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A sensitivity analysis of the New Zealand standard model of foot and mouth disease

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Summary

Disease simulation models can be a valuable tool for planning a response to exotic disease incursions, as they provide a fast, low-cost mechanism for identifying the likely outcomes of a range of outbreak scenarios and disease control strategies. To use these tools effectively and with confidence, decision-makers must understand the simplifications and framing assumptions that underlie a model's structure. Sensitivity analysis, the analytical process of identifying which input variables are the key drivers of the model's output, is a crucial process in developing this understanding.

This paper describes the application of a sampling-based sensitivity analysis to the New Zealand standard model (NZSM). This model is a parameter set developed for the InterSpread Plus model platform to allow the exploration of different outbreak scenarios for an epidemic of foot and mouth disease in New Zealand. Based on 200 iterations of the NZSM, run for a simulation period of 60 days, settings related to farm-to-saleyard movements and the detection of disease during the active surveillance phase of the epidemic had the greatest influence on the predicted number of infected premises. A small number of counter-intuitive findings indicated areas of model design, implementation and/or parameterisation that should be investigated further. A potentially useful result from this work would be information to aid the grouping or elimination of non-influential model settings. This would go some way towards reducing the overall complexity of the NZSM, while still allowing it to remain fit for purpose.

Keywords

Disease simulation model – Epidemiology – Foot and mouth disease – Modelling – New Zealand – New Zealand standard model – Sensitivity analysis.

Introduction

In countries with good biosecurity controls at their borders, incursions of exotic diseases such as foot and mouth disease (FMD) are rare. Thus, predictions of the likely outcomes of a given outbreak scenario are difficult because animal health authorities generally have little experience of disease behaviour, given the (often) unique geographical distribution of susceptible livestock species and the way in which farm enterprises interact with each other. During an incursion of an exotic infectious disease, such as FMD, a range of strategies may be applied, including various combinations of culling infected herds, pre-emptive culling of herds at risk and mass vaccination. Depending on the speed with which it is implemented, each strategy is typically accompanied by a range of positive and negative consequences or 'knock-on effects' for various participants in the agricultural sector. Timely and informed decisions must be made about which control and eradication strategies should be adopted at a time of crisis. In this environment, it is important that the evidence used to inform decision-making is transparent in its assumptions and that decisions taken about a particular course of action are able to incorporate differing views, value judgements and framing assumptions (22).

Regardless of discipline, the fundamental objective of modelling is to provide an accurate representation (as

opposed to replication) of a system of interest (22). A model that meets these objectives provides a low-cost and quick mechanism for identifying the likely outcome of a range of complex situations and scenarios. This, in turn, improves understanding of the system as a whole and can be used as an aid for decision-making (7, 9).

In animal health, infectious disease models have the potential to combine knowledge of the population at risk, epidemiological characteristics of the infectious agent, and the logistics of control efforts and their economic consequences, making them a valuable tool for supporting decision-making (29). This said, a lack of transparency in the way that models work and their framing assumptions can result in decision-makers losing confidence in their outputs and, consequently, not using them to their full potential. On the other hand, decision-makers may ignore or be unaware of the key simplifications inherent in a model, and may place too much confidence in its outputs, resulting in inappropriate ('risky') decision-making (15). The only way to mitigate these potential problems is to increase the decision-maker's awareness of:

– what the whole modelling process entails

– what constitutes good practice for using models

– how the results of models should be viewed

– what sorts of questions users should be asking of modellers.

This amounts to specifying good model practice in terms of development, reporting and critical review (13). Sensitivity analysis, the analytical process of identifying which input variables are key drivers of the model's output, should be regarded as a key component of good model practice.

InterSpread Plus (IS+) (23, 28) is a simulation model of infectious disease designed for use with domestic animal populations. Within the IS+ framework, the unit of interest is the farm: a defined location in space containing one or more of the animal species susceptible to the disease of interest. InterSpread Plus is a state-transition model (5, 14), with a set of defined states in which farms may be at a given point in time:

– susceptible

– infected

– clinical

– detected

– immune.

The structure of IS+ allows for a range of model definitions, from relatively simple spread models with few parameters (for instance, a single, local spread mechanism using a radial transmission kernel) to more complex models, with a range of spread mechanisms (e.g. local, airborne, and direct- and indirect-contact transmission pathways). It also provides the ability to apply a range of control strategies, including: resource-constrained depopulation, surveillance, movement controls, tracing activities and vaccination. The settings used to define each of the parameters needed to drive an IS+ model vary but, in general, require either numeric values declared as point estimates, defined distributions and/or look-up tables.

In 2005, the New Zealand Ministry of Agriculture and Forestry commissioned the development of a set of IS+ parameters to best represent the behaviour of an FMD epidemic if the virus entered the country, causing an outbreak. The intention was that this parameter set, termed the 'New Zealand standard model' (NZSM) (27), would be used to provide decision support before, and at the time of, an epidemic of FMD. The NZSM incorporates the known epidemiology of the disease with current knowledge of animal movement patterns between farms and/or saleyards (animal markets) in New Zealand. This allows researchers to explore different outbreak scenarios to compare size, duration or economic impacts under different control and surveillance strategies.

This paper describes the application of a sampling-based sensitivity analysis technique to the NZSM. The authors' aim was to contribute to the corroboration of the NZSM by identifying those settings in the model that had the greatest influence on the predicted number of infected premises in a simulated outbreak of FMD in New Zealand.

Materials and methods

The settings used in the NZSM model can be placed into two broad categories:

– those settings defining how disease spreads from one location to another

– settings defining how the disease will be controlled, once it has been detected.

The settings defining disease spread include details of:

– off-farm movement events (their frequency and the distance over which they occur)

– local spread (the probability of infection occurring on destination premises at given space-time separations from an infected source)

– characteristics of the FMD virus being modelled (e.g. the number of days from infection to the onset of clinical signs, and the number of days from infection to the onset of infectiousness).

The settings defining disease control include:

– details of the intensity of surveillance

– the timing, extent and effectiveness of movement restrictions, tracing activities and depopulation of farm premises.

Three distinct movement restrictions are defined within the NZSM:

– a national animal movement standstill for 14 days

– an infected-zone standstill (covering the affected region of the country)

– a 10-km surveillance zone standstill around detected infected premises.

In total, the NZSM is composed of 107 individual settings within 51 parameters. Details of these parameters and the settings within each parameter are provided in Tables I to IV.

The approach adopted for the sensitivity analysis described in this paper closely follows the methodology used by Blower and Dowlatabadi (2). In their 1994 paper, Blower and Dowlatabadi conducted a sensitivity analysis of a deterministic model of human immunodeficiency virus. Their model comprised 34 differential equations containing 20 parameters. These authors assigned a probability density function to each of the 20 parameters and used Latin hypercube sampling (11, 16) to sample from each distribution, ensuring that the entire range of possible values in the distribution was represented. The authors took a slightly different approach, since many of the input parameters in the NZSM were themselves defined as probability distributions. For the authors' analyses, the lower and upper bounds of the range of biologically plausible settings for each parameter of each probability distribution defined within the NZSM were specified. These bounds were then used to define the lower and upper bounds of a uniform distribution. For example, if the number of off-farm movements per day from a dairy farm was parameterised using a Poisson distribution with mean $\lambda = 0.04$ (equivalent to, on average, one off-farm movement event every 25 days), the authors specified the plausible range of values for λ as 0.01 to 0.1. That is, they believe that a single movement from a dairy farm might occur as infrequently as every 100 days ($\lambda = 0.01$) or as frequently as every 10 days ($\lambda = 0.1$). Settings defined as empirical distribution functions were entered into the model as look-up tables, and a set of three alternative candidate table definitions were defined. As an example, the probability that disease will be detected on a farm as a function of the number of days since the onset of clinical signs and three candidate distributions is shown in Figure 1.

To produce a set of data suitable for sensitivity analysis, the authors made a random draw from each uniform distribution to generate appropriate settings for each of the 107 settings of interest. For settings defined as look-up tables, a number between one and four was selected at random and the details for the corresponding look-up table were selected. A vector of length k was generated (composed of samples for each of the $k = 107$ input settings in the NZSM) and these values were then used as the settings for a single model run. At the conclusion of the single model run, the total predicted number of infected premises after a simulation period of 60 days was calculated and stored. This process was repeated 200 times, generating a matrix comprising 108 columns (the settings for the 107 input settings plus the single numeric value representing the predicted number of infected premises) and 200 rows (the number of model runs).

Sensitivity analyses were performed by calculating partial rank correlation coefficients (PRCCs) for each input parameter and the outcome variable, using the approach described by Iman and Conover (10), Iman and Helton (11) and Iman *et al*. (12). The significance of a non-zero PRCC value was tested by computing a t test statistic which approximated a student's t distribution with N-2 degrees of freedom, where N equalled the number of model runs.

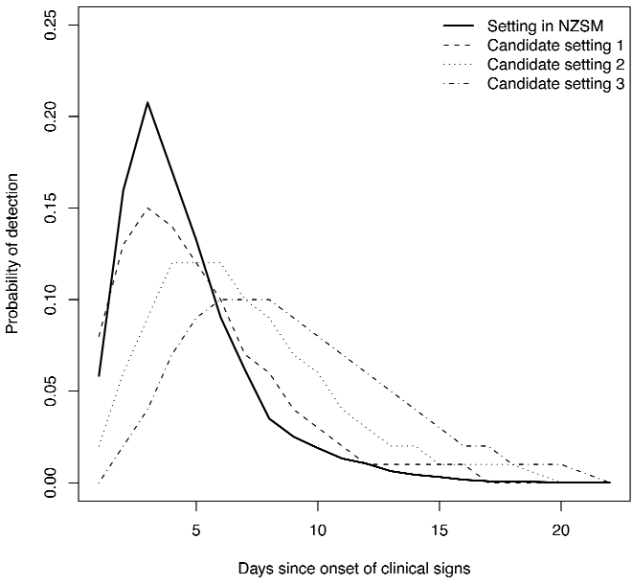


Fig. 1

Line plot showing the probability that a pig or dairy farm will be detected as positive for the disease, as a function of the number of days since the onset of clinical signs

The solid line shows the settings used in the New Zealand standard model (NZSM). The dashed lines show the three candidate settings used in the sensitivity analyses

Table I

Details of the ten parameters defining farm-to-farm and farm-to-saleyard movements within the New Zealand standard model

Also shown are the settings used in the New Zealand standard model and candidate settings for the sensitivity analysis

Parameter	Setting in NZSM	Candidate settings
1. Pastoral livestock, high risk to farm:		
Number per time period	Poisson (λ = 0.03)	λ = uniform (0, 0.1)
Number of direct contacts	Constant *n* = 1	*n* = uniform (0, 5)
Probability of transmission	Table (6, 11, 16; 0.525, 0.8, 1)[a]	6, 11, 16; 0.12, 0.52, 1 6, 11, 16; 0.25, 0.62, 1 6, 11, 16; 0.525, 0.8, 1 6, 11, 16; 0.7, 0.88, 1
2. Dairy, high risk to farm:		
Number per time period	Poisson (λ = 0.042)	λ= uniform (0, 0.1)
Number of direct contacts	Constant *n* = 1	*n* = uniform (0, 5)
Probability of transmission	Table (6, 11, 16; 0.62, 0.8, 1)	6, 11, 16; 0.12, 0.52, 1 6, 11, 16; 0.25, 0.62, 1 6, 11, 16; 0.525, 0.8, 1 6, 11, 16; 0.7, 0.88, 1
3. Dry grazing, high risk to farm:		
Number per time period	Poisson (λ= 0.1152)	λ = uniform (0,1)
Number of direct contacts	Constant *n* = 1	*n* = uniform (0, 5)
Probability of transmission	Table (6, 11, 16; 0.673, 0.8, 1)	6, 11, 16; 0.12, 0.52, 1 6, 11, 16; 0.25, 0.62, 1 6, 11, 16; 0.525, 0.8, 1 6, 11, 16; 0.7, 0.88, 1
4. Pig breeding, high risk to farm:		
Number per time period	Poisson (λ= 0.131)	λ= uniform (0, 1)
Number of direct contacts	Constant *n* = 1	*n* = uniform (0, 5)
Probability of transmission	Table (6, 11, 16; 0.458, 0.8, 1)	6, 11, 16; 0.12, 0.52, 1 6, 11, 16; 0.25, 0.62, 1 6, 11, 16; 0.525, 0.8, 1 6, 11, 16; 0.7, 0.88, 1
5. Medium risk to farm:		
Number per time period	Poisson (λ = 0.4743)	λ = uniform (0, 1)
Number of direct contacts	Constant *n* = 1	*n* = uniform (0, 5)
Probability of transmission	Constant *n* = 0.05	*n* = uniform (0, 0.1)
6. Low risk to farm:		
Number per time period	Poisson (λ = 0.0595)	λ = uniform (0, 0.1)
Number of direct contacts	Constant *n* = 1	*n* = uniform (0, 5)
Probability of transmission	Constant *n* = 0.01	*n* = uniform (0, 0.1)
7. Pastoral livestock to saleyard:		
Number per time period	Poisson (λ = 0.0135)	λ = uniform (0, 0.1)
Number of secondary contacts	Poisson (λ = 1.942)	λ = uniform (0, 5)
Probability of transmission	Table (6, 11, 16; 0.458, 0.776, 1)	6, 11, 16; 0.12, 0.52, 1 6, 11, 16; 0.25, 0.62, 1 6, 11, 16; 0.525, 0.8, 1 6, 11, 16; 0.7, 0.88, 1
8. Dairy to saleyard:		
Number per time period	Poisson (λ = 0.005)	λ = uniform (0, 0.1)
Number of secondary contacts	Poisson (λ = 1.942)	λ = uniform (0, 5)
Probability of transmission	Table (6, 11, 16; 0.458, 0.776, 1)	6, 11, 16; 0.12, 0.52, 1 6, 11, 16; 0.25, 0.62, 1 6, 11, 16; 0.525, 0.8, 1 6, 11, 16; 0.7, 0.88, 1
9. Dry grazing to saleyard:		
Number per time period	Poisson (λ = 0.003)	λ = uniform (0, 0.01)
Number of secondary contacts	Poisson (λ = 1.942)	λ = uniform (0, 5)
Probability of transmission	Table (6, 11, 16; 0.458, 0.776, 1)	6, 11, 16; 0.12, 0.52, 1 6, 11, 16; 0.25, 0.62, 1 6, 11, 16; 0.525, 0.8, 1 6, 11, 16; 0.7, 0.88, 1
10. Pig breeding to saleyard:		
Number per time period	Poisson (λ = 0.036)	λ = uniform (0, 0.1)
Number of secondary contacts	Poisson (λ = 1.942)	λ = uniform (0, 5)
Probability of transmission	Table (6, 11, 16; 0.458, 0.776, 1)	6, 11, 16; 0.12, 0.52, 1 6, 11, 16; 0.25, 0.62, 1 6, 11, 16; 0.525, 0.8, 1 6, 11, 16; 0.7, 0.88, 1

NZSM: New Zealand standard model

a) Table (6,11,16; 0.525, 0.8,1) is interpreted as:

6	11	16
0.525	0.8	1

This specifies the probability that a destination farm will be infected, given the difference in the number of days between the onset of clinical signs on the source farm and the time when the movement occurs. In the above example, if an off-farm movement occurs from an infected farm six days after the onset of clinical signs, the probability that transmission will occur is 0.525

Table II

Details of the six parameters defining surveillance before and after detection of the outbreak within the New Zealand standard model

Also shown are the settings used in the New Zealand standard model and candidate settings for the sensitivity analysis

Parameter	Setting in NZSM	Candidate settings
1. Background surveillance:		
All farm types selection probability	Constant $n = 1$	n = uniform (0, 1)
Pastoral livestock detection probability	Table[a]	
Dairy detection probability	Table[a]	
Dry grazing detection probability	Table[a]	
Pig detection probability	Table[a]	
2. Self report surveillance:		
All farm types selection probability	Constant $n = 1$	n = uniform (0, 1)
Pastoral livestock detection probability	Table[a]	
Dairy detection probability	Table[a]	
Dry grazing detection probability	Table[a]	
Pig detection probability	Table[a]	
3. Surveillance following HR contact:		
All farm types selection probability	Constant $n = 1$	n = uniform (0, 1)
Beef cattle detection probability	Constant $n = 1$	n = uniform (0, 1)
Dairy cattle detection probability	Constant $n = 1$	n = uniform (0, 1)
Deer detection probability	Constant $n = 1$	n = uniform (0, 1)
Goats detection probability	Constant $n = 1$	n = uniform (0, 1)
Pigs detection probability	Constant $n = 1$	n = uniform (0, 1)
Sheep detection probability	Constant $n = 1$	n = uniform (0, 1)
4. Surveillance following MR contact:		
All farm types selection probability	Constant $n = 0.9$	n = uniform (0, 1)
Beef cattle detection probability	Constant $n = 1$	n = uniform (0, 1)
Dairy cattle detection probability	Constant $n = 1$	n = uniform (0, 1)
Deer detection probability	Constant $n = 1$	n = uniform (0, 1)
Goats detection probability	Logistic (0.25, 0.8, 0.74, 1.7)[b]	0.25, 0.2, 0.74, 1.7 0.25, 0.4, 0.74, 1.7 0.25, 0.6, 0.74, 1.7 0.25, 0.8, 0.74, 1.7 0.25, 1.0, 0.74, 1.7
Pigs detection probability	Constant $n = 1$	n = uniform (0, 1)
Sheep detection probability	Logistic (0.25, 0.8, 0.74, 1.7)[b]	0.25, 0.2, 0.74, 1.7 0.25, 0.4, 0.74, 1.7 0.25, 0.6, 0.74, 1.7 0.25, 0.8, 0.74, 1.7 0.25, 1.0, 0.74, 1.7
5. Surveillance following LR contact:		
All farm types selection probability	Constant $n = 0.5$	n = uniform (0, 1)
Beef cattle detection probability	Constant $n = 1$	n = uniform (0, 1)
Dairy cattle detection probability	Constant $n = 1$	n = uniform (0, 1)
Deer detection probability	Constant $n = 1$	n = uniform (0, 1)
Goats detection probability	Logistic (0.25, 0.8, 0.74, 1.7)[b]	0.25, 0.2, 0.74, 1.7 0.25, 0.4, 0.74, 1.7 0.25, 0.6, 0.74, 1.7 0.25, 0.8, 0.74, 1.7 0.25, 1.0, 0.74, 1.7
Pigs detection probability	Constant $n = 1$	n = uniform (0, 1)
Sheep detection probability	Logistic (0.25, 0.8, 0.74, 1.7)[b]	0.25, 0.2, 0.74, 1.7 0.25, 0.4, 0.74, 1.7 0.25, 0.6, 0.74, 1.7 0.25, 0.8, 0.74, 1.7 0.25, 1.0, 0.74, 1.7
6. Surveillance following patrol visit:		
All farm types selection probability	Constant $n = 1$	n = uniform (0, 1)
Beef cattle detection probability	Constant $n = 1$	n = uniform (0, 1)
Dairy cattle detection probability	Constant $n = 1$	n = uniform (0, 1)
Deer detection probability	Constant $n = 1$	n = uniform (0, 1)
Goats detection probability	Logistic (0.25, 0.8, 0.74, 1.7)[b]	0.25, 0.2, 0.74, 1.7 0.25, 0.4, 0.74, 1.7 0.25, 0.6, 0.74, 1.7 0.25, 0.8, 0.74, 1.7 0.25, 1.0, 0.74, 1.7
Pigs detection probability	Constant $n = 1$	n = uniform (0, 1)
Sheep detection probability	Logistic (0.25, 0.8, 0.74, 1.7)[b]	0.25, 0.2, 0.74, 1.7 0.25, 0.4, 0.74, 1.7 0.25, 0.6, 0.74, 1.7 0.25, 0.8, 0.74, 1.7 0.25, 1.0, 0.74, 1.7

a) See Fig. 1 for details

b) Logistic $(a,b,c,d) = a + \frac{c}{1+exp[-b(x-m)]}$

HR: high risk

LR: low risk

MR: medium risk

NZSM: New Zealand standard model

Table III

Details of the eight parameters defining tracing efficiency within the New Zealand standard model

Also shown are the settings used in the New Zealand standard model and candidate settings for the sensitivity analysis

Parameter	Setting in NZSM	Candidate settings
1. Pastoral livestock, high risk:		
Probability of forgetting a movement off the property	Constant $n = 0.11$	n = uniform (0, 1)
Delays in tracing a movement off the property	Table (0.5, 1; 0,1)[a]	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
Probability of forgetting a movement onto the property	Constant $n = 0.082$	n = uniform (0, 1)
Delays in tracing a movement onto the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75,1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
2. Dairy high risk:		
Probability of forgetting a movement off the property	Constant $n = 0.11$	n = uniform (0, 1)
Delays in tracing a movement off the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
Probability of forgetting a movement onto the property	Constant $n = 0.082$	n = uniform (0, 1)
Delays in tracing a movement onto the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
3. Dry grazing:		
Probability of forgetting a movement off the property	Constant $n = 0.11$	n = uniform (0, 1)
Delays in tracing a movement off the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
Probability of forgetting a movement onto the property	Constant $n = 0.082$	n = uniform (0, 1)
Delays in tracing a movement onto the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
4. Pig breeding:		
Probability of forgetting a movement off the property	Constant $n = 0.11$	n = uniform (0, 1)
Delays in tracing a movement off the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
Probability of forgetting a movement onto the property	Constant $n = 0.082$	n = uniform (0, 1)
Delays in tracing a movement onto the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
5. Medium risk:		
Probability of forgetting a movement off the property	Constant $n = 0.212$	n = uniform (0, 1)
Delays in tracing a movement off the property	BetaPert ($a = 1$, $b = 2$, $c = 3$)	b = uniform (1, 3)
Probability of forgetting a movement onto the property	Constant n = 0.194	n = uniform (0, 1)
Delays in tracing a movement onto the property	BetaPert ($a = 1$, $b = 2$, $c = 3$)	b = uniform (1, 3)
6. Low risk:		
Probability of forgetting a movement off the property	Constant $n = 0.36$	n = uniform (0, 1)
Delays in tracing a movement off the property	BetaPert ($a = 2$, $b = 3$, $c = 4$)	b = uniform (2, 4)
7. Dairy tanker:		
Probability of forgetting a movement off the property	Constant $n = 0.014$	n = uniform (0, 1)
Delays in tracing a movement off the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
Probability of forgetting a movement onto the property	Constant $n = 0.014$	n = uniform (0, 1)
Delays in tracing a movement onto the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
8. Saleyard, high risk:		
Probability of forgetting a movement off the property	Constant $n = 0.063$	n = uniform (0, 1)
Delays in tracing a movement off the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3
Probability of forgetting a movement onto the property	Constant $n = 0.058$	n = uniform (0, 1)
Delays in tracing a movement onto the property	Table (0.5, 1; 0, 1)	0.5, 1; 0, 1 0.25, 0.75, 1.00; 0, 1, 2 0.25, 0.50, 0.75, 1; 0, 1, 2, 3

NZSM: New Zealand standard model

a) Table (0.5, 1; 0, 1) is interpreted as:

0.5	1
0	1

This specifies the number of time periods it takes to trace the specified movement type in the specified direction. In the above example, 50% of movements will be traced on the same day as the day of detection and 100% will be traced within one day of detection

Table IV
Details of the three parameters defining the efficacy of movement restrictions and the single parameter defining resources available for depopulation within the New Zealand standard model
Also shown are the settings used in the New Zealand standard model and candidate settings for the sensitivity analysis

Parameter	Setting in NZSM	Candidate settings
1. Probability restriction HR movements:		
Initial standstill	Constant $n = 0.914$	n = uniform (0, 1)
Inside infected zone	Constant $n = 0.942$	n = uniform (0, 1)
Inside surveillance zone	Constant $n = 0.951$	n = uniform (0, 1)
Outside control area	Constant $n = 0.951$	n = uniform (0, 1)
2. Probability restriction MR movements:		
Initial standstill	Constant $n = 0.604$	n = uniform (0, 1)
Inside infected zone	Constant $n = 0.804$	n = uniform (0, 1)
Inside surveillance zone	Constant $n = 0.850$	n = uniform (0, 1)
Outside control area	Constant $n = 0.850$	n = uniform (0, 1)
3. Probability restriction LR movements:		
Initial standstill	Constant $n = 0.238$	n = uniform (0, 1)
Inside infected zone	Constant $n = 0.390$	n = uniform (0, 1)
Inside surveillance zone	Constant $n = 0.520$	n = uniform (0, 1)
Outside control area	Constant $n = 0.520$	n = uniform (0, 1)
4. Depopulation number per time period:		
Pastoral livestock	Triangular ($a = 0$, $b = 0$, $c = 5$)	b = uniform (0, 5)
Dairy	Triangular ($a = 0$, $b = 1$, $c = 3$)	b = uniform (0, 3)
Dry grazing	Triangular ($a = 0$, $b = 0$, $c = 3$)	b = uniform (0, 3)
Pig	Triangular ($a = 0$, $b = 0$, $c = 3$)	b = uniform (0, 3)

HR: high risk
LR: low risk
MR: medium risk
NZSM: New Zealand standard model

Since PRCCs indicate the degree of monotonicity between two variables, care was taken to ensure that only those settings monotonically related to the output variable were used. A monotonic relationship is one in which an outcome variable moves in only one direction (up or down) as an explanatory variable increases, but the relationship is not necessarily (but can be) linear. Plots of the number of infected premises as a function of the simulated setting values were generated to identify those settings where the monotonicity assumption was satisfied (11).

Partial rank correlation coefficients provide two useful pieces of information. First, the sign of the PRCC indicates the qualitative relationship between the input setting and the output: positive PRCCs arise when increases in the value of an input setting result in increases in the output variable; negative PRCCs arise when increases in the value of an input setting result in decreases in the output variable. Secondly, the magnitude of the PRCC indicates the importance of the input setting in contributing to the value of the outcome variable. The further the PRCC from zero, the greater the influence of the variable on the outcome. Thus, the relative importance of each of the input settings can be directly evaluated by comparing their PRCC values.

Results

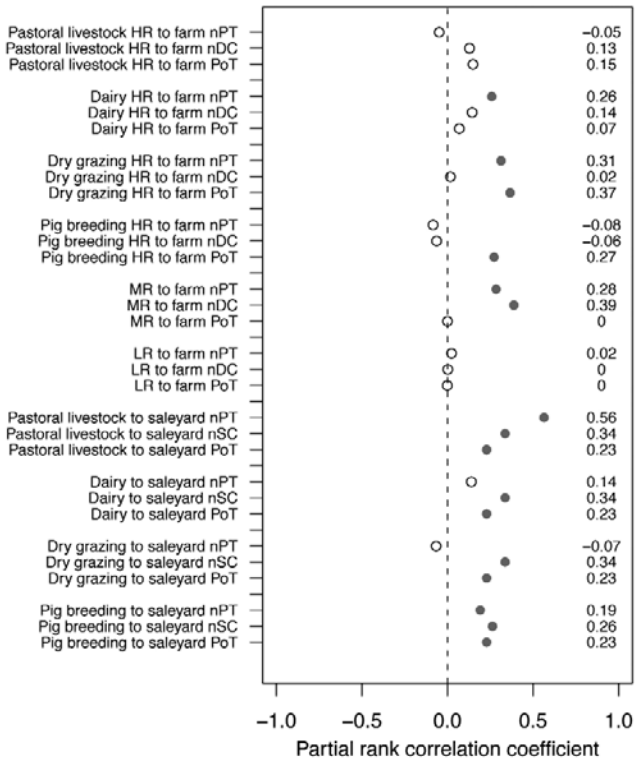
For these analyses, the population of interest comprised farms located in the North Island of New Zealand. Each outbreak was initiated by seeding infection into a single farm located in the lower half of the North Island. The median predicted number of infected premises (based on 200 iterations) after 60 days was 7 (minimum 1; maximum 99). The median outbreak duration was 22 days (minimum 1; maximum 60).

Scatterplots of the predicted number of infected premises as a function of the simulated values for each setting showed that the assumption of monotonicity held for all 107 settings evaluated, and that the sampling technique provided a set of candidate values that were adequately distributed across the plausible range of values for a given setting (results not presented).

Details of settings within the parameters defining farm-to-farm and farm-to-saleyard movements, surveillance before and after detection of the outbreak, tracing and movement restrictions are shown in Tables I, II, III and IV, respectively. Table IV also provides details of the parameters defining resources available for depopulation. Partial rank correlation coefficient values for settings related to movement, surveillance, tracing and movement restrictions, and depopulation resources are shown in Figures 2, 3, 4 and 5, respectively. In Figures 2 to 5, PRCC values significantly greater or less than zero are indicated by solid circles.

Of all the movement settings used in the NZSM, farm-to-saleyard movements collectively had the greatest influence on the predicted number of infected places at 60 days (Fig. 2). The settings defining the frequency of movement events off pastoral livestock and pig-breeding farms to saleyards per time period; the number of secondary contacts generated from movements of pastoral livestock, dairy, dry-grazing and pig-breeding farms to saleyards; and the probability of disease transmission from the movements of pastoral livestock, dairy, dry-grazing and pig-breeding farms had PRCC values that were positive and statistically significant at the alpha level of 0.05. Other movement types with significant PRCCs included the frequency of high-risk movements off dairy and dry-grazing farms; the frequency of medium-risk movements (off all farm types), and the probability of transmission after high-risk movements off dry-grazing and pig-breeding farms.

In the NZSM, the 'background' surveillance setting defined the degree of pre-epidemic surveillance for FMD that would ultimately result in detection of the first infected premises and initiation of control activities. Increases in the probability of detection during background surveillance on dry and pastoral livestock enterprises decreased the predicted number of infected premises (Fig. 3). Increases in the probability of detection on dry-grazing and pig-breeding farms that self-report the presence of disease significantly decreased the number of infected premises. Increases in the probability of detection in enterprises involving beef cattle, pigs and deer, which received low- and medium-risk contacts, decreased the predicted number of infected premises. Increases in the probability of detection on deer farms receiving low-risk contacts were associated with a significant increase in the predicted number of infected premises.



HR: high risk
LR: low risk
MR: medium risk
nDC: number of direct contacts
nPT: number per time period
nSC: number of secondary contacts
PoT: probability of transmission

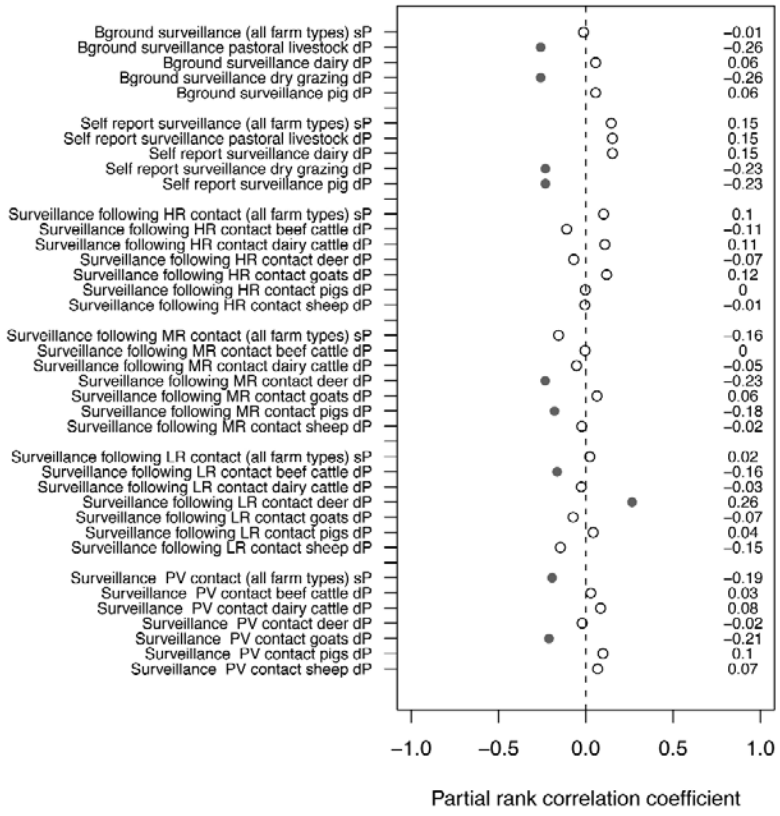
Fig. 2

Partial rank correlation coefficients for settings within the ten parameters defining farm-to-farm and farm-to-saleyard movements within the New Zealand standard model

Solid circles (•) identify settings whose partial rank correlation coefficient values were significant at the alpha level of 0.05

Partial rank correlation coefficient values for each of the monitored tracing parameters are shown in Figure 4. Increases in the probability of forgetting movement events off and onto pastoral livestock farms were associated with a decrease in predicted epidemic size. Increases in the delay in tracing high-risk movements onto dairy and pig-breeding farms were also associated with a decrease in predicted epidemic size. Increases in the probability of forgetting off-farm low-risk movements and on-farm dairy tanker movements were associated with an increase in predicted epidemic size.

For control activities, increases in the proportion of restricted high-risk movements inside the infected zone, high-risk movements out of the control area, and low-risk movements within defined surveillance areas significantly decreased the predicted number of infected premises (Fig. 5). Increases in the probability of medium-risk movements being restricted during the initial standstill period, and increases in the probability of medium-risk movements being restricted outside the control area, were associated with an increase in the predicted number of infected premises.



Bground: background
dP: detection probability
HR: high risk
LR: low risk
MR: medium risk
PV: patrol visit
sP: selection probability

Fig. 3
Partial rank correlation coefficients for settings within the six parameters defining surveillance within the New Zealand standard model
Solid circles (•) identify those settings whose partial rank correlation coefficient values were significant at the alpha level of 0.05

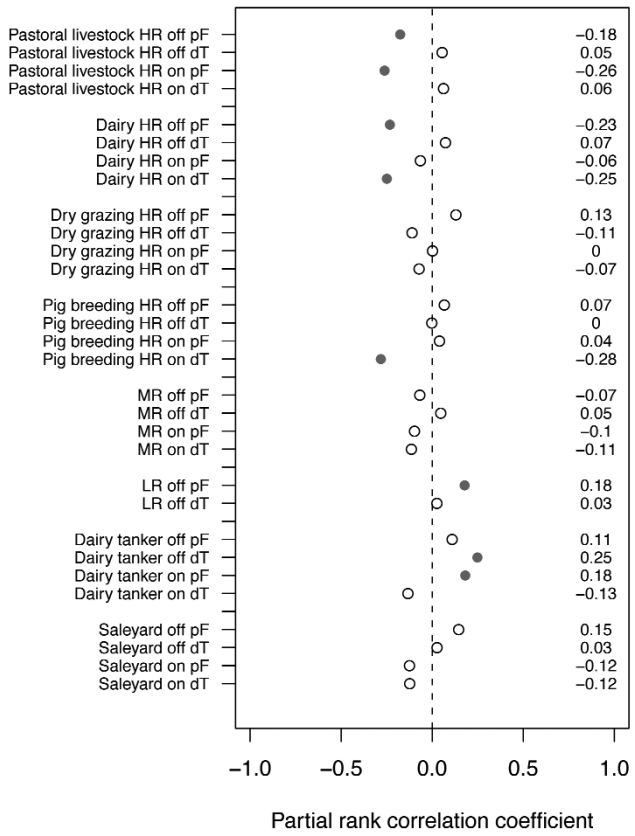
Discussion

On the whole, the authors' findings made biological sense and provided indirect confidence that the NZSM parameter set provides an appropriate indication of the way FMD might spread if it were introduced into the farm animal population in New Zealand. Collectively, the settings defining farm-to-saleyard animal movements had the greatest influence on the predicted number of infected premises (Fig. 2): a finding consistent with analyses of the data from the FMD outbreak that occurred in the United Kingdom in 2001 (8, 19, 30). This implies that efforts taken to accurately record the frequency of farm-to-saleyard movements, the number of secondary contacts and estimates of the probability of disease transmission following a movement event should enhance the accuracy of NZSM predictions.

To the best of the authors' knowledge, the work of Sanson (25) is the only study to document details of farm-to-saleyard movements of livestock in New Zealand. Given the impact of farm-to-saleyard movement patterns on model output, it is essential that the frequency and distance estimates provided by studies of this type are updated regularly, since the propensity of livestock owners to shift animals to saleyards will vary over time and depend on the slaughter value of individual animals, as well as the costs of grazing, transport and seasonal conditions. Implementation of the National Animal Identification and Tracing System (www.nait.co.nz) and routine analysis of data recorded by this system would partly meet this requirement. Additional studies would still be required, however, to provide an estimate of disease transmission probabilities when a movement takes place.

Nine of the ten detection probability surveillance settings had significant PRCC values that were negative. This means that increases in the probability of detection were associated with a decrease in the predicted number of infected premises. A single setting, the probability of detection on premises with deer after a low-risk contact, had a positive PRCC (Fig. 3). This finding was counter-intuitive.

Detailed analyses of the model's behaviour – i.e. following the step-by-step sequence of infection events following low-risk movement events onto farms with deer – would



dT: tracing delay (days)
HR: high risk
LR: low risk
MR: medium risk
pF: probability of forgetting an on- or off-farm movement

Fig. 4
Partial rank correlation coefficients for settings within the eight parameters defining efficacy of tracing within the New Zealand standard model
Solid circles (•) identify those settings whose partial rank correlation coefficient values were significant at the alpha level of 0.05

be an obvious approach for investigating this anomaly further. This is an example of another benefit of the sensitivity analysis process. By identifying counter-intuitive model behaviour, a sensitivity analysis allows us to identify specific areas of the model that should be investigated in detail for possible errors in design, implementation and/or parameterisation.

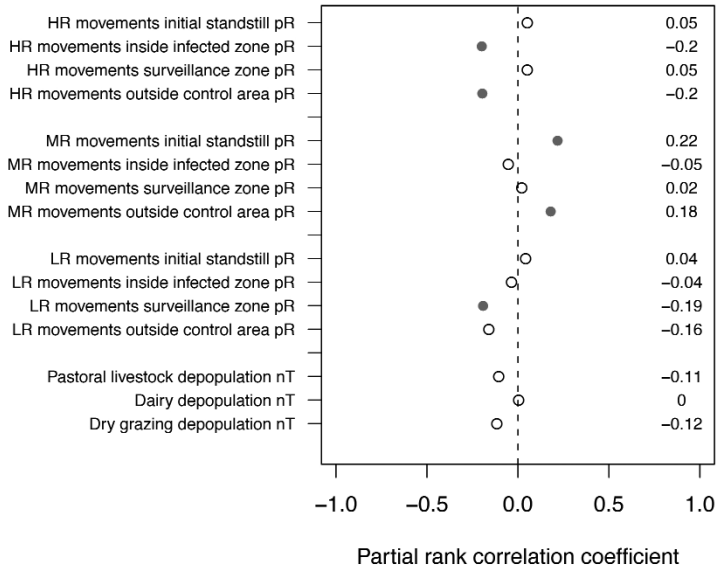
Sensitivity analysis of the tracing parameters related to high-risk pastoral livestock and dairy-farm movements also presented findings that were counter-intuitive. Analyses to clarify the mechanism of these effects, using an approach similar to that described above, are required to investigate these anomalies further. An additional explanation is that the number of simulation days specified (n = 60) was insufficient to allow the full effect of changes in tracing efficacy to be reflected in model output.

Increases in the probability of restricting high-risk movements inside the infected zone and outside the control area were associated with a decrease in the predicted number of infected premises (Fig. 5). This finding is consistent with the known biology of FMD (24). Increases in the probability of restricting medium-risk movements during the initial standstill period and outside the control area were associated with an increase in the predicted number of infected premises. This was yet another finding that was counter-intuitive. Further analyses are required to investigate this.

If a model is non-linear or non-additive, the influence of a variable will change at different points in the input space due to interactions with other variables. In these situations, where linearity and additivity cannot be assumed, local sensitivity methods are inappropriate. Global approaches that are independent of the model, or at least assume monotonicity rather than linearity or independence, should be used (18, 21). Global methods involve simultaneous adjustments, which allow the entire parameter domain, or at least a substantial area of the domain, to be analysed. A range of global techniques have been described to explore the behaviour of models used in economics, engineering, chemistry and physics. These techniques include 'elementary effects' methods (for example, that of Campolongo *et al*. [3], based on the so-called 'Morris' method [17]); variance-based methods, and sampling-based methods, using parametric tests of ranked data of the type described in this study (2). Of this group, the most suitable approaches for complex disease simulation models include the elementary effects methods and sampling-based methods using parametric tests of ranked data.

Type II errors (the failure to identify a factor of considerable influence on the model) are recognised as potential problems when using parametric tests of ranked data (A. Saltelli, personal communication). An alternative would be to use an elementary effects approach, such as the adapted Morris method (3). The Morris method is no more computationally demanding than the method described here and has the advantage of being more resilient to type II errors. A benefit of applying multiple sensitivity analysis techniques to the same model is that the combined knowledge provides a more detailed picture of how the parameters interact and contribute to model output uncertainty, and thus results in deeper insight into the model's behaviour (4).

Although good practices are well established for sensitivity analysis of models used in chemical engineering, biostatistics and risk analysis (13, 20), the uptake of these techniques appears to be relatively poor in the wider scientific community. Sensitivity analysis is an important component of good scientific practice and should be regarded as an integral part of model development, rather than as an additional and non-essential set of analyses (20). The approach described in this paper should be seen as one element that contributes to the corroboration of IS+



HR: high risk
LR: low risk
MR: medium risk
nT: number of herds able to be processed per time period (days)
pR: probability of restriction

Fig. 5
Partial rank correlation coefficients for settings within the three parameters defining efficacy of movement restrictions, and the single parameter defining the resources required for depopulation, within the New Zealand standard model
Solid circles (•) identify those settings whose partial rank correlation coefficient values were significant at the alpha level of 0.05

and the NZSM, in the context of a specific problem and particular management scenarios. Other approaches that are currently being applied are the multiple model comparisons of similar outbreak scenarios (6, 26) and continuous seeking of expert opinion.

Simulation models of disease in human and animal populations are typically composed of a series of logical processes that allow a response (usually the presence or absence of disease at a given location) to be predicted as a function of a set of defined decision rules (1). These models can be tactically useful as they follow a logical, biologically valid process that is flexible and can incorporate a high degree of detail (29). Although the flow of logic in disease simulation models tends to be straightforward, attempts to incorporate a high level of detail make it difficult for developers to provide a concise description of a model's overall design to non-technical personnel. This is particularly the case with 'generic' simulation models (i.e. those designed to simulate a range of infectious disease conditions, such as IS+), since these often incorporate settings that may not be directly applicable to a given disease scenario of interest. Thus, a balance needs to be struck between complexity and simplification to ensure that simulation models provide sufficient information about the system under investigation without being so complex that they cannot be widely understood.

The analyses presented in this paper represent the first of a number of steps that may be applied to refine the NZSM. A potentially useful result of this work would be information that informs the grouping of non-influential settings (e.g. the low- and medium-risk movement parameters). This would go some way towards reducing the overall complexity of the NZSM, while still allowing it to remain fit for its purpose. This simplified model would potentially offer greater transparency to decision-makers but retain the benefits of the parent model's complexity. Results from the simplified model could be compared with the fully parameterised version for validation.

Several other possibilities should be considered for further work. In particular, it is important to carry out sensitivity analyses at various times during the simulation; for example, at the time the disease is first detected, then at regular intervals throughout the control and eradication phase of the epidemic. This process would identify how the sensitivity of the model changes during the simulation period, quantifying the way in which prediction precision changes over time and the effect of time on both the values of the PRCC and their relative rankings.

Analyse de la sensibilité du modèle standard pour la fièvre aphteuse appliqué en Nouvelle-Zélande

K. Owen, M.A. Stevenson & R.L. Sanson

Résumé
Les modèles de simulation des maladies présentent un grand intérêt au moment de planifier les activités de riposte en cas d'incursion d'une maladie exotique, car ils offrent un mécanisme permettant d'identifier de manière rapide et peu onéreuse les effets probables de divers scénarios d'apparition de foyers ainsi que des stratégies de prophylaxie envisageables. Pour une utilisation efficace et raisonnée de ces instruments, les décideurs doivent être parfaitement conscients des simplifications et des hypothèses initiales qui sous-tendent la structure d'un modèle. L'analyse de la sensibilité d'un modèle est un processus analytique visant à déterminer quelles sont les variables d'entrée qui ont le plus d'influence sur les données de sortie du modèle. Il s'agit d'une étape indispensable pour bien comprendre le fonctionnement d'un modèle.
Les auteurs rapportent un exemple d'analyse de la sensibilité axée sur l'échantillonnage appliquée pour évaluer le modèle standard néo-zélandais (NZSM) pour la fièvre aphteuse. Le modèle réunit un ensemble de paramètres développés pour la plate-forme de modélisation InterSpread Plus afin d'explorer différents scénarios d'apparition de foyers lors d'une épidémie de fièvre aphteuse en Nouvelle-Zélande. A l'issue de 200 itérations du modèle NZSM couvrant une période de simulation de 60 jours, les paramètres ayant exercé la plus grande influence sur les projections du nombre d'exploitations infectées étaient les mouvements d'animaux entre les exploitations et les lieux de vente, d'une part, et le fait que la maladie ait été détectée précocement au cours de la phase de surveillance active de l'épidémie, d'autre part. L'analyse a également conduit à des constatations déroutantes qui ont fait ressortir les aspects qu'il conviendrait d'approfondir concernant la conception et la mise en œuvre du modèle ainsi que le choix des paramètres utilisés. L'un des résultats les plus utiles de ce travail serait d'obtenir des informations permettant de regrouper et d'éliminer les paramètres dont l'influence est nulle. Cela permettrait de réduire un peu la complexité globale du modèle NZSM, tout en conservant les caractéristiques qui le rendent apte à l'emploi qui lui est assigné.

Mots-clés
Analyse de sensibilité – Épidémiologie – Fièvre aphteuse – Modèle de simulation de maladie – Modèle standard néo-zélandais – Modélisation – Nouvelle-Zélande.

Análisis de sensibilidad del modelo estándar de la fiebre aftosa neozelandés

K. Owen, M.A. Stevenson & R.L. Sanson

Resumen
Los modelos de simulación de enfermedades pueden ser una herramienta útil para planificar la respuesta a la penetración de enfermedades exóticas, pues ofrecen un mecanismo rápido y barato para determinar las probables consecuencias de hipotéticos brotes y eventuales estrategias de lucha. Para

utilizar esas herramientas eficazmente y con un alto grado de confianza los responsables de adoptar decisiones deben entender las simplificaciones y premisas que subyacen a la estructura de un modelo. El análisis de sensibilidad, proceso analítico que consiste en discernir cuáles son las variables de partida que en lo esencial van a determinar los resultados del modelo, es un proceso fundamental para adquirir tal comprensión.
Los autores describen la aplicación al modelo estándar neozelandés de un análisis de sensibilidad basado en un muestreo. Dicho modelo consiste en un conjunto de parámetros definidos para el programa genérico *InterSpread Plus* con el fin de poder evaluar distintas hipótesis de brote epidémico de fiebre aftosa en Nueva Zelanda. Atendiendo a los resultados de 200 pases del modelo efectuados durante un periodo de simulación de 60 días, los parámetros con mayor influencia en el número predicho de explotaciones infectadas eran los relativos al movimiento de animales entre la explotación y el punto de venta y a la detección de la enfermedad durante la fase de vigilancia activa de la epidemia. Se obtuvieron asimismo unas pocas conclusiones contrarias al sentido común, lo que indica que se deben analizar más a fondo ciertos aspectos de la concepción, aplicación y/o parametrización del modelo. Un resultado posiblemente útil de esta labor sería la obtención de información que ayudara a agrupar o eliminar especificaciones del modelo carentes de influencia, lo que hasta cierto punto reduciría la complejidad global del modelo sin por ello reducir su grado de idoneidad.

Palabras clave
Análisis de sensibilidad – Elaboración de modelos – Epidemiología – Fiebre aftosa – Modelo de simulación de enfermedad – Modelo estándar neozelandés – Nueva Zelanda.

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