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Decision-making for foot-and-mouth disease control: Objectives matter

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ABSTRACT

Formal decision-analytic methods can be used to frame disease control problems, the first step of which is to define a clear and specific objective. We demonstrate the imperative of framing clearly-defined management objectives in finding optimal control actions for control of disease outbreaks. We illustrate an analysis that can be applied rapidly at the start of an outbreak when there are multiple stakeholders involved with potentially multiple objectives, and when there are also multiple disease models upon which to compare control actions. The output of our analysis frames subsequent discourse between policy-makers, modellers and other stakeholders, by highlighting areas of discord among different management objectives and also among different models used in the analysis. We illustrate this approach in the context of a hypothetical foot-and-mouth disease (FMD) outbreak in Cumbria, UK using outputs from five rigorously-studied simulation models of FMD spread. We present both relative rankings and relative performance of controls within each model and across a range of objectives. Results illustrate how control actions change across both the base metric used to measure management success and across the statistic used to rank control actions according to said metric. This work represents a first step towards reconciling the extensive modelling work on disease control problems with frameworks for structured decision making.

1. Introduction

Epidemiological modelling is a demonstrably useful tool in providing exploration of proposed response measures in the event of a disease outbreak. Such models have two main uses: (1) to identify and uncover mechanistic understanding of the system in question, and (2) to project the outbreak to explore potential outcomes under different conditions. For foot-and-mouth disease (FMD), a highly-contagious, viral disease of several economically-important, cloven-hoofed species (such as cattle, sheep, and pigs), model outputs have been used extensively to inform policy-makers of the likely next steps in an outbreak and to explore the efficacy

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of various control actions (Keeling et al., 2001, 2003; Ferguson et al., 2001; Morris et al., 2001; Carpenter, 2001; Bates et al., 2003; Kao, 2003; Tildesley et al., 2006; Thornley and France, 2009; Ward et al., 2009; Backer et al., 2012a; Dürr et al., 2014; McReynolds et al., 2014). Such extensive use of models is due, in part, to the large economic ramifications of trade-bans once FMD infection is detected. Simulation models allow exploration of management strategies that may be seen as too risky (or impossible) to be trialled in a real outbreak setting (Milner-Gulland et al., 2001; Kao, 2002).

Evaluating control actions for FMD in such a manner requires the choice of a currency for comparison. The literature on FMD control provides myriad examples, including the number of livestock slaughtered (Durand and Mahul, 2000), number of infected farms on which animals are culled (Schoenbaum and Disney, 2003), the number of farms where animals are pre-emptively slaughtered (Velthuis and Mourits, 2007), export losses from trade bans (Paarlberg et al., 2008), livestock slaughter compensation costs (Sanson et al., 2014), total number of farms vaccinated (Tildesley et al., 2006), spatial area of the outbreak (Dubé et al., 2007), and outbreak duration (Morris et al., 2001). In choosing any particular metric to compare control actions, a statement is implicitly being made about the objective of management. That is, different stakeholders may have different management objectives and therefore different metrics of management success that they are most interested in optimising.

Not all of these metrics of management success are positively correlated, potentially leading to stakeholder conflict. For instance, taking a 'scorched-earth' approach to FMD management where susceptible animals are culled in a wide area surrounding a confirmed case, may be highly effective in reducing outbreak duration, minimising the time that trade embargoes are enforced, and thus benefiting exporters. However, this same scorched-earth approach would result in devastating economic losses to individual farmers and emotional toll to those with premises in the culling area, and the total number of culled livestock and associated control costs may be very high locally and/or unacceptably high to the general public.

Even if a single metric for evaluation can be identified, more detailed questions remain in order to compare control actions. For outbreak duration, a number of statistics have been used in the literature for summarising this metric such as the average time until disease eradication (Morris et al., 2001), the median outbreak duration (Roche et al., 2014a), the probability of disease eradication within 200 days (Morris et al., 2001), the 95th percentile of outbreak duration (Velthuis and Mourits, 2007), and sophisticated comparisons of the whole distribution in outcome metrics (Dubé et al., 2007). These are all statistics of outbreak duration yet, as with the choice of metric, not all statistics of outbreak duration are positively correlated with one another and the choice of statistic will also influence which control action is recommended. A scorched-earth approach, as described above, may result in a short mean outbreak duration and the variability surrounding this estimate may be low. Alternatively, only culling confirmed infected premises (IPs) may also lead to a small mean outbreak duration but this control action may have a high likelihood of a large number of infected premises and thus a greater chance of a very long outbreak (i.e. high variability in outbreak duration).

A suitable management objective should motivate the choice of metric and evaluation function, and thus the definition of a management objective is the first step in phrasing a control problem. We define what we mean by an objective in order to clarify this discussion and highlight the benefits of clearly defining management objectives.

Four types of objectives can be defined (Keeney, 2007): strategic, fundamental, means, and process objectives. Strategic objectives define the general direction of all decisions made by the decision-maker. The mission statement of the United States Department of Agriculture (USDA) is a strategic objective, part of which aims to "provide leadership on food, agriculture, natural resources, rural development, nutrition, and related issues" (USDA). Strategic objectives, being broad and aspirational, can be useful for motivation and cooperation of stakeholders, such as was recognised in the eradication of smallpox (Fenner et al., 1988; Henderson, 2011). However, useful as they are, strategic objectives offer little guidance as to how to directly prioritise response actions and resources for control.

Fundamental objectives define the overarching goal of the decision problem currently at hand and the term 'objective' shall refer to fundamental objectives in this manuscript unless otherwise qualified. For example, a policy-maker may decide that minimising outbreak duration, thereby lifting trade bans on products from FMD-susceptible animals as soon as possible, is most important. The FMD Red Book, for instance, offers a surveillance objective for the period 72 h post FMD outbreak declaration to "detect existing infected animals and premises as quickly as possible to determine the extent of the outbreak" (APHIS, 2014). A clearly stated fundamental objective is unambiguous, quantifiable, states the metric that is used to evaluate control actions, and, for clarity, states how said metric should be optimised (Keeney, 1992; Runge and Walshe, 2014). That is, are we interested in maximising or minimising the metric? Finally, since a fundamental objective is the criterion by which control actions are evaluated and compared it is important to include relevant constraints on time (e.g. when is it desired that this objective be met?).

Means objectives are those which are needed insofar as they help reach fundamental objectives. It is not of interest to pursue them for their own sake. Learning is a common example of a means objective. For instance, improving mechanistic understanding of the spread of FMD will likely improve management success. However, improving this understanding is not the fundamental goal of controlling an outbreak, so this is a means objective. In the case of learning, obfuscating means objectives with fundamental objectives might lead to the conclusion that any action that obtains information will be part of an optimal control strategy. In an outbreak situation, when time and resources are limited, such an assumption can be dangerous if spending time and resources to learn prevents other management activities from being carried out in a timely fashion. Managers are faced with a huge number of uncertainties in an outbreak situation so there is a need to be able to distinguish between which uncertainties are a hindrance to management, and therefore a priority to resolve, and which uncertainties do not affect the best choice of management action (i.e. uncertainties for which, were they resolved, the recommended management action would not change). Put bluntly, it is a waste of resources to resolve uncertainties in an outbreak situation that ultimately are not going to lead to a substantive improvement in management.

Determining which uncertainties should be resolved requires a manager to quantify the value of learning, which can be a difficult task. Learning can be quantified in a number of ways. However, from a management point of view, the currency most pertinent to evaluating the benefit of learning are the units of the fundamental objective, that is, the units in which control actions are compared. For instance, if a policy maker is most interested in minimising outbreak duration (the fundamental objective), then the benefit of resolving uncertainty in, say, the rate of disease transmission to susceptible individuals is best evaluated when the reduction in uncertainty surrounding the transmission rate is stated in terms of an expected reduction in outbreak duration. That is, answering the question, what is the expected reduction in outbreak duration that will result from resolving our uncertainty surrounding the transmission rate? Thus, speaking more generally, once a fundamental objective and a metric of management success have been defined, it is possible to evaluate the expected improvement in management provided by the resolution of each uncertainty (Runge et al., 2011; Shea et al., 2014). Uncertainties expected to most influence fundamental objectives can then be prioritised.

Process objectives are concerned with the making of decisions and not the outcome of decisions. Process objectives do not directly affect the choice of control action. Ensuring that decision-making is kept transparent and the public regularly informed may be process objectives adopted by a government so as to keep the trust and confidence of the public, or to maintain the cooperation of different stakeholders and personnel involved in carrying out control actions. Process objectives thus influence the likelihood of successfully containing an FMD outbreak. Weekly stakeholder meetings that were set up on each Friday during the 2001 UK outbreak are one such example of enacted process objectives (Anderson, 2002).

The benefits of being clear in the definition of objectives, particularly fundamental objectives, has been recognised in a number of contexts beyond FMD control, including in the success of projects leading to the eradication of smallpox (Fenner et al., 1988; Henderson and Klepac, 2013), in the eradication of rinderpest (Mariner et al., 2012), in evaluating influenza vaccination plans (Medlock and Galvani, 2009), in deciding vaccination strategies against avian influenza (Akey, 2003; Senne et al., 2005), and in many areas outside disease control, such as in wildlife management (Walters and Hilborn, 1976; Shea et al., 2002; Nicholson and Possingham, 2006; Probert et al., 2011), weed control (Shea et al., 2010), and in the management of social welfare programs (Rossi and Williams, 1972; Austin, 1973). Despite this acknowledgement of the importance of clear management objectives in the success of control projects for high-profile diseases, the topic of objectives, in itself, appears to be rarely discussed in the literature on FMD control, or even infectious disease control in general.

Here, we illustrate the dependence of the preferred choice of control action on the fundamental objective of outbreak management using an example of emergency response control to a hypothetical FMD outbreak in Cumbria, UK. We focus on the phenomenon of contrasting different control actions in light of different objectives, rather than the specific metrics of comparison, so as to illustrate the method of phrasing a decision-making problem. We evaluate seven control actions using five independent, rigorously-studied disease spread models and using a range of quantified fundamental objectives. We explore three metrics of management success, outbreak duration, number of livestock culled, and a cost metric that includes both compensation costs of the number of animals culled and costs of vaccine doses administered. Using these metrics we construct objectives which differ not only in the base metric being used but also in the statistic used to summarise each metric for ranking.

Consulting multiple models may complicate an analysis aiming to identify the optimal control policy, particularly when model results are in conflict against each other. However, it is likely that policy-makers will consult multiple modelling groups during a real outbreak (e.g. the 2001 FMD outbreak in UK (Kao, 2002; Woolhouse, 2003)) so it is important to study how to identify optimal control policies when faced with results from several models. Several research groups have previously compared multiple models in the evaluation of FMD control strategies (e.g. Dubé et al., 2007; Roche et al., 2014a; Halasa et al., 2014). A multi-model situation illustrates that, while concordance in recommended control action across models may provide validation and reassurance, differences in control action recommendation within the same objective but across different models may highlight potentially useful differences in models and the assumptions governing those models.

2. Methods

2.1. Data

Data are from simulations of an FMD outbreak using five independently-developed disease spread models: (1) AusSpread, developed by the Australian Government Department of Agriculture, Fisheries, and Forestry (Garner and Beckett, 2005; Roche et al., 2014b); (2) the Davis Animal Disease Simulation model, developed at the University of California, Davis (Bates et al., 2003); (3) Interspread Plus, developed at Massey University, New Zealand (Sanson, 1993; Stern, 2003; Stevenson et al., 2013); (4) the North American Animal Disease Spread Model, jointly developed by the US and Canada, and with continued development by the Animal and Plant Health Inspection Service of the United States Department of Agriculture (Harvey et al., 2007); and (5) the Warwick model, originally developed at Cambridge University during the 2001 UK outbreak but then further developed at Warwick University from 2003 onward (Keeling et al., 2001; Tildesley et al., 2008). All the models are spatially-explicit, stochastic, state-transition simulation models. Beyond this classification, each model differs in several respects, from the units upon which infection acts (at the farm-level or the animal-level) to the type of control actions allowed. All models have been used for planning purposes for FMD and several studies have validated results from several of these simulation models against each other (e.g. Dubé et al., 2007; Halasa et al., 2014). Results are presented with models anonymised.

Demographic parameters for the hypothetical outbreak scenario were chosen to be consistent with the county of Cumbria in the UK (Fig. S1). Such parameters included the sizes of the farms and the proportion of sheep and cattle in each farm (other cloven-hoofed species were ignored in this analysis). Spread was simulated across 7837 farms with a spatial distribution consistent with Cumbria. All models were run from the start of the control program with 10 infected farms. The method used to generate which 10 infected farms for each simulation varied slightly between models. Some models used the same index farms for each simulation, with a configuration of infected farms consistent with a single point of FMD introduction, and some models used a new set of index farms at each simulation (subject to clustering constraints to simulate a single point of infection). After the first farm was reported with infection it was assumed a livestock movement ban was implemented with 90–100% efficacy.

In addition to the movement ban, five control actions were evaluated in the simulations: (1) culling of infected farms only (IP); (2) culling of infected farms and of those that have been identified as at risk through tracing of dangerous contacts (DC); (3) culling of infected farms and of all those within 3 km of each infected farm (RC); (4) culling of all infected farms and vaccination of cattle on all farms within 3 km of each infected farm (V3L); and (5) culling of all infected farms and vaccination of cattle on all farms within 10 km of each infected farm (V10L). Note that culling of infected premises was performed in all control strategies. Only one of these management actions was implemented per simulated outbreak (one action per outbreak). Each modelling team ran each management action for 100 simulation runs (model B only ran 99 simulation runs per control). Culling was constrained to a maximum of 50 farms per day and vaccination had a capacity of 10,000 animals per day. Vaccine efficacy was between 80 and 90%, specific to each model, with no limit on the number of vaccine doses available. Owing to constraints on action specification, ring culling was not possible in model B. Control actions may be nested within each other (such as IP culling within the other actions), or it may not be possible to evaluate some control actions in some models (as presented here) and, although this situation is not complete, from the point of view of presenting the results in a consistent manner, these situations may present themselves to decision-makers in real outbreaks so methods need to be prepared for them. Additionally, models themselves may not have been constructed with the same aims and so it may not be appropriate to use such models in a comparison across a full range of control actions.

Two further control actions accounted for vaccination. While vaccination was not used during the 2001 UK outbreak, the subsequent public feedback and concern for animal welfare prompted more serious discussion about using vaccination as a viable control action in future outbreaks. Vaccinated animals are not conferred lifelong immunity after vaccination and so two vaccination regimes are recognised: a vaccinate-to-kill regime, where vaccinated animals are removed from the population (V3K, V10K) and a vaccinate-to-live regime, where vaccinated animals are allowed to remain in the population to live out their normal commercial lives (V3L, V10L). These vaccination regimes reflect differences in approaches by FMD-free countries and the ramifications of those strategies with respect to gaining disease-free status from the World Organisation for Animal Health (OIE) and re-establishing international market access for livestock and livestock products (OIE, 2013, see Article 8.6.9; Knight-Jones and Rushton, 2013; Backer et al., 2012b). In all simulations it was assumed that only cattle were vaccinated.

For each simulation, the duration of the simulated outbreak, the total number of livestock culled by species, and the total number of vaccine doses administered were recorded. Data are provided in the supplement.

3. Objectives

Objectives are constructed from three metrics used to evaluate control actions in the literature: (1) a cost metric, in this case as a function of both the number of livestock culled and livestock vaccinated (in units of £); (2) duration of the epidemic (in days); and (3) simply the number of culled livestock. The first metric, denoted as C, includes both compensation to farmers of culled livestock and vaccine cost of administered doses. This metric was calculated as $C = C_{\text{cow}}N_{\text{cow}} + C_{\text{sheep}}N_{\text{sheep}} + C_{\text{vacc}}N_{\text{vacc}}$, where C_{cow}, C_{sheep}, and C_{vacc} are the relative per-animal costs of compensation for cattle and sheep, and the cost of a vaccine dose, respectively (1000, 100, and 1, respectively). Model C reported some farms that were a mix of cattle and sheep without specifying the relative numbers of each species. In this case, an additional term was added to the cost metric, $C_{\text{mix}}N_{\text{mix}}$, where C_{mix} took a value of 500 (as a midpoint between 100 and 1000). The variables N_{cow}, N_{sheep}, N_{mix}, and N_{vacc}, are the culled numbers of cattle, sheep, cattle and sheep (on mixed farms), and the number of vaccine doses used, respectively. Note that values of C calculated for the vaccinate-to-kill actions assume that vaccine cost and compensation cost are the same, $C_{\text{vacc}} = C_{\text{cow}}$, since under this action vaccinated cows are culled and thus compensation is paid. Note too that although minimising the number of livestock lost is generally not a fundamental objective of FMD outbreak control, it does represent a significant logistical constraint (de Klerk, 2002). Unless explicitly specified, it is assumed vaccination actions are vaccinate-to-live.

For each of the three metrics, five summary statistics were used to reflect the risk attitude of the decision maker. All of these statistics have previously been used to construct objective functions in the FMD literature (e.g. Morris et al., 2001; Halasa et al., 2014). Statistics used were the mean, the median, the variance, the 90th quantile, and the empirical probability of having the metric over a particular threshold. Note that a shortcoming of using a threshold-type objective is that values falling on either side of the chosen threshold, no matter how small a difference, are given completely different values with respect to the objective. An alternative approach would be to discount values of the metric in decreasing increments above the set threshold. The five statistics are calculated over each of the three metrics, giving fifteen objective functions for ranking management actions. Any ranking of control actions presented, using any one of these objectives, is performed on results from only one model at a time. For example, the objective of minimising the median outbreak duration was included (calculated for each model separately), and so was the objective of minimising the probability of an outbreak that resulted in indemnity and vaccine costs totalling more than £20 million (calculated for each model separately). When ties occur within the same model and objective the smallest rank of the tied actions is given to all tied actions.

4. Results

Simulation output from multiple models and multiple objective/metric combinations produces an enormous quantity of output. The goal here is not necessarily to identify a best action or model, but rather to begin to explore the space of action-outcome combinations in order to facilitate richer discussion between modelling and decision-making groups. Rather than a complete enumeration of all outcomes, here we focus on highlighting specific patterns that emerge from our comparison of outcomes across potential actions and models; the full results from all combinations of model, action, metric, and statistic are presented in the supplement. Results are shown using only the statistics of median, the 90th quantile, and the empirical probability of having a value over a particular threshold due to similarities of results between the mean with median, and variance with the 90th quantile, respectively (results for all five statistics are presented in the supplement).

In a conventional, single-model analysis, one would rank candidate actions with respect to their projected outcome within a single metric and statistic. For example, simulation results from model D using vaccination at a 3 km radius under a vaccinate-to-live regime (V3L) produce a median cost of compensation of livestock culled and vaccine doses administered of £2.96 million (Fig. 1, Fig. S3). Under an objective to minimise the median cost this was the best (i.e. smallest) control action using model D; the next most highly ranked control under model D, and using the same objective, was vaccinating-to-live at a 10 km radius (V10L), with a median cost of £2.97 million, followed by culling of infected premises only (IP, £4.68 million), ring culling at 3 km (RC, £5.47 million), dangerous contacts culling (DC, £6.06 million), vaccination at 3 km under a vaccinate-to-kill regime (V3K, £28.85 million), and vaccination at 10 km under a vaccinate-to-kill regime (V10K, £125.51 million), respectively.

Within a given metric, the recommended control actions may vary across objectives that use different statistics to form a ranking. In particular, statistics based on measures of central tendency will reflect expected outcomes, but statistics based on higher order moments (e.g. variance, skewness) may be more influenced by a small number of extreme outcomes. For instance, for the metric of the combined cost of compensation of culled livestock and vaccine doses administered, culling only infected farms is ranked highly for objectives of minimising statistics of central tendency such as the mean or median cost (Fig. 1, Fig. S3). However, this control strategy ranks poorly for metrics of variation or minimising extreme values, with the exception of results from model A (Fig. 1, Fig. S3). This comparison highlights that the IP strategy, which is the least severe culling alternative (in that it never recommends culling of farms for which infection has not yet been detected) results in low expected costs associated with compensation and vaccine doses, but is not robust to very large outbreaks, during which transmission outpaces the ability to respond. Thus, stakeholders that have

Control		Model	Median	Quantile90	EmpProb20
Infected premises culling (IP)		A	3	3	0.00
		B	75	97	0.85
		C	6	18	0.06
		D	5	13	0.04
		E	5	54	0.19
Dangerous contacts culling (DC)		A	7	9	0.00
		B	77	95	0.84
		C	6	19	0.06
		D	6	13	0.04
		E	7	21	0.13
Ring culling at 3km (RC)		A	30	46	0.92
		B	NA	NA	NA
		C	7	10	0.00
		D	5	13	0.04
		E	12	36	0.26
Vaccinate at 3km	to live (V3L)	A	3	3	0.00
		B	5	14	0.02
		C	4	12	0.03
		D	3	7	0.00
		E	5	9	0.00
	to kill (V3K)	A	28	40	0.84
		B	47	89	0.92
		C	10	20	0.11
		D	29	50	0.79
		E	24	47	0.64
Vaccinate at 10km	to live (V10L)	A	3	4	0.00
		B	4	7	0.00
		C	4	10	0.01
		D	3	5	0.00
		E	4	8	0.00
	to kill (V10K)	A	125	149	1.00
		B	143	178	1.00
		C	26	39	0.83
		D	126	155	1.00
		E	116	178	1.00

Fig. 1. Cost of both compensation for culled livestock and vaccine doses administered (£ million), for a range of control actions (grouped rows) evaluated against three objectives (columns) under five models (A–E, rows). Column titles represent the statistic used for ranking the control actions. Cells are rounded to integer values, except the column for the empirical probability, and are coloured according to rank (within both a model and objective) with red representing worst performing control actions and blue representing best performing control action. The final column is the empirical probability of the combined cost of compensation of culled livestock and vaccine doses administered being greater than £20 million.

strong aversion to such rare, but extreme, outcomes would do best to choose another strategy.

The ranking of control actions may also vary across objectives that use different metrics but the same statistic. For instance, while the control action of vaccinate-to-kill at a 10 km radius (V10K) performs poorly under an objective that minimises median cost (Fig. 1), this control action performs well under an objective to minimise outbreak duration with the same statistic (Figs. 2 and 3). With the exception of model D, ring culling performs very well for minimising median outbreak duration but poorly across other median metrics (Fig. 3). This conflict among metrics may lead to conflict among stakeholders in a decision-making setting as different groups may favour one metric of management success over another.

While trade-offs between metrics or statistics used to create rankings may lead to conflict among stakeholders, consistency in the rankings of control actions allows decision-makers to simplify the decision problem by identifying "win-win" or "lose-lose" situations. Vaccinating at a 10 km radius under a vaccinate-to-live regime, for instance, performs well under all statistics, across all models, and across all three metrics investigated (Figs. 1–3, Figs. S2–S7). Across the same range of criteria, the action of only culling infected premises performs consistently poorly. Identifying such "lose–lose" actions in advance might allow decision-makers to remove these options from consideration, and simplify future simulation exercises. Isolated exceptions to such consensuses are useful to know too. For instance, the only metric for which vaccinating at a 10 km radius under a vaccinate-to-kill regime does perform well is the metric of outbreak duration (Figs. 1 and 2, Figs. S2–S7). Knowing this exception forces decision-makers to express whether this metric of management success is of primary importance.

It is not only useful to look at ordinal rankings of control measures but also the actual numerical output that leads to this ordinal scale. Fig. 4 and Figs. S8–S14 present scatterplots of the performance of each control action for each model and across a range of objectives. For any given model and objective, statistics of the chosen measure of success for each control action are scaled by subtracting the value of said statistic of the worst performing control action and dividing by the range of values of the statistic across all control actions for that model and objective. Under this rescaling, the worst control strategy has a score of 1 and the best a score of 0 within each model and objective, allowing control actions to

Control	Model	Median	Quantile90	EmpProb50
Infected premises culling (IP)	A	27	41	0.01
	B	408	564	0.99
	C	123	258	0.89
	D	60	107	0.60
	E	70	396	0.63
Dangerous contacts culling (DC)	A	26	39	0.02
	B	404	538	0.95
	C	122	267	0.90
	D	40	56	0.21
	E	74	182	0.76
Ring culling at 3km (RC)	A	22	30	0.01
	B	NA	NA	NA
	C	13	27	0.00
	D	63	111	0.65
	E	31	74	0.21
Vaccinate at 3km (V3L/V3K)	A	26	41	0.02
	B	118	220	0.99
	C	96	224	0.90
	D	42	64	0.32
	E	61	101	0.68
Vaccinate at 10km (V10L/V10K)	A	25	41	0.00
	B	102	171	0.92
	C	89	200	0.83
	D	36	49	0.10
	E	68	110	0.69

Fig. 2. Outbreak duration (days) of control actions (grouped rows) evaluated against several objectives (columns) under five models (rows). Column titles represent the statistic used for ranking the control actions. Cells are rounded to integer values, except the column for the empirical probability, and are coloured according to rank with red representing worst performing control actions and blue representing best performing control action (within both a model and objective). The final column is the empirical probability of the outbreak duration being longer than 50 days.

be compared independently of the raw numerical output of simulation models. For instance, the mean outbreak duration under model B for the strategy of dangerous contacts culling was 384 days while the best and worst performing actions under model B, according to mean outbreak duration, were vaccinating at 10 km (114 days) and infected premises culling (394 days), respectively. This gives a score for dangerous contacts culling for model B of (384–114)/(394–114) = 0.96 (Fig. 4).

Correlations between metrics provide broader insight into the relationship between metrics and functions of metrics. Some metrics, such as outbreak duration, are generally positively correlated across all investigated statistics, with the exception of the empirical probability of an extreme event, and in almost all models (Fig. S9). Therefore, any stakeholder interested in outbreak duration, whether it be expectation or risk, may campaign for the same control action. The metrics of cost and the number of livestock culled are also highly correlated (Figs. S11–S14).

Clustering of actions in the space of different objectives allows discussion of latent logistical costs of actions, trade-offs in actions among different objectives, and constraints inherent in the system in question. For instance, relative to the worst actions, vaccinating at 10 km and at 3 km under a vaccinate-to-live regime (V3L, V10L) cluster together in multiple dimensions: outbreak duration, cost, and number of livestock culled (Fig. 4, Fig. S11–S12). Although vaccinating at 10 km under a vaccinate-to-live regime was previously identified as a consistently well-performing action, this clustering forces decision-makers to decide whether the implementation costs associated with vaccinating at 10 km over vaccinating at 3 km are warranted given marginal improvement across a wide range of objectives. Actions that cluster in one dimension but disperse in another highlight the importance of trade-offs. For example, in all models except model B, dangerous contacts culling (DC) resulted in a mean outbreak duration that is similar to vaccinating at 10 km under a vaccinate-to-live regime (V10L) while resulting in a greater number of mean livestock culled (Fig. 4). Therefore, if it is deemed by policy-makers that the mean number of livestock culled is not an important measure then the relatively small increase in outbreak duration may be warranted so as to avoid the implementation costs associated with vaccination at a 10 km radius.

5. Discussion

Our analysis illustrates how differences in the definition of a management objective for disease control really matter. The importance of a clearly stated management objective is illustrated in our results by the change in recommended control actions across (1) the choice of metric of management success, as has been noted elsewhere in disease control (e.g. Medlock and Galvani, 2009), and (2) the statistic used to summarise the metric to create a ranking. Our analysis shows how qualitatively comparing rankings of actions allowed identification of consistently well or poorly performing control actions, broad-scale correlations among objectives, and clustering of actions in the space of management objectives. All such findings either simplify the subsequent decision-making process or focus further discussion between modellers and decision-makers on points of interest. Exceptions to consensus in the best choice of control action across different objectives explicitly shows where conflicts between different

Control		Model	Cost	Duration	Livestock culled
Infected premises culling (IP)		A	3	27	10
		B	75	408	251
		C	6	123	12
		D	5	60	14
		E	5	70	19
Dangerous contacts culling (DC)		A	7	26	23
		B	77	404	259
		C	6	122	11
		D	6	40	19
		E	7	74	26
Ring culling at 3km (RC)		A	30	22	100
		B	NA	NA	NA
		C	7	13	13
		D	5	63	18
		E	12	31	42
Vaccinate at 3km	to live (V3L)	A	3	26	10
		B	5	118	22
		C	4	96	8
		D	3	42	10
		E	5	61	16
	to kill (V3K)	A	28	26	35
		B	47	118	64
		C	10	96	14
		D	29	42	36
		E	24	61	36
Vaccinate at 10km	to live (V10L)	A	3	25	10
		B	4	102	20
		C	4	89	8
		D	3	36	10
		E	4	68	16
	to kill (V10K)	A	125	25	131
		B	143	102	160
		C	26	89	29
		D	126	36	133
		E	116	68	131

Fig. 3. Median performance of control actions (grouped rows) evaluated against several objectives under five models (rows). The median is used as the statistic to form a ranking of control actions under each metric (columns). Column titles represent the metric use for the ranking, and units for each column are, respectively: £ million, days, and thousand head of livestock culled. Cells are rounded to integer values and are coloured according to rank within each model and objective (red signifies worst performing action, blue signifies best performing action).

stakeholders may exist, thereby forcing policy-makers to express their fundamental objective(s) of management. Reconciling any highlighted discordance in action recommendation across different objectives may require multiple rounds of discussion and modelling.

Elicitation of objectives is a non-trivial task which may involve many stakeholders with competing interests. Ultimately, the appropriate management objective(s) is a choice to be made by policy-makers in consultation with stakeholders. While it may be unrealistic to expect a policy-maker to provide modellers with a statistic they wish to optimise in simulation experiments, it should be possible to deduce whether a policy-maker is interested in minimising an expectation or in minimising the risk of an extreme event occurring. Stating an explicit objective is in line with having a clear policy, and so should be encouraged. In the absence of clear objectives from policy-makers (such as prior to discussions with policy-makers), our analysis shows how performing comparisons across a range of objectives can highlight consensuses and trade-offs of control actions across the space of candidate objectives, which can then focus discussion to elicit a preference from policy-makers. Subsequently obtaining a clearly-defined fundamental objective of management then makes most efficient use of modellers' resources, which is particularly important in an outbreak situation when speed is needed, and allows uncertainties that have the greatest impact on FMD control to be prioritised. In cases where it is not possible to identify one objective of interest and decision makers require a combination of objectives, it may be appropriate to consider techniques from the literature on multiple criterion decision analysis (e.g. Keeney and Raiffa, 1976). Further discussion of risk tolerance of decision makers may be found in the risk analysis literature (e.g. Raiffa, 1968; Keeney and Raiffa, 1976).

Our analysis, which used several objectives, was complicated by output from multiple peer-reviewed models rather than from a single model. This situation is likely when dealing with important diseases of humans and livestock, and one that will only become more common in the future. Broad scale consensus across different models provides corroboration for whatever patterns are highlighted by our analyses. One such pattern was identifying actions that perform consistently well (vaccinating at 10 km under a vaccinate-to-live regime) or poorly (culling of infected premises

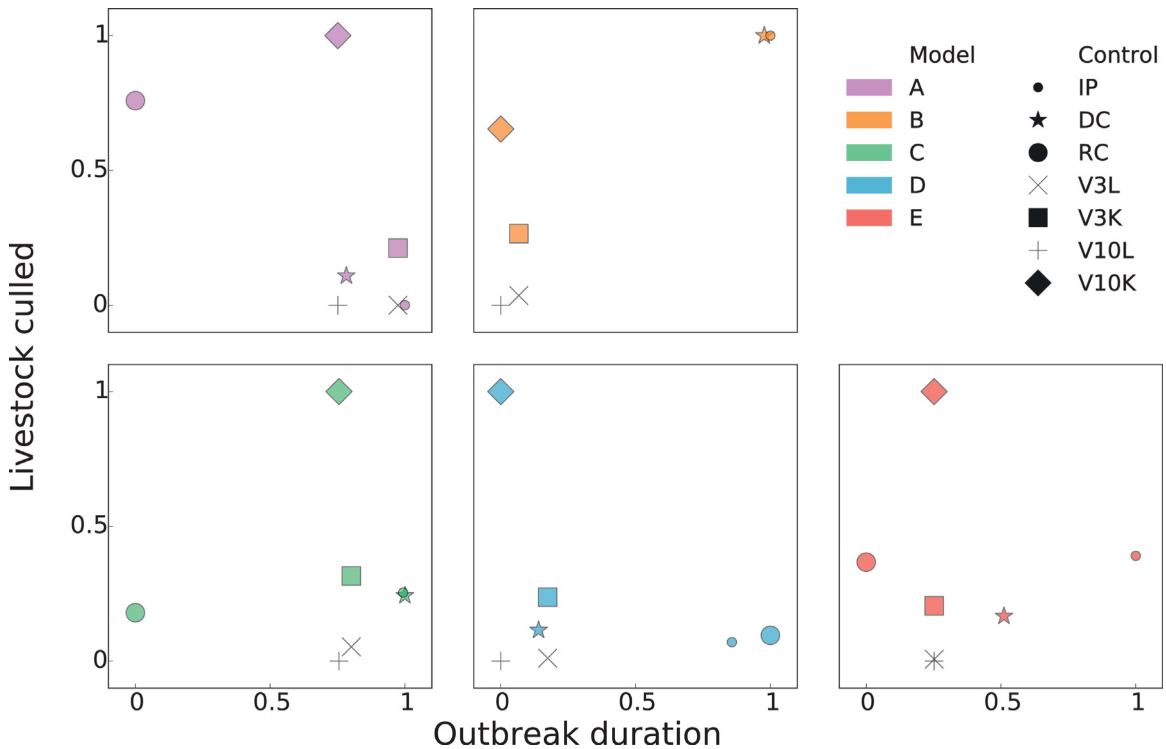

Fig. 4. Performance of control strategies under both mean outbreak duration and mean number of livestock culled across five simulation models of FMD spread. Mean values from simulation output under each model and under each measure of success (outbreak duration and livestock culled) have been scaled so that the worst control strategy has a score of 1 and the best a score of 0 within each model.

only) across different management objectives. The positive correlation observed in several statistics of outbreak duration was also consistent across models, adding weight to this phenomenon.

In several situations models differed in their recommendations of the best control action. All models stood out at some point in our analysis as an exception to a norm. We present no formal guide for choosing between control actions when there exist discrepancies in the recommended control strategy across different models. However, there is merit in taking the broad-scale view that we present, at least in the initial stages of the decision-making process. The goal of the decision-making process is to choose the best course of action and therefore the role of modelling, as a part of the decision-making process, is not necessarily to produce a single recommended management action but to augment the decision-making process in the way that most effectively helps decision-makers choose the course of action that is most in-line with the objectives of management. This aim holds, regardless of the number of models available for comparison. By not choosing between models, or by not combining model outputs, our presented approach avoids (1) conditioning results on a single model (assuming only one model is true), (2) assuming that all models will give similar results, (3) making assumptions about the commensurability of model outputs, and (4) having an upper limit on the number of models that can be included (besides considering the practicalities of interpreting the simulation output). Underlying mechanisms that lead to divergence among models may be caused by different assumptions and parameterisations, uncontrollable differences in computation, or they may be reflective of underlying mechanisms that different models take into account, and therefore have a real-world interpretation. Ultimately, only by taking a broad view across several models can we identify patterns in measures of management success that are robust to model choice, and identify where resolution in model outputs is needed. Our analysis can highlight where resolution is needed, therefore framing subsequent discussion between decision-makers and modellers, and taking steps towards prioritising which uncertainties are impeding decision-making. If it is found that several uncertainties in the system have led to discordance in models then an uncertainty analysis may be an appropriate next step, such as a value-of-information analysis (Runge et al., 2011; Shea et al., 2014). As with reconciling differences across objectives, reconciling the highlighted discordance in action recommendation across different models may require multiple rounds of discussion and modelling. Methods exist for combining outputs from multiple models into a single prediction or action recommendation (e.g. Lindström et al., 2015) and employing such an approach can mean added transparency in the decision-making process as it requires explicit quantification of how to combine different model outputs. It is worth noting that discovering differences in model recommendations is potentially more informative when the teams developing the contributing models are working independently of each other, as such a situation means it is more likely for different mechanistic approaches to modelling to have been used.

For the analysis presented, subsequent discussions between modellers highlighted that discrepancies in output between the models could have been caused by movement restrictions associated with implementing control actions. For example, the poor ranking of ring culling in model D under an objective of minimising outbreak duration (Fig. 2), being an exception compared to other models, is likely a reflection that model D does not implement additional movement constraints in areas where ring culling is occurring whereas the other models do, and thus highlights the importance of maintaining movement constraints in areas where control actions are taking place. Additionally, models differ in how they account for resource constraints. Some models assume detection of infected farms is a function of time while others assume detection depends on the availability of surveillance resources to undertake investigations. Daily vaccination rates also depend on farm size in some of the models. While parameter differences across models were minimised, there is also the possibility of these causing differences in model output. These factors, highlighted from our results, can thus frame subsequent analysis to pinpoint where lie the most pertinent differences between models.

Our analysis used a cost function that only includes compensation costs of culled livestock and the cost of vaccine doses administered. In a real world setting the economic losses caused by export losses are non-trivial (Paarlberg et al., 2008; Buetre et al., 2013). Indeed, for a country with an export-focussed livestock industry these costs can account for the majority of the economic losses associated with an FMD outbreak, and implementation costs will vary across control actions. All these costs need to be taken into account for a thorough comparison of control actions using any objective of cost. From a cost perspective, the number of vaccine doses used are the number of doses that are ordered from manufacturers, rather than doses that are administered. Unused vaccine doses are a sunk cost, and this has not been taken into account in the cost function in the presented analysis.

The current analysis calculates outbreak duration as the time from the first reported cases to when there are no more infected or exposed animals in the simulation. This represents the minimum duration of an outbreak, since in reality addition time would be required to complete control operations, undertake surveillance to demonstrate disease freedom, and to regain international market access. The duration of sanctions placed upon FMD-infected countries by the OIE and trade partners is dependent on whether vaccination is used and whether or not vaccinated animals are culled (OIE, 2013 see Article 8.6.9) so it may be pertinent to include such allowances when calculating outbreak duration. In our analysis, the definition of outbreak duration provides no difference in outcome between vaccinate-to-kill and vaccinate-to-live actions, whereas duration of these two control actions when defined according trade restrictions would be very different.

Our analysis is straight-forward and rapid, assuming that models are already available, and the results presented are easily understandable, requiring no assumptions on combining model outputs. This analysis could also be adapted to other animal or human diseases as simulation models are widely used to test efficacy of control strategies in these fields (e.g. Medlock and Galvani, 2009; Lee et al., 2010). Conditional on the time needed to generate model outputs, it would be feasible to construct the presented tables and plots in a short time-frame consistent with the urgency of an FMD outbreak situation, thereby quickly illustrating where differences occur across choice of objective and model, and fostering discussion surrounding the factors causing any differences. Despite the presented scenario being somewhat artificial it illustrates how the rapid use of models can augment the decision-making process in disease outbreak management in this respect. This work lays the important foundation, in defining an FMD control project's objectives, for future applications of formal structured decision making in FMD control problems, and in disease control in general, thereby leading to a more transparent and reproducible framework for making the most of modelling tools used in disease outbreak control.

Data accessibility statement

Simulation data from each of the five models used in this analysis are given in the supplementary information. Models are anonymised in the data, as per the results.

Conflict of interest statement

None.

Authors' contributions

SD, TC, MS, MGG, NH, MW, and MT generated the simulation data. WP and MF analysed the simulation data. WP created the tables/figures, and drafted the manuscript. All authors contributed to conception and design of the study, interpretation of the data, editing and revising of the article, and gave final approval to be submitted.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.epidem.2015.11.002.

References

Akey, B.L., 2003. Low-pathogenicity H7N2 avian influenza outbreak in Virginia during 2002. Avian Dis. 47, 1099–1103, http://dx.doi.org/10.1637/0005-2086-47.s3.1099.

Anderson, I., 2002 July. Foot and Mouth Disease 2001: Lessons to be Learned Inquiry Report. The Stationery Office, London.

Animal Plant Health Inspection Service (APHIS), 2014. Foot-and-Mouth Disease Response Plan: The Red Book. United States Department of Agriculture Animal and Plant Health Inspection Service Veterinary Services, Washington, DC.

Austin, J.E., 1973. The management bottleneck in family planning programs. Stud. Fam. Plann. 4 (12), 343–350.

Backer, J.A., Hagenaars, T., Nodelijk, G., van Roermund, H., 2012a. Vaccination against foot-and-mouth disease I: epidemiological consequences. Prev. Vet. Med. 107, 27–40, http://dx.doi.org/10.1016/j.prevetmed.2012.05.012.

Backer, J.A., Engel, B., Dekker, A., van Roermund, H.J.W., 2012b. Vaccination against foot-and-mouth disease II: regaining FMD-free status. Prev. Vet. Med. 107 (1–2), 41–50, http://dx.doi.org/10.1016/j.prevetmed.2012.05.013.

Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2003. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. Am. J. Vet. Res. 64 (2), 195–204.

Buetre, B., Wicks, S., Kruger, H., Millist, N., Yainshet, A., Garner, G., et al., 2013. Potential Socio-Economic Impacts of an Outbreak of Foot-and-Mouth Disease in Australia. Australian Bureau of Agricultural and Resource Economics and Sciences, Canberra, Australia.

Carpenter, T.E., 2001. Evaluation of effectiveness of a vaccination program against an infectious disease at the population level. Am. J. Vet. Res. 62 (2), 202–205, http://dx.doi.org/10.2460/ajvr.2001.62.202.

de Klerk, P.F., 2002. Carcass disposal: lessons from the Netherlands after the foot and mouth disease outbreak of 2001. Rev. Sci. Tech. Off. Int. Epiz. 21 (3), 789–796.

Dubé, C., Stevenson, M.A., Garner, M.G., Sanson, R.L., Corso, B.A., Harvey, N., et al., 2007. A comparison of predictions made by three simulation models of foot-and-mouth disease. N. Z. Vet. J. 55 (6), 280–288, http://dx.doi.org/10.1080/00480169.2007.36782.

Durand, B., Mahul, O., 2000. An extended state-transition model for foot-and-mouth disease epidemics in France. Prev. Vet. Med. 47, 121–139, http://dx.doi.org/10.1016/S0167-5877.(00)00158-6).

Dürr, S., Fasel-Clemenz, C., Thür, B., Schwermer, H., Perler, L., Doherr, M.G., et al., 2014. Evaluation of the benefit of emergency vaccination in a foot-and-mouth disease free country with low livestock density. Prev. Vet. Med. 113 (1), 34–46, http://dx.doi.org/10.1016/j.prevetmed.2013.10.015.
Fenner, F., Henderson, D.A., Arita, I., Jezek, Z., Ladnyi, I.D., 1988. Smallpox and its Eradication. World Health Organization, Geneva.
Ferguson, N.M., Donnelly, C.A., Anderson, R.M., 2001. The foot-and-mouth epidemic in Great Britain: pattern of spread and impact of interventions. Science 292, 1155–1160, http://dx.doi.org/10.1126/science.1061020.
Garner, M.G., Beckett, S.D., 2005. Modelling the spread of foot-and-mouth disease in Australia. Aust. Vet. J. 83 (12), 758–766, http://dx.doi.org/10.1111/j.1751-0813.2005.tb11589.x.
Halasa, T., Boklund, A., Stockmarr, A., Enøe, C., Christiansen, L.E., 2014. A comparison between two simulation models for spread of foot-and-mouth disease. PLoS ONE 9 (3), e92521, http://dx.doi.org/10.1371/journal.pone.0092521.
Harvey, N., Reeves, A., Schoenbaum, M.A., Zagmutt-Vergara, F.J., Dubé, C., Hill, A.E., et al., 2007. The North American animal disease spread model: a simulation model to assist decision making in evaluating animal disease incursions. Prev. Vet. Med. 82, 176–197, http://dx.doi.org/10.1016/j.prevetmed.2007.05.019.
Henderson, D.A., Klepac, P., 2013. Lessons from the eradication of smallpox: an interview with D. A. Henderson. Philos. Trans. R. Soc. London, Ser. B 368, 1–7, http://dx.doi.org/10.1098/rstb.2013.0113.
Henderson, D.A., 2011. The eradication of smallpox—an overview of the past, present, and future. Vaccine 29s, D7–D9, http://dx.doi.org/10.1016/j.vaccine.2011.06.080.
Kao, R.R., 2002. The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. TRENDS Microbiol. 10 (6), 279–286, http://dx.doi.org/10.1016/S0966-842X.(02)02371-5).
Kao, R.R., 2003. The impact of local heterogeneity on alternative control strategies for foot-and-mouth disease. Proc. R. Soc. London, Ser. B 270, 2557–2564, http://dx.doi.org/10.1098/rspb.2003.2546.
Keeling, M.J., Woolhouse, M.E.J., Shaw, D.J., Matthews, L., Chase-Topping, M., Haydon, D.T., et al., 2001. Dynamics of the 2001 UK foot and mouth epidemic: stochastic dispersal in a heterogeneous landscape. Science 294, 813–817, http://dx.doi.org/10.1126/science.1065973.
Keeling, M.J., Woolhouse, M.R.J., May, R.M., Davies, G., Grenfell, B.T., 2003. Modelling vaccination strategies against foot-and-mouth disease. Nature 421, 136–142, http://dx.doi.org/10.1038/nature01343.
Keeney, R.L., Raiffa, H., 1976. Decisions with Multiple Objectives: Preferences and Value Tradeoffs. Wiley, New York, NY.
Keeney, R.L., 1992. Value-focused thinking: a path to creative decision-making. Harvard University Press, Cambridge, MA.
Keeney, R.L., 2007. Developing objectives and attributes. In: Edwards, W., Miles Jr., R.F., von Winterfeldt, D. (Eds.), Advances in Decision Analysis. From Foundations to Applications. Cambridge University Press, Cambridge, MA, pp. 104–128.
Knight-Jones, T.J.D., Rushton, J., 2013. The economic impacts of foot and mouth disease - what are they, how big are they and where do they occur? Prev. Vet. Med. 112, 161–173, http://dx.doi.org/10.1016/j.prevetmed.2013.07.013.
Lee, B.Y., Brown, S.T., Korch, G.W., Cooley, P.C., Zimmerman, R.K., Wheaton, W.D., et al., 2010. A computer simulation of vaccine prioritization, allocation, and rationing during the 2009 H1N1 influenza pandemic. Vaccine 28, 4875–4879, http://dx.doi.org/10.1016/j.vaccine.2010.05.002.
Lindström, T., Tildesley, M., Webb, C., 2015. A bayesian ensemble approach for epidemiological projections. PLoS Comput. Biol. 11 (4), e1004187, http://dx.doi.org/10.1371/journal.pcbi.1004187.
Mariner, J.C., House, J.A., Mebus, C.A., Sollod, A.E., Chibeu, D., Jones, B.A., et al., 2012. Rinderpest eradication: appropriate technology and social innovations. Science 337, 1309–1312, http://dx.doi.org/10.1126/science.1223805.
McReynolds, S.W., Sanderson, M.W., Reeves, A., Hill, A.E., 2014. Modeling the impact of vaccination control strategies on a foot and mouth disease outbreak in the Central United States. Prev. Vet. Med. 117, 487–504, http://dx.doi.org/10.1016/j.prevetmed.2014.10.005.
Medlock, J., Galvani, A.P., 2009. Optimizing influenza vaccine distribution. Science 325, 1705–1708, http://dx.doi.org/10.1126/science.1175570.
Milner-Gulland, E.J., Shea, K., Possingham, H.P., Coulson, T., Wilcox, C., 2001. Competing harvesting strategies in a simulated population under uncertainty. Anim. Conserv. 4, 157–167, http://dx.doi.org/10.1017/S1367943001001184.
Morris, R.S., Wilesmith, J.W., Stern, M.W., Sanson, R.L., Stevenson, M.A., 2001. Predictive spatial modelling of alternative control strategies for the foot-and-mouth disease epidemic in Great Britain. Vet. Rec. 149, 137–144, http://dx.doi.org/10.1136/vr.149.5.137.
Nicholson, E., Possingham, H.P., 2006. Objectives for multiple-species conservation planning. Conserv. Biol. 20 (3), 871–881, http://dx.doi.org/10.1111/j.1523-1739.2006.00369.x.
OIE, 2013. World organisation for animal health. In: Terrestrial Animal Health Code, 22nd ed. OIE, Paris.
Paarlberg, P.L., Seitzinger, A.H., Lee, J.G., Mathews Jr., K.H., 2008. Economic impacts of foreign animal disease. In: Technical Report Economic Research Report Number 57. USDA.
Probert, W.J.M., Hauser, C.E., McDonald-Madden, E., Runge, M.C., Baxter, P.W.J., Possingham, H.P., 2011. Managing and learning with multiple models: objectives and optimization algorithms. Biol. Conserv. 144, 1237–1245, http://dx.doi.org/10.1016/j.biocon.2010.07.031.
Raiffa, H., 1968. Decision Analysis. Addison-Wesley, Reading, MA.
Roche, S.E., Garner, M., Sanson, R., Cook, C., Birch, C., Backer, J., et al., 2014a. Evaluating vaccination strategies to control foot-and-mouth disease: a model comparison study. Epidemiol. Infect., http://dx.doi.org/10.1017/S0950268814001927.
Roche, S.E., Garner, M.G., Wicks, R.M., East, I.J., de Witte, K., 2014b. How to resources influence control measures during a simulated outbreak of foot and mouth disease in Australia? Prev. Vet. Med. 113, 436–446, http://dx.doi.org/10.1016/j.prevetmed.2013.12.003.
Rossi, P.H., Williams, W., 1972. Evaluating Social Programs: Theory, Practice and Politics. Seminar Press, New York and London.
Runge, M.C., Walshe, T., 2014. Identifying objectives and alternative actions to frame a decision problem. In: Guntenspergen, G.R. (Ed.), Application of Threshold Concepts in Natural Resource Decision Making. Springer-Verlag, New York, pp. 29–44.
Runge, M.C., Converse, S.J., Lyons, J.E., 2011. Which uncertainty? Using expert elicitation and expected value of information to design an adaptive program. Biol. Conserv. 144, 1214–1223, http://dx.doi.org/10.1016/j.biocon.2010.12.020.
Sanson, R.L., Dubé, C., Cork, S.C., Frederickson, R., Morley, C., 2014. Simulation modelling of a hypothetical introduction of foot-and-mouth disease into Alberta. Prev. Vet. Med. 114, 151–163, http://dx.doi.org/10.1016/j.prevetmed.2014.03.005.
Sanson, R.L., 1993. The Development of a Decision Support System for an Animal Disease Emergency. Massey University, Palmerston North, NZ, PhD Thesis.
Schoenbaum, M.A., Disney, W.T., 2003. Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. Prev. Vet. Med. 58, 25–52, http://dx.doi.org/10.1016/S0167-5877.(03)00004-7).
Senne, D.A., Holt, T.J., Akey, B.L., 2005. An overview of the 2002 outbreak of low-pathogenic H7N2 avian influenza in Virginia, West Virginia and North Carolina. In: Schrijver, R.S., Koch, G. (Eds.), Avian Influenza: Prevention and Control. Wageningen UR Frontis Series. Springer, New York, pp. 41–47.
Shea, K., Possingham, H.P., Murdoch, W.W., Roush, R., 2002. Active adaptive management in insect pest and weed control: intervention with a plan for learning. Ecol. Appl. 12 (3), 927–936.
Shea, K., Jongejans, E., Skarpaas, O., Kelly, D., Sheppard, A.W., 2010. Optimal management strategies to control local population growth or population spread may not be the same. Ecol. Appl. 20 (4), 1148–1161, http://dx.doi.org/10.1890/09-0316.1.
Shea, K., Tildesley, M.J., Runge, M.C., Fonnesbeck, C.J., Ferrari, M.J., 2014. Adaptive management and the value of information: learning via intervention in epidemiology. PLoS Biol. 12 (10), e1001970, http://dx.doi.org/10.1371/journal.pbio.1001970.
Stern, M., 2003. InterSpread plus user guide. In: Institute of Veterinary, Animal and Biomedical Sciences. Massey University, Palmerston North, New Zealand.
Stevenson, M.A., Sanson, R.L., Stern, M.W., O'Leary, B.D., Sujau, M., Moles-Benfell, N., et al., 2013. InterSpread plus: a spatial and stochastic simulation model of disease in animal populations. Prev. Vet. Med. 109, 10–24, http://dx.doi.org/10.1016/j.prevetmed.2012.08.015.
Thornley, J.H.M., France, J., 2009. Modelling foot and mouth disease. Prev. Vet. Med. 89, 139–154, http://dx.doi.org/10.1016/j.prevetmed.2009.02.019.
Tildesley, M.J., Savill, N.J., Shaw, D.J., Deardon, R., Brooks, S.P., Woolhouse, M.E.J., et al., 2006. Optimal reactive vaccination strategies for a foot-and-mouth outbreak in the UK. Nature 440, 83–86, http://dx.doi.org/10.1038/nature04324.
Tildesley, M.J., Deardon, R., Savill, N.J., Bessell, P.R., Brooks, S.P., Woolhouse, M.E.J., et al., 2008. Accuracy of models for the 2001 foot-and-mouth epidemic. Proc. R. Soc. London, Ser. B: Biol. Sci. 275 (1641), 1459–1468, http://dx.doi.org/10.1098/rspb.2008.0006).
U.S.Department of Agriculture (USDA), 2014. Strategic Plan FY 2014–2018. United States Department of Agriculture, pp. 45 (cited 4th January 2016), Available from http://www.usda.gov/documents/usda-strategic-plan-fy-2014-2018.pdf.
Velthuis, A.G.J., Mourits, M.C.M., 2007. Effectiveness of movement-prevention regulations to reduce the spread of foot-and-mouth disease in The Netherlands. Prev. Vet. Med. 82, 262–281, http://dx.doi.org/10.1016/j.prevetmed.2007.05.023.
Walters, C.J., Hilborn, R., 1976. Adaptive control of fishing systems. J. Fish. Res. Board Can. 33, 145–159.
Ward, M.P., Highfield, L.D., Vongseng, P., Garner, M.G., 2009. Simulation of foot-and-mouth disease spread within an integrated livestock system in Texas, USA. Prev. Vet. Med. 88, 286–297, http://dx.doi.org/10.1016/j.prevetmed.2008.12.006.
Woolhouse, M.E.J., 2003. Foot-and-mouth disease in the UK: what should we do next time? J. Appl. Microbiol. 94, 126S–130S.