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A dynamic, optimal disease control model for foot-and-mouth disease: I. Model description

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Abstract

A dynamic optimization model was developed and used to evaluate alternative foot-and-mouth disease (FMD) control strategies. The model chose daily control strategies of depopulation and vaccination that minimized total regional cost for the entire epidemic duration, given disease dynamics and resource constraints. The disease dynamics and the impacts of control strategies on these dynamics were characterized in a set of difference equations; effects of movement restrictions on the disease dynamics were also considered. The model was applied to a three-county region in the Central Valley of California; the epidemic relationships were parameterized and validated using the information obtained from an FMD simulation model developed for the same region. The optimization model enables more efficient searches for desirable control strategies by considering all strategies simultaneously, providing the simulation

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model with optimization results to direct it in generating detailed predictions of potential FMD outbreaks.

Keywords: Optimization modeling; Infectious livestock disease; Foot-and-mouth disease; Disease control strategies; Economic analysis

1. Introduction

Management of contagious livestock diseases such as foot-and-mouth disease (FMD) is a complex and dynamic decision problem (Morris et al., 2002; Speers et al., 2004). A decision maker faces tradeoffs between effectiveness and cost of different control options (Barnett et al., 2002; Morris et al., 2002; Bates et al., 2003a). Radical or comprehensive measures can quickly contain an epidemic but often with high costs and economic disruptions, while conservative or limited responses increase the chance of the epidemic growing in duration and size and potentially becoming more costly or difficult to control. Physical and manpower capacities also limit the scope and scale of disease control options (Morris et al., 2002). In preparation for a potential outbreak, decision makers would benefit from knowing the expected epidemic and economic outcomes of alternative disease control strategies under existing and alternative disease control capacities.

Studies on the effectiveness of different disease control strategies (Morris et al., 2001; Tomassen et al., 2002; Bates et al., 2003a; Kao, 2003; Schoenbaum and Disney, 2003) typically used epidemic simulation models, and cost assessments were made on simulated outbreaks. For example, Bates et al. (2003a) evaluated cost-effectiveness of different FMD control strategies using a simulation model developed for a three-county region in the Central Valley of California. Schoenbaum and Disney (2003) simulated the consequences of alternative control strategies in a hypothetical FMD outbreak in the US and estimated national-level economic impacts, including potential losses associated with lost red-meat export opportunities.

These simulation-based studies typically consider pre-determined levels of disease control measures. For example, in Bates et al. (2003a), the radius of ring vaccination for FMD was specified at 5, 10, 25, and 50 km and that of ring depopulation at 1, 3, and 5 km, and cost-benefit analyses were performed on the simulation output under each specification. This approach allows evaluation of only a subset of all possible control strategies, leaving the possibility of missing the optimal one. Moreover, specifications of strategy parameters are usually fixed for an entire simulation run, ruling out flexible strategies that can vary over time. For example, aggressive preemptive depopulation may be most effective in early stages of an FMD outbreak, while in later stages vaccination may be preferable.

Optimization modeling, a common approach in economics, overcomes the above limitations. An example of optimization modeling is least-cost feed ration identification (e.g., Heady and Bhide, 1983). In an optimization model, the levels of decision variables are determined *endogenously* (by the model and not the analyst) in the process of maximizing or minimizing the objective function, e.g., profit maximization or cost minimization. For example, the optimal radius for a ring vaccination strategy would be determined in the model, rather than the researcher *exogenously* specifying alternative radius levels. Furthermore, optimization models can generate dynamically optimal solutions because flexible daily strategies can be accommodated readily. The optimization approach was adopted for the problem of infectious livestock disease control in the linear programming models by Carpenter (1976) and Carpenter and Howitt (1980). With advances in dynamic optimization theory and microcomputer processing power, limitations identified in these early applications, such as representation of realistic disease dynamics, can now be addressed. However, to our knowledge, there is no recent published application of optimization technique to livestock disease control problems.

In this study, the FMD management problem was modeled in a dynamic cost-minimization framework, formulated as a discrete-time optimal control problem. The model solved for daily combinations of FMD control strategies (depopulation and vaccination) while minimizing the total regional cost for the entire epidemic. Although the optimization approach considerably increases computational complexity, reasonably detailed epidemiology relationships were incorporated in the model. The model allowed efficient search for desirable FMD control strategies by considering all strategies simultaneously. The model was applied to a three-county region in the Central Valley of California (Fresno, Kings, and Tulare counties).

Table 1
List of parameters and variables used in an optimal FMD-control model

Symbol		Description
Herd number variables		
Prevalence	Incidence	
P^{S}		Susceptible herd
P^{L}	I^{L}	Latently infected herd
	$I^{L}_{i,j}$	Latently infected herd from herd type i to j
P^{SI}	I^{SI}	Subclinically infectious herd
P^{CI}	I^{CI}	Clinically infectious herd
P^{V}		Vaccinated herd
P^{I}		Total infectious herds ($P^{SI} + P^{CI}$)
N		Total herd population ($P^{S} + P^{L} + P^{SI} + P^{CI} + P^{V}$)
Epidemic parameters		
β^{ij}		Daily disease transmission parameter from herd type i to j
λ		Duration of latent period (days)
σ		Duration of subclinically infectious period (days)
Decision variables		
r^{B}		Rate of baseline slaughter (% of herds/day)
r^{P}		Rate of preemptive slaughter (% of herds/day)
v		Rate of vaccination (% of herds/day)

Note: Subscripts for herd type (i) and/or time (t) are suppressed.

2. Materials and methods

2.1. Model formulation

A population of FMD-susceptible livestock herds and its subgroups were considered. In our application, livestock herds in the study region were grouped according to operation types (beef, dairy, swine, etc.). The disease dynamics were modeled for the herds in each operation type and on a daily basis. For herd type i on day t, prevalence (the number of herds in each disease status) was denoted as follows: susceptible ($P^{\mathrm{S}}_{i,t}$), latently infected ($P^{\mathrm{L}}_{i,t}$), subclinically infectious ($P^{\mathrm{SI}}_{i,t}$), clinically infectious ($P^{\mathrm{CI}}_{i,t}$), and vaccinated ($P^{\mathrm{V}}_{i,t}$) (the list and description of all parameters and variables included in the model is provided in Table 1). Disease control options considered included: depopulation of FMD-infected herds (baseline depopulation), preemptive depopulation of potentially infected herds, vaccination of susceptible herds, and movement restrictions on animals, vehicles, and personnel.

Due to the daily discrete-time specification, the following order of events within a day was assumed: (1) the prevalence variables representing the number of herds in each status at the beginning of the day; (2) a herd's transition in disease status, i.e., from latently infected to subclinically infectious and from subclinically to clinically infectious; (3) latent incidence; and then (4) implementation of depopulation and vaccination controls.

The disease dynamics and the impacts of control actions on the dynamics were represented in a set of difference equations. For herd type i, the daily dynamics for susceptible herds were modeled as:

$$P^{\mathrm{S}}_{i,t+1} = (1 - r^{\mathrm{P}}_{i,t} - v_{i,t})(P^{\mathrm{S}}_{i,t} - I^{\mathrm{L}}_{i,t}), \tag{1}$$

where $r^{\mathrm{P}}_{i,t}$ and $v_{i,t}$ denote the proportion of herds that is preemptively depopulated and vaccinated, respectively, and $I^{\mathrm{L}}_{i,t}$ is the incidence of latent infections. Latent incidence in herd type j on day t was modeled as:

$$I^{\mathrm{L}}_{j,t} = \sum_i I^{\mathrm{L}}_{i,j,t} = P^{\mathrm{S}}_{j,t} \sum_i \beta^{ij} \frac{P^{\mathrm{I}}_{i,t}}{N_{i,t}}, \tag{2}$$

where $I^{\mathrm{L}}_{i,j,t}$ is the latent incidence in herd type j due to transmission from herd type i; β^{ij} is the disease transmission parameter from herd type i to herd type j; $P^{\mathrm{I}}_{i,t}$ is the prevalence of infectious herds ($P^{\mathrm{SI}}_{i,t} + P^{\mathrm{CI}}_{i,t}$); and $N_{i,t}$ is the total number of herds ($P^{\mathrm{S}}_{i,t} + P^{\mathrm{L}}_{i,t} + P^{\mathrm{SI}}_{i,t} + P^{\mathrm{CI}}_{i,t} + P^{\mathrm{V}}_{i,t}$).

The daily dynamics for latently infected herds were modeled as:

$$P^{\mathrm{L}}_{i,t+1} = (1 - r^{\mathrm{P}}_{i,t} - v_{i,t})(P^{\mathrm{L}}_{i,t} + I^{\mathrm{L}}_{i,t} - I^{\mathrm{SI}}_{i,t}), \tag{3}$$

where

$$I^{\mathrm{SI}}_{i,t} = \left(\prod_{k=1}^{\lambda_i}(1 - r^{\mathrm{P}}_{i,t-k} - v_{i,t-k})\right) I^{\mathrm{L}}_{i,t-\lambda_i}, \quad t - \lambda_i \geq 0, \tag{4}$$

denotes the subclinically-infectious incidence on day t, with λ_i being the duration of latent period for type i herds (if $t - \lambda_i < 0$, then $I^{\mathrm{SI}}_{i,t} = 0$).

The daily dynamics for subclinically infectious herds were characterized as:

$$P^{\mathrm{SI}}_{i,t+1} = (1 - r^{\mathrm{P}}_{i,t} - v_{i,t})(P^{\mathrm{SI}}_{i,t} + I^{\mathrm{SI}}_{i,t} - I^{\mathrm{CI}}_{i,t}), \tag{5}$$

where

$$I^{\mathrm{CI}}_{i,t} = \left(\prod_{k=1}^{\sigma_i}(1 - r^{\mathrm{P}}_{i,t-k} - v_{i,t-k})\right) I^{\mathrm{SI}}_{i,t-\sigma_i}, \quad t - (\lambda_i + \sigma_i) \geq 0, \tag{6}$$

denotes the clinically-infectious incidence on day t, with σ_i being the subclinically-infectious duration for type i herds (if $t - (\lambda_i + \sigma_i) < 0$, then $I^{\mathrm{CI}}_{i,t} = 0$).

The daily dynamics of clinically infectious herds were modeled as:

$$P^{\mathrm{CI}}_{i,t+1} = (1 - r^{\mathrm{B}}_{i,t})(P^{\mathrm{CI}}_{i,t} + I^{\mathrm{CI}}_{i,t}), \tag{7}$$

where $r^{\mathrm{B}}_{i,t}$ denotes the proportion of clinically-infected herds that is depopulated on day t. Finally, the daily dynamics of vaccinated herds were modeled as:

$$P^{\mathrm{V}}_{i,t+1} = P^{\mathrm{V}}_{i,t} + v_{i,t}(P^{\mathrm{S}}_{i,t} + P^{\mathrm{L}}_{i,t} + P^{\mathrm{SI}}_{i,t} - I^{\mathrm{CI}}_{i,t}). \tag{8}$$

In case of an actual FMD outbreak, decision makers may want to improve the efficiency of preemptive depopulation and vaccination by applying these strategies to a target sub-population. For preemptive depopulation, the decision maker would clearly like to target subclinically-infected herds. For vaccination, determining the target is not trivial because vaccination can be used both to protect susceptible herds and to reduce virus shedding by infected herds (Golde et al., 2005). In practice, without an accurate, real-time test, only clinically-infected or vaccinated herds can be differentiated from other herds. A practical alternative may be to apply these strategies to dangerous contacts (DCs) and contiguous premises (CPs) to infected premises, or other herds considered at high risk of infection (Bates et al., 2003b; Honhold et al., 2004). However, without spatially explicit treatment of herds, the optimization model is unable to accommodate such targeting of control strategies. Accordingly, in this model, preemptive depopulation and vaccination were applied uniformly to the total of susceptible herds and subclinically-infected, non-vaccinated herds $(P^{\mathrm{S}}_{i,t} + P^{\mathrm{L}}_{i,t} + P^{\mathrm{SI}}_{i,t})$.

While depopulation and vaccination affect the latent incidence by changing the number and proportion of susceptible and infectious herds, movement restrictions on animals and other vectors also reduce latent incidence by decreasing direct and indirect contacts between herds (Bates et al., 2001). In this model, impacts of movement restrictions were specified in terms of reduced values of disease transmission parameter β^{ij}. While other control strategies ($r^{\mathrm{B}}_{i,t}$, $r^{\mathrm{P}}_{i,t}$, $v_{i,t}$) are choice variables whose levels are endogenously determined in the cost-minimization process, β^{ij}'s are treated as exogenously-given parameters.

The objective of the problem was to minimize total regional cost for an entire epidemic by choosing the levels of control strategies ($r^{\mathrm{B}}_{i,t}$, $r^{\mathrm{P}}_{i,t}$, $v_{i,t}$) for all i and t. That is, the cost-minimizing depopulation and vaccination levels are chosen for each herd type on a daily basis. The disease dynamics Eqs. (1)–(8) serve as constraints of the problem. Explicit constraints on disease control resource availability may also be included. The problem was set up for a sufficient number of days to cover an entire epidemic. Detailed cost specifications are provided in the parameterization section that follows.

2.2. Model parameterization

2.2.1. Herds

The conceptual model formulated in the previous subsection was numerically applied to herds in a three-county region in the Central Valley of California (Fresno, Kings, and Tulare counties). An FMD simulation model (Bates et al., 2003b) developed for the same region is available and the specification of the current model draws on a modification of the simulation model. In the development of the simulation model, 2238 herds and 5 salesyards were identified in the region. The simulation model treats each of them individually in a spatially explicit manner. In the current optimization model, the herds and the salesyards were aggregated into six groups based on operation types: (1) beef, (2) dairy, (3) swine, (4) sheep and goat, (5) backyard herds, and (6) salesyards. The herd types were indexed with subscripts or superscripts i and j.

According to the 2002 Census of Agriculture, published by National Agricultural Statistics Service (NASS-USDA, 2004), the three-county region houses about 1.8 million head of FMD-susceptible livestock (cattle, hogs, sheep, and goats). Mean herd sizes for commercial operations (farms with at least 10 cattle or 25 head of other livestock) were estimated using NASS data (Table 2). NASS provides beef/dairy distinction only for the inventory of breeding cows and replacement heifers, and assumptions were made on the distribution of other types of cattle. It was assumed that beef cattle include bull and heifer calves, other heifers, steers, and bulls, while dairy cattle include heifer calves and bulls, in addition to breeding cows and replacement heifers. A backyard herd was assumed to contain an average of 5 animals.

In this model, a salesyard was considered as a transitory destination where animals come and go during the day but do not stay overnight. Because depopulation and vaccination were assumed to be implemented at the end of each day, these control measures are not applicable to animals at salesyards. Thus, average herd size was not defined for this herd type (Table 2).

Table 2
Herd-type-specific parameters used in an optimal FMD-control model

	Herd type (i)					
	Beef	Dairy	Swine	Sheep and goat	Backyard	Salesyard
Herd number[a]	664	576	79	131	788	5
Mean herd size[b]	853	1727	2519	558	5	na
Mean herd-level latent period[c] (days) (λ_i)	4	4	6	4	4	na
Mean herd-level subclinically infectious period[c] (days) (σ_i)	3	3	5	3	3	na

na: Not applicable.

[a] Drawn from the three-county survey (Bates et al., 2001).

[b] Calculated using data from 2002 Census of Agriculture (NASS-USDA, 2004).

[c] Based on calculations from experimental transmission trials (Bates et al., 2003b).

2.2.2. Epidemic parameters

Parameterization of epidemic relationships was based on the FMD simulation model (Bates et al., 2003b). For the herd-level duration of latent period (λ_i) and subclinically-infectious period (σ_i), the mean values from the probability distributions used in the simulation model were used (Table 2). On average, herds show clinical signs 7–11 days after infection. Unlike other herds, a salesyard was assumed to become infectious immediately after getting infected, and an infected salesyard was assumed to remain infectious until it was closed. Thus, latent and subclinically-infectious periods were not defined, and closure was the only control strategy applied to salesyards. For backyard operations, only baseline depopulation was applied. Movement restrictions were implemented for all herd types.

Disease transmission parameters (β^{ij}) were estimated for transmission within the same herd type and between different herd types using output generated with the simulation model. Two datasets were generated: with and without movement restrictions. For movement restrictions, it was assumed that the entire three-county region was placed under a "surveillance zone," where all animal movements are stopped while movements of other vectors such as humans and vehicles are reduced and biosecurity increased. It was also assumed that all five salesyards in the region were closed under the movement-restriction policy. In both cases, the simulation model was run for 180 days with a randomly selected index case and without depopulation or vaccination control strategies. The procedure was repeated for a total of 100 times, generating 18,000 data points. Observations on I_i^{L}, P_i^{S}, P_i^{I}, and N_i were stored and indexed with $l = 1, \ldots, 18{,}000$.

Following Eq. (2), the estimation equation was specified as:

$$I_{i,j,l}^{\mathrm{L}} = \beta^{ij} P_{j,l}^{\mathrm{S}} \frac{P_{i,l}^{\mathrm{I}}}{N_{i,l}} + \varepsilon_{i,j,l}, \tag{9}$$

where $\varepsilon_{i,j,l}$ is the error term, assumed to be a white noise. A first-order autoregressive error was also specified, but the prediction did not improve. In total, two sets of 36 β^{ij}'s were estimated.

The β^{ij} coefficients were first estimated by least squares, but numerical implementation of Eq. (2) with the estimated coefficients resulted in some cases of larger incidence of latent infection than susceptible prevalence (i.e., $I_i^{\mathrm{L}} > P_i^{\mathrm{S}}$). In order to ensure sensible predictions, restrictions were imposed such that $0 \leq \beta^{ij} \leq 1$, and the coefficients were estimated using the generalized maximum entropy (GME) estimation technique (Golan et al., 1996). Imposing restrictions on coefficients is conveniently handled in GME estimation, where a feasible range, called the "support space," is specified for each coefficient to estimate. Movement restrictions were expected to reduce β^{ij} values relative to no movement restrictions. Accordingly, the support space for β^{ij} under movement restrictions was modified using the previous β^{ij} estimates under no movement restrictions as its upper bound. The support space for the error term allows the errors to be between plus and minus the maximum value of the dependent variable.

GME returned β^{ij} coefficient estimates that generate epidemic curves very similar to those generated by the simulation model. (Overall goodness of fit of the model is examined below.) The estimated coefficients are listed in Tables 3a and 3b as well as the 90%

Table 3a
Generalized maximum entropy (GME) estimates of daily FMD-transmission parameters β^{ij} in Eq. (9) with simulation output used as data, without movement restrictions

Herd type *ji*	Beef	Dairy	Swine	Sheep/goat	Backyard	Salesyard
Beef	0.009 (0.000, 0.017)	0.026 (0.000, 0.049)	0.019 (0.000, 0.035)	0.009 (0.000, 0.018)	0.008 (0.000, 0.014)	0.676 (0.000, 0.966)
Dairy	0.031 (0.000, 0.058)	0.345 (0.000, 0.647)	0.157 (0.000, 0.295)	0.052 (0.000, 0.097)	0.042 (0.000, 0.079)	0.781 (0.052, 0.975)
Swine	0.003 (0.000, 0.005)	0.021 (0.000, 0.039)	0.014 (0.000, 0.026)	0.005 (0.000, 0.009)	0.004 (0.000, 0.007)	0.786 (0.062, 0.976)
Sheep/goat	0.002 (0.000, 0.004)	0.011 (0.000, 0.021)	0.014 (0.000, 0.027)	0.006 (0.000, 0.011)	0.002 (0.000, 0.004)	0.631 (0.000, 0.961)
Backyard	0.007 (0.000, 0.014)	0.046 (0.000, 0.087)	0.030 (0.000, 0.056)	0.011 (0.000, 0.020)	0.012 (0.000, 0.023)	0.548 (0.000, 0.948)
Salesyard	0.000 (0.000, 0.000)	0.004 (0.000, 0.007)	0.002 (0.000, 0.003)	0.001 (0.000, 0.002)	0.001 (0.000, 0.001)	0.579 (0.000, 0.953)

90% Probability intervals in parentheses, calculated by linear interpolation between the support values.

Table 3b

Generalized maximum entropy (GME) estimates of daily FMD-transmission parameters β^{ij} in Eq. (9) with simulation output used as data, with movement restrictions

Herd type *ji*	Beef	Dairy	Swine	Sheep/goat	Backyard	Salesyard
Beef	0.002 (0.000, 0.006)	0.008 (0.000, 0.021)	0.008 (0.000, 0.017)	0.003 (0.000, 0.008)	0.002 (0.000, 0.006)	0
Dairy	0.007 (0.000, 0.022)	0.113 (0.000, 0.295)	0.049 (0.000, 0.131)	0.013 (0.000, 0.039)	0.010 (0.000, 0.031)	0
Swine	0.001 (0.000, 0.002)	0.008 (0.000, 0.019)	0.005 (0.000, 0.012)	0.002 (0.000, 0.004)	0.001 (0.000, 0.003)	0
Sheep/goat	0.001 (0.000, 0.002)	0.003 (0.000, 0.009)	0.006 (0.000, 0.013)	0.001 (0.000, 0.004)	0.001 (0.000, 0.002)	0
Backyard	0.002 (0.000, 0.005)	0.009 (0.000, 0.031)	0.008 (0.000, 0.024)	0.003 (0.000, 0.008)	0.002 (0.000, 0.007)	0
Salesyard	0	0	0	0	0	0

90% Probability intervals in parentheses, calculated by linear interpolation between the support values.

Table 4
Herd-type-specific value parameters used in an optimal FMD-control model

	Herd type (*i*)					
	Beef	Dairy	Swine	Sheep and goat	Backyard	Salesyard
Unit value ($/head)	598[a]	1,669[a]	130[b]	121[b]	0	na
Herd value ($/herd)	509,830	2,881,919	327,470	66,960	0	na
Euthanasia/disposal cost ($/head)	16.50[c]	16.50[c]	4.40[d]	2.31[d]	7.73[d]	na
Cleaning/disinfection cost[e] ($/herd)	9,513[e]	31,710[e]	9,513[e]	9,513[e]	5,000[c]	31,710[e]
Vaccination cost 1[c] ($/head)	6	6	6	6	na	na
Vaccination cost 2[e] ($/herd)	885	664	664	885	na	na

na: Not applicable.
[a] Estimated using USDA (2005) and NASS-USDA (2005).
[b] Drawn from USDA (2005).
[c] Drawn from Schoenbaum and Disney (2003).
[d] Calculated based on Schoenbaum and Disney (2003) and USDA (2006).
[e] Calculated based on Bates et al. (2003a).

probability intervals that were calculated by linear interpolation between the support values and the corresponding probability estimates. According to the β^{ij} estimates, movement restrictions reduce disease transmission parameter values by 55–82%, with the exception of salesyards where it was reduced 100%.

2.2.3. *Costs*

Only the costs incurred at the three-county level were included in this study. The costs included in the current model have three components: (1) value of livestock herds depopulated for disease control, (2) direct costs of disease control, and (3) daily operational costs during the epidemic that the local administration incurs. The costs taken into account in the optimization model are identical to direct government costs if the government were to fully compensate producers for lost livestock assets, i.e., if indemnity costs reflect the true livestock values.

Unit values of commercial livestock used to calculate the value of slaughtered livestock were obtained from a publication by US Department of Agriculture (USDA, 2005). Figures for California in 2004 were used (Table 4). The sheep unit value was used for the "sheep and goat" herd type. USDA (2005) provides an average unit value of all cattle in California ($1130/head). In order to obtain separate unit values for beef and dairy cattle, the value of total cattle inventory ($6.1 billion) was split according to the ratio of 2004 gross farm incomes for the two sectors (NASS-USDA, 2005) and then divided by the respective total inventory in California. For each commercial herd type, the unit livestock value was multiplied by the mean herd size to obtain the mean herd value. Due to a lack of information, no monetary values were assigned to backyard herds. Because salesyards were assumed not to have animals at the end of the day, assignment of values to salesyards was not applicable.

Direct expenses related to depopulation and vaccination were included in the model (Table 4). Following Bates et al. (2003a) and Schoenbaum and Disney (2003), these costs have per-animal and per-herd components. For each slaughtered animal, euthanasia and carcass disposal (E&D) cost was applied; for each depopulated herd, cleaning and disinfection (C&D) cost was applied. For E&D cost, the figure reported in Schoenbaum and Disney (2003) ($16.50/head) was used for cattle and is scaled down according to the relative live-weights (USDA, 2006) for animals in other herd types. For the unit live-weight of a backyard animal, a simple average of that of other species was used.

C&D cost parameters for commercial herds were derived from the estimates for a typical dairy herd found in Bates et al. (2003a). Bates et al. (2003a) estimated that the total cost of C&D and E&D for a typical dairy operation in the region is $60,205. By subtracting our assumed E&D cost for a dairy herd ($28,495 = $16.50/head × 1727 head), the estimate of per-herd C&D cost for a dairy herd was $31,710. Following Bates et al. (2003a), C&D cost for other commercial herd types was assumed to be 30% of that for a dairy herd. For a backyard herd, the C&D cost for a "small herd" in Schoenbaum and Disney (2003) was used. C&D cost was also applied to all infected salesyards, the level of which was assumed to be the same as that for a dairy herd.

The per-head component of vaccination cost was set at $6/head as in Schoenbaum and Disney (2003). For per-herd vaccination cost, the following was assumed. Bates et al. (2003a) estimated that the cost of a vaccination team is $2656/day. Given the intensive nature of dairy and swine operations and extensive nature of beef cattle and small ruminant production in California, it was assumed that such a full-time team could vaccinate 3 beef/sheep and goat herds and 4 dairy/swine herds per day. Because vaccination was not applied to backyard herds in this model, vaccination cost parameters were not defined for this herd type.

Finally, daily operational costs that the local government incurs during the epidemic were included. The estimate was obtained in an FMD simulation exercise "Operation Aphtosa" in Tulare, California, November 2004 (Jonas and Speers, 2004). The figure $157,968/day was considered to include the cost of enforcing movement restrictions. The daily operational cost was added to the other costs from the day the control measures are implemented until the epidemic was over.

2.3. Model implementation

The model was implemented using non-linear programming software GAMS (GAMS Development Corporation, Washington, D.C.). Several notes must be made on the technical specifications. First, because control measures were applied to proportions of herds in the model, the solutions may contain fractions of herds, e.g., 2.5 herds to depopulate. While integer programming techniques are available, it was not practical in this application given the size of the problem. All numbers of herds and days reported in this study were rounded to the closest integers. Another implication was that a herd fraction can still be infected at the end of the optimization duration. Thus, the epidemic was defined to be over when the total number of infected herds $\sum_i (P^{\mathrm{L}}_{i,t} + P^{\mathrm{SI}}_{i,t} + P^{\mathrm{CI}}_{i,t})$ declines below one.

In order to obtain sensible solutions, the value of infected herds was included in the objective function instead of that of depopulated herds. This specification does not bias optimization results because all infected herds are expected to be depopulated once

Table 5
Comparison of optimization and simulation model outputs, with baseline slaughter and movement restrictions

	Index case					
	Beef	Dairy	Swine	Sheep and goat	Backyard	Salesyard
1. Epidemic duration (days)						
Optimization	38	44	43	42	37	52
Simulation						
Mean	34	52	44	40	40	58
Median	30	51	43	40	38	57
95% PI[a]	(23, 62)	(32, 78)	(30, 69)	(23, 70)	(23, 69)	(47, 76)
2. Cumulative incidence (herds)						
Optimization	22	54	45	43	19	218
Simulation						
Mean	11	52	21	23	20	209
Median	8	44	16	13	11	213
95% PI[a]	(6, 38)	(9, 146)	(8, 66)	(6, 82)	(6, 76)	(44, 360)

[a] Probability interval.

diagnosed. When vaccination was implemented, however, there were differentials between the number of infected herds and the number of herds to be depopulated, but the magnitude of this discrepancy was small.

3. Results

3.1. Model validation

The optimization model output was validated against the epidemic simulation model (Bates et al., 2003b). Output on epidemic duration and cumulative incidence from the two models were compared, and the results from the optimization model were tested whether they fell within the 95% probability intervals formed with the results of the simulation model. For the results of the two models to be directly comparable, only baseline depopulation (depopulation of clinically-infected herds) and movement restrictions were introduced. The simulation model was run with a randomly selected index herd from each of the six herd types; for each index herd type, the model was run 1000 times. The optimization model was also run with an index case from each herd type. Movement restrictions were specified in an equivalent way in the two models. In both models, all control strategies were implemented on day 21 and after.

The results suggest that the two models produced a very similar output (Table 5). In comparing the output of the optimization model with the means and medians of the simulation output, the differences in epidemic duration were within 8 days, with the largest differences observed when beef, dairy, or salesyard was the index case. The optimization model appeared to overestimate the cumulative incidence up to 30 herds. The difference was the largest when a swine or sheep and goat herd was the index case. However, in all cases, the results of the optimization model fell within the 95% probability intervals of the simulation output.

Table 6
Selected optimal FMD-control model results under alternative objective functions when index case is a salesyard, under vaccinate-to-live policy

	Objective function		
	Cost minimization	Infected herd minimization with budget constraint:	
		$700 million	$1 billion
Total cost (million$)	424	700	1000
Epidemic duration (days)	38	35	34
Cumulative incidence (herds)	202	193	187
Cumulative incidence (000head)	277.6	262.5	252.8
Vaccinated (herds)	417	408	269
Vaccinated (000head)	720.3	660.1	465.1
Preemptively depopulated (herds)	0	306	436
Preemptively depopulated (000head)	0	440.0	663.1

3.2. Model results

While detailed analyses of the optimal FMD control strategies are conducted in a companion paper (Kobayashi et al., 2007), selected results are presented here for demonstration purpose (Table 6). The model was run with a salesyard as the index case, with the assumption that vaccination is allowed and vaccinated animals will not be slaughtered subsequently. In addition to cost-minimization, optimization was also implemented with an alternative non-economic objective functions. Specifically, minimization of the number of infected commercial herds was implemented with overall budget constraints of 700 million dollars and one billion dollars. The exercises simulated the behavior of decision makers that try to minimize the total incidence while meeting the budget constraints in disease control.

The results (Table 6) indicated that epidemic duration and cumulative incidence were reduced under the objective of infection minimization relative to that under the objective of cost minimization. However, the lower incidence was achieved at higher overall costs. The higher costs in turn were primarily the result of preemptive herd depopulation. While preemptive depopulation was not optimal under the cost-minimization objective, it was optimally adopted under the infection-minimization objective. Since it was costly, the extent of preemptive depopulation depended on the budget. When the budget was smaller, lower preemptive depopulation was supplemented with higher vaccination, the other preemptive control measure.

Optimization was implemented with another objective function, where total number of herds depopulated (i.e., baseline plus preemptive depopulation) was minimized. The results (not shown in the table) were very close to the cost-minimization results except that more herds were vaccinated as opposed to depopulated. The total cost under herd-depopulation-minimization objective was 440 million dollars, instead of 424 million dollars under the cost-minimization objective.

4. Discussion

In developing the model, we were privileged to have access to a state-of-the-art FMD epidemic simulation model initially developed for the same region (Bates et al., 2003b). The simulation model was designed for multiple species and parameterized with locally-specific information obtained from local authorities and producer surveys. The simulation model enabled us to estimate species-specific disease-transmission parameters, which then allowed us to consider locally-specific industry structure in the region. Previous studies did not have the luxury. For example, Ekboir (1999) studied the potential impacts of FMD in a similar region of California, but the epidemic model used in the analysis was simple and unrealistic. Schoenbaum and Disney (2003) used a sophisticated spatially-explicit FMD simulation model, but they evaluated alternative FMD control strategies for hypothetical populations of single species.

The epidemic output of our optimization model was successfully validated against that of the simulation model: the current model replicates the basic average results of the simulation model. The simulation model itself, however, has not been validated as no FMD outbreak data for the region are available. Thus, our interest was in how the optimization model compares with the simulation model. The epidemic relationships incorporated in the optimization model were simplified ones derived from the detailed simulation model. Simplifications and restrictive assumptions were made on economic specifications as well. Known limitations of the current model are discussed here.

In order to limit the number of state variables, assumptions were made about the dynamics of vaccinated herds. Once vaccinated, herds left the path of disease-status transition and affect the system only via Eq. (2) as a component of total population N. By this treatment, vaccination was assumed to be immediately and perfectly effective in protecting susceptible herds and stopping and preventing infectiousness of infected herds. This is a simplification of reality because (1) FMD vaccine would take at least 4 days to be effective (Doel et al., 1994; Salt et al., 1998; Cox et al., 1999), (2) vaccine efficacy would not be 100% (Callis, 1978; Hutber et al., 1999), and (3) already infected animals would shed virus after vaccination, though the amount is significantly reduced (Golde et al., 2005). However, additional protective measures taken for vaccinated herds, especially quarantine, would partially support these assumptions. The specification of the dynamics of vaccinated herds also led to a downward bias in the number of diagnosed herds to depopulate, but it did not affect the optimization solutions because the objective function included the value of infected herds rather than value of depopulated herds. The problem of underestimation of latent incidence, though supposedly small, remained.

To keep the model tractable, the scope of the analysis was limited to the three-county area, so only those costs incurred at the three-county level were included in this model. Therefore, for example, costs associated with restrictions on US meat exports that will be incurred outside the region were not considered in the model. Moreover, only direct impacts to the livestock sector were considered. More comprehensive studies are required to thoroughly assess the economic impacts of an FMD outbreak in the region.

In this study, backyard herds were not assigned monetary values. While mean herd values for commercial herd types were estimated using published statistics, information on herd composition and animal values for backyard operations were not readily available.

Therefore, rather than assuming arbitrary figures, backyard herds were assumed to have no monetary value. Sensitivity analyses, where backyard animals were assigned the unit values of other herd types, found optimal strategies that were essentially identical to those presented here. Meanwhile, preemptive depopulation and vaccination of backyard herds were not considered in the model, because regulatory veterinarians do not seem to consider such strategies viable for this large group of small livestock owners who have relatively few contacts, compared with other herd types (Dr. Richard Breitmeyer, California State Veterinarian, personal communication). Furthermore, in a sensitivity analysis of the optimization model, these strategies were allowed for backyard herds, but the model output did not change.

It was not possible to obtain clear estimates on vaccination cost, and per-herd vaccination cost parameters were derived based on the assumption on the number of herds a vaccination crew can cover in a day. The assumption will not be realistic when teams are not permitted to visit multiple premises on a same day to avoid the risk of disease transmission. In reality, vaccination costs would depend on the nature of livestock operations as well as the spatial distribution of farms and animals. For example, large dairy operations in the Central Valley of California usually have their own capacity of routine vaccination and would be able to perform emergency FMD vaccination. Regulatory personnel would only need to supervise the vaccination process. Therefore, in this instance, overall vaccination costs that the government incurs may be lower for dairy operations than for other types of operations in the region.

The results presented in this paper suggested potentially substantial opportunity costs of pursuing alternatives to the cost-minimization objective. Quicker containment of an epidemic could be achieved than under a cost minimization objective by preemptively depopulating more herds; but the magnitude seemed limited and the costs were substantially higher, at least in the case examined in this paper. Accordingly, balancing the costs and benefits of preemptive measures will be an essential part of the control strategy decision making.

Finally, the model developed here is not intended as a substitute for simulation models. The optimization approach has its advantages and limitations. As is clearly seen through the examples presented in the companion paper (Kobayashi et al., 2007), an optimization model considerably expedites the search process of desirable strategy combinations by allowing flexible strategies that are determined endogenously in the model. Achieving the same goal would require the simulation of several thousand scenarios. An optimization model is also a powerful tool in deciding allocation strategies when resources available for control strategy implementation are limited.

At the same time, an optimization model faces limitations in the level of detail that can be incorporated regarding physical relationships characterizing the system. Though capturing the fundamental dynamics of FMD spread, the epidemic relationships used in the model developed here were simplified ones derived from the output of the detailed simulation model. Besides the limitations discussed above, the current optimization model is deterministic, using mean disease transmission parameters, whereas a stochastic representation better characterizes actual disease spread processes. The optimized strategies thus apply only to average epidemics with different index cases. In addition, the optimization model is not spatially explicit, and the herds were aggregated into herd types, so herd-level contact information was not used. Incorporating stochasticity and spatial dimension in an optimization model is a non-trivial task and will be addressed in a future project.

We propose iterative uses of optimization and simulation models to arrive at useful and meaningful policy conclusions in a minimum time. An optimization model can provide a comprehensive screening of desirable strategies, and simulation models may be used to supplement the details lacking in the results of the optimization model. Output of an optimization model also may be used as a guide to narrow down parameter ranges to be used in a simulation model. Dynamically optimal solutions identified by the optimization model will be useful in parameterizing a simulation model with non-static disease control strategies. A simulation model in turn can be used to validate the control strategies optimally identified by an optimization model. Thus, iterative teamwork between the two types of models can identify an optimal practical control strategy in the minimum time, especially when the disease-transmission parameters used in the optimization and simulation models are the same.

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