary differential equations corresponding to the schematic in Figure 1 is given by:

$$\dot{x}_{12} = (1 - d_1\theta_1 - d_2\theta_2 - d_1\theta_{12})b + (\nu_1 + \tau)y_1 + \tau y_{12} - (a_1m_1\lambda_1 + m_2\lambda_2 + I_2 + \mu + 3c_1\psi)x_{12} \quad (1)$$

$$\dot{y}_1 = d_1\theta_1b + a_1m_1\lambda_1x_{12} - (\nu_1 + \tau + \mu + c_1 + q_1 + (1 - \pi_2)(m_2\lambda_2 + I_2))y_1 \quad (2)$$

$$\dot{y}_2 = d_2\theta_2b + (m_2\lambda_2 + I_2)x_{12} + \nu_1y_{12} - ((1 - \pi_1)a_1m_1\lambda_1 + \mu + 3c_1\psi)y_2 \quad (3)$$

$$\dot{y}_{12} = d_1\theta_{12}b + (1 - \pi_1)a_1m_1\lambda_1y_2 - (\nu_1 + \tau + \mu + c_1 + q_1)y_{12} + (1 - \pi_2)(m_2\lambda_2 + I_2)y_1 \quad (4)$$

$$\dot{q}_d = q_1(y_1 + y_{12}) - (\mu + 3c_1\psi)q_d \quad (5)$$

where

$$1 = x_{12} + y_1 + y_2 + y_{12} + q_d \quad (6)$$

$$b = \mu + 4c_1(y_1 + y_{12}) \quad (7)$$

$$\psi = (y_1 + y_{12}) / (x_{12} + y_2 + q_d) \quad (8)$$

$$\lambda_i = \beta_i(y_i + y_{12}) \quad (i = 1, 2). \quad (9)$$

The parameters in the model (1)–(9) either relate to the dynamics of the transmission of the pathogens (*model parameters*), or correspond to a potential control measure (*control parameters*). The model parameters are given by:

- μ , the average turnover of lactating cows in the herd;
- θ_i , the proportion of quarters entering the lactating herd already infected with major pathogens ($i = 1$), minor pathogens ($i = 2$) or both classes of pathogens ($i = 12$);
- ν_1 , the average recovery rate from major pathogen infection;
- β_i , the transmission rate of major ($i = 1$) or minor ($i = 2$) pathogens;
- π_1 (π_2), the level of cross-protection against major (minor) or pathogen infection provided by minor (major) pathogen infection.

These parameters can have values that are specific to each herd, such as θ_1 , θ_2 , θ_{12} , β_1 and β_2 , or they can take the same value for all herds, such as μ , ν_1 , π_1 and π_2 . The values used in this paper are those obtained by White *et al.* (2004), which are given in Table 1 for the herd-specific parameters and the non herd-specific values are $\mu = 0.0045$ (day⁻¹), $\nu_1 = 0.01$ (day⁻¹), $\pi_1 = 0.867$ and $\pi_2 = -2.64$. The values for π_1 and π_2 indicate that infection with minor pathogens provides protection against infection with major pathogens, whilst infection with major pathogens enhances susceptibility to minor ones (indicated by the minus sign for π_2).

The control parameters represent:

Table 1. Values obtained by White *et al.* (2004) used for the model parameters.

Herd	θ_1	θ_2	θ_{12}	β_1	β_2
1	0.011	0.559	0.031	0.066	0.007
2	0.010	0.414	0.059	0.024	0.010
3	0.049	0.338	0.013	0.019	0.004
4	0.023	0.503	0.023	0.046	0.014
5	0.045	0.545	0.045	0.089	0.006
6	0.030	0.384	0.026	0.026	0.007
7	0.017	0.514	0.017	0.038	0.005

Postmilking teat disinfection: modelled by a proportional reduction in susceptibility of quarters to major and minor pathogens by factors m_1 and m_2 , respectively;

Quarter drying: modelled as a removal of major pathogen infected quarters (from the lactating herd) at a first order rate with constant q_1 ;

Culling: modelled as a removal of major pathogen infected quarters at a first order rate with constant c_1 ; and a corresponding removal of quarters not infected with major pathogens at a rate that is directly proportional (coefficient c_1) to the ratio of the proportions of quarters infected with major pathogens to those that are not (ψ);

Lactation therapy: modelled as a first order recovery of major pathogen infected quarters, with rate constant τ , arising from antibiotic treatment in the lactation period;

Dry cow therapy: modelled as a reduction in the proportion of quarters entering the herd infected with major pathogens, by a factor d_1 , minor pathogens, by a factor d_2 , or both classes of pathogen, by a factor d_{12} ;

Inoculation: modelled as an additional force of infection, I_2 , for minor pathogens arising from inoculation with iodine resistant minor pathogens;

Antibody: modelled as a proportional reduction in the susceptibility of quarters to major pathogen infection by a factor a_1 , resulting from vaccination with topical antibody.

White *et al.* (2004) performed parameter estimation using data from a split-udder trial to consider the efficacy of postmilking teat disinfection (PMTD) (Lam *et al.*, 1996). As a result, estimates for the effectiveness of PMTD for each of the herds considered were obtained in terms of estimates \hat{m}_1 and \hat{m}_2 for the control parameters m_1 and m_2 . These estimates are given in Table 2.

Table 2. Values obtained by White *et al.* (2004) for PMTD control parameters.

Herd:	1	2	3	4	5	6	7
\hat{m}_1	≈ 0	0.23	0.36	0.46	0.04	0.38	0.32
\hat{m}_2	0.21	0.37	0.56	0.16	0.36	0.69	0.001

All of the values of \hat{m}_1 and \hat{m}_2 are less than 1, which indicates that PMTD reduces susceptibility to major and minor pathogen infection. Since PMTD involves dipping the teat in an iodine-

based dip following milking, and so is either applied or not, the control parameters m_1, m_2 will be restricted to two values: the value 1 corresponding to the control not being applied, and the appropriate value \hat{m}_1, \hat{m}_2 (from Table 2) when it is.

3. THE CONTROL PROBLEM

In the absence of any control measures the proportions of quarters in each of the different classes tends to a disease-persistent steady state. These values are given in Table 3 and are used as the herd-specific initial conditions for the system (1)–(5) when considering the control problem.

Table 3. Disease-persistent steady states in the absence of control measures

Herd:	1	2	3	4	5	6	7
\bar{x}_{12}	0.101	0.172	0.376	0.108	0.060	0.242	0.211
\bar{y}_1	0.029	0.005	0.024	0.006	0.052	0.012	0.018
\bar{y}_2	0.748	0.788	0.577	0.844	0.650	0.714	0.734
\bar{y}_{12}	0.122	0.035	0.023	0.042	0.237	0.032	0.037

The principal objective of any control is to reduce the proportion of quarters infected with major pathogens ($y_1 + y_{12}$), since clinical mastitis has the most adverse effects. Since the presence of quarters infected with minor pathogens also adversely affects milk production and quality, a secondary objective is to simultaneously reduce the proportion of quarters infected with these. To reduce the economic impact of applying controls it is also necessary to minimise the amount of ‘control effort’ applied. This is done by minimising the deviation of the control parameter values from those corresponding to the control not being applied. However, since it is the effect on milk production resulting from quarter drying that is the principal cost associated with this control measure, it is the deviation of the variable q_d (rather than the parameter) from 0 that is considered.

A superscript will be used to denote the herd for which a particular parameter or variable is used. Hence, let $\mathbf{z}^i = (x_{12}^i, y_1^i, y_2^i, y_{12}^i, q_d^i)^T$ be the state vector and $\mathbf{v}^i = (m_1^i, m_2^i, c_1^i, \tau^i, d_1^i, d_2^i, I_2^i, a_1^i)^T$ so that $\mathbf{u}^i = ((\mathbf{v}^i)^T, q_1)^T$ is the vector of control parameters for Herd i . The common infection-free target state is denoted by $\mathbf{z}_* = (1, 0, 0, 0, 0)^T$, while $\mathbf{u}_* = ((\mathbf{v}_*)^T, 0)^T = (1, 1, 0, 0, 1, 1, 0, 1, 0)^T$ is the control parameter vector that corresponds to no control measures being applied. The objective for the control of Herd i can be expressed in the form of a quadratic cost function that one wishes to minimise:

$$J^i(\mathbf{u}^i) = (\mathbf{v}^i - \mathbf{v}_*)^T \mathbf{R}^i (\mathbf{v}^i - \mathbf{v}_*) + \int_0^T (\mathbf{z}^i(t) - \mathbf{z}_*)^T \mathbf{Q}^i (\mathbf{z}^i(t) - \mathbf{z}_*) dt$$

where $\mathbf{R}^i \in \mathbb{R}^{8 \times 8}$ is positive definite, $\mathbf{Q}^i \in \mathbb{R}^{5 \times 5}$ is positive semi-definite and $T > 0$ denotes the length of the intervention. This minimisation can be subject to constraints on the control parameter vectors, such that $\mathbf{u}^i \in \mathcal{U}^i \subset \Omega^9$, to reflect limitations on the effectiveness of treatment or delays/errors in diagnosis.

Assuming that the costs associated with each herd are identical and independent, the weighting matrices, \mathbf{Q}^i and \mathbf{R}^i , are the same for each herd and diagonal. Similarly, the constraints on the control parameter values (except m_1 and m_2), are assumed to be the same across herds and are taken from (Evans *et al.*, 2005). The weights (diagonal entries) are based on a relative daily cost (RDC) estimated from the costs (for the 1000 days intervention) given in (Evans *et al.*, 2005), where minimisation was performed with respect to RMS error (see Table 4). The greatest difficulty lies in ensuring consistency in the costs between those for the variables and those for the parameters. Since the mean recovery period for major pathogen infected quarters is $1/\nu_1 = 100$ days, the estimated cost for an infected cow is \$180. The proportion of major pathogen infected cows culled is c_1 , so that the estimated maximum cost per infected cow for culling is $0.02 \times \$905 = \18.1 . The daily cost associated with major pathogen infected quarters is \$1.8 giving a RDC of \$0.181 for culling. The RDC for each of the remaining parameters is determined by multiplying the cost from (Evans *et al.*, 2005) by $0.181/905 = 0.0002$. The weights for the variables are set at the square of the RDC; while those for the parameters, since they remain constant throughout the intervention, are set at 1000 (i.e., T) times the square of the normalised (with respect to its range) RDC.

Table 4. Weights and admissible ranges for control parameters and variables; costs taken from (Evans *et al.*, 2005)

	Range	Cost	RDC	Weight
x_{12}	0–1	0	0	1
y_1	0–1	\$1800	\$1.80	3.24
y_2	0–1	\$225	\$0.225	0.0506
y_{12}	0–1	\$1800	\$1.80	3.24
q_d	0–1	\$1875	\$1.875	3.5156
m_1	Discrete	\$130	\$0.026	$0.676/(1 - \hat{m}_1)^2$
m_2	Discrete	\$130	\$0.026	$0.676/(1 - \hat{m}_2)^2$
q_1	0–0.02	-	-	-
c_1	0–0.02	\$905	\$0.181	81903
τ	0–0.01	\$51	\$0.0102	1040.4
d_1	0.3–1	\$18	\$0.0036	0.0264
d_2	0.3–1	\$18	\$0.0036	0.0264
I_2	0–0.0135	\$10	\$0.002	21.9479
a_1	0.15–1	\$10	\$0.002	0.0055

We consider two control problems relating to the transmission of mastitis-causing pathogens within seven herds: in the first, the herds are controlled separately with different control strategies ap-

plied. More formally, controls $\mathbf{u}^1, \dots, \mathbf{u}^7$ are sought that minimise the associated cost criteria:

$$\min_{\mathbf{u}^1 \in \mathcal{U}^1} J^1(\mathbf{u}^1), \dots, \min_{\mathbf{u}^7 \in \mathcal{U}^7} J^7(\mathbf{u}^7). \quad (10)$$

In the second problem, a common strategy is applied across all of the herds, that is, controls $\hat{\mathbf{u}}^1, \dots, \hat{\mathbf{u}}^7$ are sought that minimise a linear combination of the herd cost criteria:

$$\min \left\{ \sum_{i=1}^7 w_i J^i(\hat{\mathbf{u}}^i) : \hat{u}_j^1 = \dots = \hat{u}_j^7, j = 3 \dots 9 \right.$$

$$\left. \text{for } p = 0, 1 \quad \hat{u}_j^i = 1 - p(1 - \hat{m}_j^i) \quad j = 1, 2 \right\} \quad (11)$$

where $w_i > 0$ are weights that can be used to normalise $J^i(\mathbf{u}_*)$ to distribute cost evenly over the herds, or to assign the relative importance of each. Note that the last 7 components of the controls are common across the herds and there is a common policy of whether to apply PMTD, where $p = 0$ corresponds to no PMTD and $p = 1$ corresponds to PMTD being applied in (11).

Since the controls are present in the model only as parameters, these control problems can be tackled using commonly available parameter estimation algorithms.

4. SOLVING THE CONTROL PROBLEMS

Parameter fitting for the two control problems was performed within the software package FACSIMILE (MCPA Software, UK). The control parameter values obtained for each herd, in the case of the first problem, and the common control across all herds, for the second, are given in Table 5. Since the performance index for each herd gives a relative cost, the weights, w_i , in (11) were set equal to 1 for each herd.

Table 5. Values for control parameters that minimise the appropriate cost

	m_1	m_2	q_1	c_1	τ	d_1	d_2	I_2	a_1
\mathbf{u}^1	≈ 0	0.21	0	0.0097	0.01	0.3	0.3	0	1.00
\mathbf{u}^2	0.23	0.37	0	0.0068	0.01	0.3	0.3	0	1.00
\mathbf{u}^3	0.36	0.56	0	0.0037	0.01	0.3	0.3	0	0.15
\mathbf{u}^4	0.46	0.16	0	0.0069	0.01	0.3	0.3	0	1.00
\mathbf{u}^5	0.04	0.36	0	0.0132	0.01	0.3	0.3	0	1.00
\mathbf{u}^6	0.38	0.69	0	0.0071	0.01	0.3	0.3	0	1.00
\mathbf{u}^7	0.32	0.001	0	0.0048	0.01	0.3	0.3	0	0.50
$\hat{\mathbf{u}}^i$	\hat{m}_1^i	\hat{m}_2^i	0	0.0081	0.01	0.3	0.3	0	1

With the exception of quarter drying (q_1), culling (c_1), inoculation (I_2) and antibody treatment (a_1), the controls are applied to their maximum extent. With a fixed value of q_1 throughout the period of intervention, a nonzero value would lead to prohibitive costs compared to the benefits of quarter drying. Similarly, inoculation leads to infection with minor pathogens, from which there is no ready route of recovery, and any reduction

in major pathogen infections does not offset the costs associated with this.

The fitted values for c_1 for the individual herds correspond to the best ones necessary to minimise costs associated with infection, whilst balancing costs resulting from culling. These values vary quite widely, from a minimum of 0.0037 day^{-1} (Herd 3) to a maximum of 0.0132 day^{-1} (Herd 5), with a standard deviation of 0.0032 day^{-1} and a mean of 0.0075 day^{-1} . With a common control strategy across all herds, a culling rate of 0.0081 day^{-1} is obtained, which corresponds to a mean time from major pathogen infection to cull of $1/c_1 = 123$ days.

The steady states achieved as a result of the applied control measures (\mathbf{u}^i or $\hat{\mathbf{u}}^i$) are given in Table 6, with the corresponding value of the cost function $J^i(\mathbf{u}^i)$ or $J^i(\hat{\mathbf{u}}^i)$. For comparison the value of the cost function, $J^i(\mathbf{u}_*)$, when no controls are applied is also given. It should be noted that the disease-free state \mathbf{z}_* is not a steady state for any herd with any control vector $\mathbf{u}^i \in \Omega^i$.

Table 6. Steady states resulting for each of the herds resulting from \mathbf{u}^i or $\hat{\mathbf{u}}^i$

Herd	1	2	3	4	5	6	7
\bar{x}_{12}	0.769	0.692	0.821	0.747	0.737	0.634	0.840
\bar{y}_1	0.000	0.001	0.002	0.003	0.002	0.002	0.001
\bar{y}_2	0.229	0.304	0.176	0.242	0.259	0.358	0.156
\bar{y}_{12}	0.001	0.003	0.001	0.001	0.002	0.002	0.001
$J^i(\mathbf{u}^i)$	159	211	103	189	156	228	113
$J^i(\mathbf{u}_*)$	888	721	409	837	1096	605	657
Common strategy							
\bar{x}_{12}	0.769	0.693	0.822	0.747	0.735	0.635	0.838
\bar{y}_1	0.000	0.001	0.002	0.003	0.002	0.002	0.001
\bar{y}_2	0.229	0.304	0.175	0.242	0.261	0.357	0.156
\bar{y}_{12}	0.001	0.003	0.001	0.001	0.002	0.001	0.001
$J^i(\hat{\mathbf{u}}^i)$	159	211	105	189	160	228	114

The results for Herd 5 show the greatest improvement in the cost function (from 1096 to 156, an 85.8% decrease), while Herd 6 exhibits the smallest decrease in cost (from 605 to 228, a 62.4% decrease). There is a mean decrease of 76.6% (standard deviation, SD, of 8.1) in cost across herds as a result of the individual herd strategies.

Applying a common control strategy across all herds a similar situation is seen; namely, the greatest decrease in cost occurs for Herd 5 (85.4%) and least for Herd 6 (62.4%). There is a mean decrease in cost across herds of 76.4% (SD 8.0) resulting from the common strategy. The overall cost, obtained from summing the costs associated with each herd, increases by 0.7% as a result of applying a common strategy, compared to applying ones individually tailored to each herd.

Figures 2 and 3 show the output of model simulations for Herd 5 in the case of no control and individual control, respectively. The output

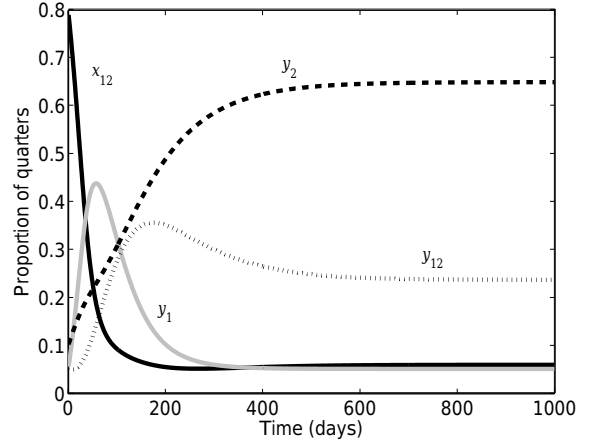


Fig. 2. Simulated output of model with no controls applied, Herd 5.

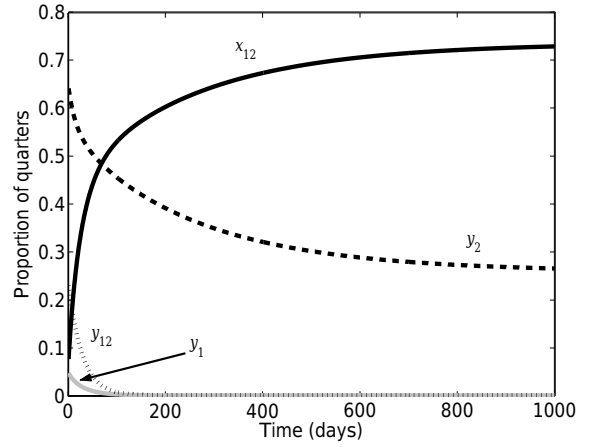


Fig. 3. Simulated output of model with individual control strategy applied, Herd 5.

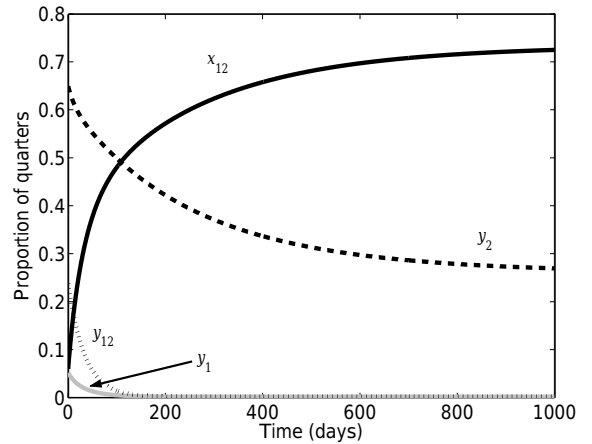


Fig. 4. Simulated output of model with control strategy common to all herds, except Herd 5, is applied to Herd 5.

of simulation with common control is indistinguishable from that for individual control. Even for Herd 3, which exhibits the greatest variation in cost between individual and common strategies, there is no visual difference between the simulated output of the model for the two controls.

These results suggest that there is only a small decrease in performance when the control strategy is tuned for simultaneous control of multiple, heterogeneous herds. In practice, one might only tune a control strategy to a number of ‘seen’ herds and then apply this strategy to ‘unseen’ herds too. To test this, a common control strategy, \tilde{u}^i , was determined for all of the herds except for Herd 5, since this has the largest cost in the absence of controls. The common control strategy was then applied to Herd 5, the output of which is shown in Figure 4. The results are displayed in Table 7.

Table 7. Results of applying control strategy developed for all herds except Herd 5 to each of the herds

\tilde{u}^i	m_1 \hat{m}_1^i	m_2 \hat{m}_2^i	q_1 0	c_1 0.0068	τ 0.01	d_1 0.3	d_2 0.3	I_2 0	a_1 1
Herd	1	2	3	4	5	6	7		
\bar{x}_{12}	0.769	0.692	0.822	0.747	0.735	0.634	0.838		
\bar{y}_1	0.000	0.001	0.003	0.003	0.002	0.002	0.001		
\bar{y}_2	0.229	0.304	0.175	0.242	0.261	0.358	0.156		
\bar{y}_{12}	0.001	0.003	0.001	0.001	0.002	0.002	0.001		
$J^i(\tilde{u}^i)$	160	211	104	189	163	228	113		

There are only small differences to the results for each herd as a result of determining the control from 6 herds. Even for Herd 5, which again has the greatest decrease in cost (85.1%), the results are similar to those obtained for a strategy common for all 7 herds. There is a mean decrease in cost across herds of 76.4% (8.0 SD) resulting from the new strategy, which is almost identical to the previous common strategy. The overall cost (sum of the costs associated with each herd) increases by 0.8% as a result of applying a common strategy, compared to applying ones individually tailored to each herd.

5. CONCLUSIONS

Parameter fitting was used as a tool to determine control strategies for preventing the transmission of mastitis-causing pathogens in dairy herds. Two control problems were considered: the first was to determine individual strategies for the seven herds, which yielded controls that resulted in significant decreases in major pathogen infected quarters (from a mean of 9.63%, SD 9.35, to a mean of 0.31%, SD 0.12); the second problem was to determine a common strategy across seven herds, which resulted in a comparable decrease in major pathogen infected quarters (from a mean of 9.63%, SD 9.35, to a mean of 0.30%, SD 0.12). It would appear from the results in this paper that a strategy developed simultaneously for a number of herds does not perform significantly worse than if individual strategies were obtained.

A common feature across all control strategies was the absence of any inoculation or quarter drying,

demonstrating that the benefits of these measures do not outweigh their cost. However, this might be an artifact of the length of time of intervention and the fixed value for the control parameters. It needs to be investigated whether a strategy that allows different values, particularly in the transient phase, uses these controls and achieves a greater reduction in cost.

The principal differences between the controls is the value of the culling rate. Generally, a higher rate is needed if the initial cost, with no controls applied, is high. Parameter fitting, as applied in this paper, yields values for all of the control parameters that balances the costs associated with infection and treatment.

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