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Optimal surveillance against foot-and-mouth disease: the case of bulk milk testing in Australia*

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Previous foot-and-mouth disease (FMD) outbreaks and simulation-based analyses suggest substantial payoffs from detecting an incursion early. However, no economic measures for early detection have been analysed in an optimising framework. We investigate the use of bulk milk testing (BMT) for active surveillance against an FMD incursion in Australia. We find that BMT can be justified, but only when the FMD entry probability is sufficiently high or the cost of BMT is low. However, BMT is well suited for post-outbreak surveillance, to shorten the length of time and size of an epidemic and to facilitate an earlier return to market.

Key words: Australia, bulk milk testing, dynamic optimisation, foot-and-mouth disease, surveillance.

1. Introduction

Foot-and-mouth disease (FMD) is considered to be one of the most contagious animal diseases, affecting cloven hoofed animals (OIE and FAO, 2012). The FMD virus (FMDV) can survive for a long period of time in many parts of the environment and in recovered animals, as well as spread rapidly via various pathways to other animals (Grubman and Baxt 2004). The disease produces debilitating effects including weight loss, decrease in milk production, loss in productivity and high mortality in young animals. For these reasons, FMD brings significant trade barriers and substantial economic losses to affected countries.

To avoid large potential damages, FMD-free countries have focused on attempts to minimise the entry and spread of FMD. Measures include stringent quarantine at ports of entry and across main disease pathways

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(GAO 2002).[1] No matter how aggressive these measures are, complete prevention has proved to be impossible, as seen in a loss of roughly $US25 billion over the last 15 years in countries that were previously free of FMD (Knight-Jones and Rushton 2013). In fact, with FMD being prevalent in two-thirds of the world, coupled with rapid increases in global trade and mobility, FMD-free countries continuously face the threat of FMD outbreaks (Muroga *et al.* 2012). As a result, in these countries, there have been calls for more attention to be paid to postborder measures, namely active surveillance in the local animal population for early detection and rapid response to an incursion (GAO 2002; Matthews 2011). However, to our best knowledge, there are no current active surveillance activities conducted in any FMD-free countries.

Delayed detection of FMD has been a key reason that recent outbreaks have been so widespread and debilitating, due to its rapid spread (Yang *et al.* 1998; Ferguson *et al.* 2001; Bouma *et al.* 2003; Muroga *et al.* 2012; Park *et al.* 2013). These delays often stem from the fact that infected (and infectious) animals experience a long incubation period before showing any clinical signs (Orsel *et al.* 2009) while FMD detection traditionally relies on visual inspection (Bates *et al.* 2003; Matthews 2011). But even when clinical symptoms are evident, FMD can be easily misdiagnosed since it is clinically almost indistinguishable from other more common diseases, as seen in several past epidemics (Bates *et al.* 2003). Existing analyses using simulation-based modelling suggest substantial economic payoffs from detecting an FMD incursion early (Ward *et al.* 2009; Hayama *et al.* 2013). However, specific measures to achieve early detection are as yet unknown, as is how early detection should optimally be, comparing all costs to potential net benefits in terms of avoided losses.

Since early detection requires considerable upfront investment, while delays in detection result in potentially large economic losses, there is a clear trade-off between the two costs. The challenge in defining the optimal detection level, which basically minimises the sum of these two costs, is rooted in complications surrounding the growth and spread of the disease. As FMD spreads across time and space, its proliferation is formally described by a spatial dynamic process. This process is further complicated by the fact that not only does FMD spread locally, it also transmits rapidly over a long distance via animal movements and human mobility, with a spread rate that varies across different animal types as well as landscapes (Kao 2001; Keeling *et al.* 2001; Grubman and Baxt 2004). These features make the spatial dynamics of FMD too complicated to simply apply recent (albeit useful) developments in the literature on spatial dynamic optimisation (Sharov 2004;

[1] See Leung *et al.* (2005); Hennessy (2008); Finnoff *et al.* (2007), among others, for analyses of the trade-offs surrounding prevention versus control.

Epanchin-Niell and Wilen 2012; Epanchin-Niell *et al*. 2012, 2015).[2] In particular, the nature of this multiregion, multihost dynamic process, so characteristic of FMD, has not been considered in any existing optimisation models. A principal reason is the 'curse of dimensionality', which makes the resulting large-scale problems difficult if not practically impossible to solve.

To find an optimal policy while retaining FMD-epidemic features, a two-step combination of simulations and dynamic optimisation has been proposed by Kobayashi *et al*. (2007). In particular, instead of using a full spread model, the authors use only its estimated transmission parameters to feed into their optimisation problem. To this end, the dimension of the problem is reduced and is thereby solvable. However, this model does not accommodate long-range dispersal patterns and the creation of local and regional clusters of infected animals which are typical for FMD.

Our contribution to the literature is twofold. First, we consider an active surveillance measure for the early detection of FMD, specifically, bulk milk testing (BMT) for the virus. We find the optimal level of spending on this measure, considering its cost and its potential benefit in reducing the economic damages that would occur from an FMD incursion in Australia. Second, our optimisation approach takes into account the features of a multihost and local and long-range spread, which best suits an FMD outbreak. To this end, our model complements the recent spatial dynamic optimisation model of Epanchin-Niell *et al*. (2012), applied to optimising surveillance against gypsy moth, by being able to consider the relationship among clusters of infected animals. We also extend the model by Kobayashi *et al*. (2007) to account for FMD dispersal over a long spatial range.

2. Surveillance for the early detection of FMD and the study area

2.1 Passive surveillance

Passive surveillance for FMD is based on notification of clinical signs in animals by 'front-line people' including farmers, meat inspectors and veterinarians. This approach is applied throughout the world, including in major livestock exporting countries, without any active surveillance measures in place, despite the serious consequences of any delay in detecting FMD (Bates *et al*. 2003; Matthews 2011). There are two inherent problems with this approach, which likely leads to a delay in detecting FMD in otherwise unaffected countries. First, with visual inspection, FMD can be easily

[2] Previous studies on optimal surveillance (i.e. search algorithms) can be found for other invasive species with more basic spatial dynamic processes, for example Mehta *et al*. (2007); Bogich *et al*. (2008); Hauser and McCarthy (2009); Kompas and Che (2009); Gramig and Horan (2011); Homans and Horie (2011). The approach largely applied in these studies is an aggregate dynamic optimisation method, which does not take into account spatial heterogeneity. The consequences of this approach are discussed in detail by Wilen (2007). A review of the literature is found in Epanchin-Niell *et al*. (2012).

misdiagnosed as one of many other clinically indistinguishable diseases (e.g. bovine viral diarrhoea, infectious bovine rhinotracheitis, bluetongue and contagious ecthyma) (Bates *et al.* 2003). The error in diagnosis can also be made worse due to strain and host-specific variations in disease severity and infection (Dunn *et al.* 1997), as well as from a lack of understanding and experience with the disease (McLaws *et al.* 2009). Second, while farmers are expected to take appropriate reporting and biosecurity safeguards under this approach, they may instead delay, and make decisions based on the perceived risk to their own enterprise from a disease incursion as well as the concern over the cost of repeated visits by a veterinarian (Palmer *et al.* 2009; East *et al.* 2013; Schembri *et al.* 2015; Hernández-Jover *et al.* 2016a,b).

2.2 Active surveillance: the bulk milk test

Active surveillance entails frequent and intensive efforts to establish the presence of a disease in an animal or an area (Paskin 1999). This approach can detect recently infected cases that might not otherwise be identified by passive surveillance, at least not until much later in the course of the disease and its spread. Active surveillance can be very expensive and time-consuming. Although a few measures have been proposed (Bates *et al.* 2003), none has been applied in practice to the best of our knowledge. In theory, BMT seems the most practical and promising measure for it can detect FMDV in the milk of FMD incubating cattle up to 4 days before clinical signs of the disease become evident (Garner *et al.* 2016). Developed using a real-time reverse transcription polymerase chain reaction (rRT-PCR) by Reid *et al.* (2006), this test is quick and sensitive to virus isolation while potentially cost-effective since milk samples need to be collected to measure somatic cell count and antimicrobial residues to determine milk quality (Bates *et al.* 2003; Garner *et al.* 2016).

2.3 Study area

The Victoria state of Australia is chosen as our study area for two reasons. First, it bears the highest risk of an FMD introduction, establishment and spread in Australia (East *et al.* 2013); a top ten largest exporting country in the world as of 2013 in terms of export value of livestock primary products that come directly from the slaughtered animals including meat, offals, raw fats, fresh hides and skins (FAO 2017). Livestock, here, is defined as cattle, buffaloes, sheep, pigs, goats, horses, mules, asses, poultry, rabbits and beehives (FAO 2017). This greater risk stems from Victoria having suitable environmental conditions for FMD survival, high human population density, and livestock production areas being relatively close to high volume air and sea ports. All these factors imply an increased risk of FMD entry and spread. Second, the distribution and composition of livestock in Victoria raises challenges to the passive surveillance system, implemented here as well as

throughout Australia, while offering opportunities for the application of BMT active surveillance. For the former, Victoria has the highest farm density in Australia while holding only 3 per cent of total land area. It is home to 62 per cent of the dairy cows, 21 per cent of the sheep and lamb and 22 per cent of the pigs of Australia (ABS 2011b). The range and mix of species mean that FMD can be easily misdiagnosed, while a large number of sheep in the state could result in delayed detection due to the mild symptoms in this species (Kitching *et al*. 2006). At the same time, pig farms, which bear the highest risk of being exposed and infected to FMD due to their omnivorous habits of eating both meat and plant products (Matthews 2011), are scattered throughout the state, thereby making the farms vulnerable to a widespread outbreak. Regarding the opportunities, Victoria is the leading dairy state in Australia, with large concentrations of dairy cattle and extensive bulk milk collection points, thereby making it the ideal place for applying BMT.

3. Methods

In this section, we describe our epidemiological economic optimisation model and its parameterisation. Our model aims to find the optimal frequency of bulk milk tests in the context of ongoing passive surveillance – a worldwide practice. That is, an outbreak is always detected by passive surveillance if it is not first detected by bulk milk tests. We consider two scenarios. The first one is to implement regular bulk milk tests before there is a known or suspected incursion, called 'BMT-pre'. In the second scenario, called 'BMT-post', bulk milk tests are carried out only after a known FMD incursion. While both scenarios seek to shorten the length of time and size of an epidemic, BMT-post avoids paying for excessive upfront investment and may be preferred in the light of a perceived low risk of FMD entry given only four incursions and establishments over the last 200 years in Australia. Finally, these two scenarios are worth consideration only if their net benefits exceed those under passive surveillance alone.

3.1 An epidemiological model of FMD spread

Consider an FMD outbreak caused by an outside source, with an arrival probability λ drawn from a Bernoulli distribution. This distribution is assumed since the chance of having more than one FMD outbreak over a particular short time period (i.e. a day) is almost zero. The outbreak starts from a pig farm of small-to-medium size, based on the prior information that pigs have the highest risk of being exposed to and infected by FMDV, and small-to-medium sized farms do not have adequate biosecurity measures (Kitching *et al*. 2006; Matthews 2011; Schembri *et al*. 2015; Hernández-Jover *et al*. 2016a,b).

From this first infected farm, FMD can spread locally and/or over a long distance to create multiple local clusters of infected farms. This spread, which can be done by way of animal movements through saleyards, wind-borne spread and local spread, as well as by direct and indirect farm-to-farm contact, all are modelled in detail in a separate FMD spatial spread model called AusSpread (Garner and Beckett 2005). To avoid the curse of dimensionality, following Kobayashi *et al.* (2007), only AusSpread simulation-based estimates of spread rates are fed into our model.

To characterise the multihost as well as local and long-range spread of FMD, our epidemiological model has two main features. The first one is the spreading mechanism which allows both local and long-range spread being dependent on farm type and region. The second feature is the probability tree which determines the chance of a 'colony' being in a particular region and having its first infected farm of a particular type. A colony is defined as a local cluster of FMD-infected farms, and is created when FMD first arrives and spreads locally. The first colony is called the mother colony while all other colonies are called child colonies. In a colony, the first infected farm is called the *seed* farm. Without the loss of generality, our model has two regions (i.e. the region set $L = \{\text{dairy}, \text{non-dairy}\}$) and two farm types (i.e. the farm type set $F = \{\text{pig}, \text{non-pig}\}$).

The local spread within a colony depends on a few factors. They include the type of its *seed* farm, the type and number of (infected and susceptible) farms in its region and the region-specific FMD transmission rates of infected farms to other susceptible farms of the same and different types. Since pigs get infected and transmit FMD differently compared to sheep and cattle, we classify farms into pig and non-pig farms, each of them has its own FMD transmission rate to farms of the same type, β^{ii}, and to farms of a different type, β^{ij} where $i \neq j$ and $i, j \in F = \{\text{pig}, \text{non-pig}\}$. Accordingly, before being detected, the growth in the number of infected farms type i in a colony in region l with a seed farm of type s is modelled by a logistic function in the following form (Verhulst 1838)

$$p_{\phi+1}^{lsi} = p_{\phi}^{lsi} + (N^{li} - p_{\phi}^{lsi}) \sum_{j} \beta^{lij} \frac{p_{\phi}^{lsj}}{N^{lj}} \quad \text{for} \quad s, i, j \in F; l \in L; \quad \text{and} \quad \phi \in [1, 2, \ldots, \Phi^{l}] \tag{1}$$

where p is the number of infected farms in a colony; φ is the colony infection 'age' which is measured in days; Φ^{l} is the number of days it would take for FMD to be detectable by passive surveillance, which varies across regions; N^{li} and N^{lj} are maximum numbers of farms i and j in a colony in region l; and β^{lij} are farm-type and location-specific FMD transmission rates. Following the Australian Veterinary Emergency Plan (AUSVETPLAN), all animals in farms in the colony of infection age equal or older than Φ^{l} are culled (Animal

Health Australia 2014). This culling is referred to as a 'stamped out' policy in AUSVETPLAN.

Long-distance spread is determined by the growth in the number of colonies. Also being logistic in functional form, this growth is modelled as

$$q_{t+1} = q_t + g \times \frac{(q\max - q_t)q_t}{q\max} \tag{2}$$

where q_t is the number of colonies in day t of an outbreak; $q_{\max}$ is the maximum number of colonies in an outbreak; and g is a colony growth parameter. We assume that no new colonies will be established once the outbreak is detected (i.e. when the first detection of an FMD incursion is made) because Australia's national livestock stand-still policy under AUSVETPLAN will be implemented, preventing all animal movements across the country (Animal Health Australia 2014). As can be seen in equation (2), the more colonies that are in existence today, the more colonies will be in existence tomorrow.

It is worth noting that the time step t in an outbreak time horizon, as indexed in equation (2), differs from the age φ of a colony in its lifespan as indexed in equation (1). An outbreak time horizon starts from the day when FMD first arrives until the day Australia declares FMD-free status. During this time horizon, one or many colonies are established. In contrast, the age of a colony starts from its establishment until the colony is eliminated. Therefore, the indices φ and t refer to two different time horizons.

The second feature of our epidemiological model is the probability tree, which connects the two equations governing the local and long-range dispersal. Indeed, the probability tree determines the locations and the types of seed farms in colonies generated by equation (2). The mother colony always has its seed farm as a pig farm, hence having only its location being probabilistic. On the other hand, the child colony has its location and the type of its seed farm being dependent on the location of the mother colony. While our probability tree is not fully detailed, it may not substantially differ from the case where the outcome of a newly established colony is conditional upon all previous colonies because an outbreak is expected to be relatively short in Australia, making the influence of the mother colony dominant. Furthermore, this simplified probability tree reduces the dimension in our optimisation problem, making it solvable.

3.2 Economic model

The size and length of an outbreak depend on how early it is detected. Our economic model is designed to exploit the trade-off between spending more on the early detection of FMD using BMT and the benefits drawn from the resulting avoided losses with this measure. That is, in each scenario, we seek the optimal frequency of bulk milk tests that minimises the sum of the BMT cost

itself and the resulting outbreak cost, both of which are linked with the outbreak outcome governed by equations (1) and (2). It is worth mentioning that the growth of colonies in equation (2) will stop under AUSVETPLAN once FMD is detected, and then all existing colonies will be detected and eliminated.

In BMT-pre, active surveillance is aggressive with bulk milk tests being carried out regularly, regardless of FMD presence, to detect FMD. Since tankers visit dairy farms every day to collect milk, let us assume that each tanker can visit h farms. If milk is tested every k day(s) for FMDV, then the daily cost of this active surveillance measure is

$$C_{\text{bmt}}^{\text{pre}} = \delta \times \frac{M_{\text{df}}}{k \times h} + E_{\text{daily}} \times M_{\text{fac}} \tag{3}$$

where δ is the unit cost per bulk milk test; M_{df} is the number of dairy farms; E_{daily} is the daily amortised cost of the testing equipment per factory; and M_{fac} is the number of milk collection points or factories in Victoria.

Bulk milk testing-post scenario, on the other hand, aims to shorten the duration and the size of an outbreak only when it occurs. Thus, its active surveillance cost is

$$C_{\text{bmt}}^{\text{post}} = \delta \times \frac{M_{\text{df}}}{k \times h} \times D_{\text{outbreak}} + E_{\text{one-off}} \times M_{\text{fac}} \tag{4}$$

where D_{outbreak} is the outbreak duration since FMD is detected and $E_{\text{one-off}}$ is the one-off cost of the testing equipment per factory for Victoria. As can be seen, the testing equipment cost differs under the two scenarios. Furthermore, the active surveillance cost under BMT-post is finite while the one under BMT-pre is in perpetuity.

For a livestock exporting country like Australia, the main components of an outbreak cost are revenue losses and its control cost, both of which occur once FMD is detected. Following the previous literature, we do not consider production loss, such as weight loss, milk yield reductions, since they are negligible due to Australia's 'stamp-out' policy of eliminating animals that are infected (Productivity Commission, 2002; Abdalla *et al.* 2005; Garner *et al.* 2012; Buetre *et al.* 2013). Revenue losses, instead, are caused mainly by immediate and prolonged export bans to Australia's FMD-sensitive markets and depressed domestic prices (Buetre *et al.* 2013). These losses can be long-lasting and are the largest in the first year (Productivity Commission, 2002). Therefore, in our model, they are calculated as

$$C_{\text{r}} = \left[c_{\text{r1}}(D_{\text{outbreak}} + D_{\text{mkt1}}) + c_{\text{r2}} D_{\text{mkt2}}\right] \tag{5}$$

where c_{r1} and c_{r2} are the net present daily revenue losses in the first and following years, D_{outbreak} is the outbreak duration; D_{mkt1} is the remaining time in the first year; and D_{mkt2} are the following years over which markets react to an FMD outbreak, inducing further revenue losses.

The control cost covers outbreak management and eradication expenses (i.e. expenses on compensation to farms, slaughtering and disposal, as well as decontamination) (FAO, 2002; Doel 2003). The outbreak management cost is calculated as

$$C_{\mathrm{m}} = c_{\mathrm{m}} \times D_{\mathrm{outbreak}} \tag{6}$$

where c_m is the daily operating cost of an FMD disease control centre(s) and D_{outbreak} is the outbreak duration.

The eradication cost is used to eradicate all infected farms in all colonies from the time the outbreak starts until it ends. The total number of infected farms is an expected number due to the underlying probability tree of the spread model. As a result, the expected eradication cost of all infected farms is

$$C_{\mathrm{e}} = E\left[\sum_q \sum_l \sum_i p^{qli} c_{\mathrm{e}}^{qli} \theta\right] \quad \text{for} \quad l \in L; i \in F; q \in Q_t \tag{7}$$

where p^{qli} is the colony's number of infected farms of type i in region l and colony q; c_{e}^{qli} is the unit cost of eradication per farm which varies by farm type and region; θ is the culling ratio of susceptible farms to an infected farm, which is typically much larger than 1 to take into account the pre-emptive culling of susceptible farms to keep an outbreak small; and Q_t is the possible number of colonies at each time step of the outbreak.

It follows that different active surveillance schemes in different scenarios bring about different outbreak durations and sizes and hence outbreak costs. Furthermore, the outbreak cost under the ongoing BMT-pre differs from that under the one-off BMT-post, since the former needs to account for the FMD arrival rate while the latter does not as BMT is initiated only after an FMD outbreak is detected. To this end, the total cost considered under BMT-pre is the expected total cost per day due to the combination of ongoing active surveillance and the chance of FMD incursion while the cost under BMT-post is considered for only an average outbreak. For this reason, our optimisation problems under each scenario are as follows:

$$\underset{k}{\text{minimise}} \quad TC^{\mathrm{pre}}(k) = \underbrace{C_{\mathrm{bmt}}^{\mathrm{pre}}}_{\text{daily BMT cost}} + \underbrace{\lambda[C_r^{\mathrm{pre}} + C_m^{\mathrm{pre}} + C_e^{\mathrm{pre}}]}_{\text{expected daily outbreak cost}} \tag{8}$$

$$\underset{k}{\text{minimise}} \quad TC^{\mathrm{post}}(k) = \underbrace{C_{\mathrm{bmt}}^{\mathrm{post}}}_{\text{BMT cost for the whole outbreak}} + \underbrace{[C_r^{\mathrm{post}} + C_m^{\mathrm{post}} + C_e^{\mathrm{post}}]}_{\text{expected outbreak cost}} \tag{9}$$

where the index *post* and *pre* on each cost component highlights their differences under the two scenarios; and *TC* is total cost. While all cost components are in real terms, a discount factor is needed for equation 9 since the total cost here is for the whole outbreak. However, we choose to ignore this factor for simplicity because the outbreak duration is typically short, being less than a year, and the prevalent discount rate in Australia is low.

A discount factor, on the other hand, is not needed in equation 8. The reason is that we assume the FMD arrival rate and the policy response are the same every day while an outbreak is to be contained and eliminated within a relatively short and finite period of time. These assumptions lead to expected losses that are constant over time such that optimising over a single period is equivalent to optimising the present discounted value of multiple periods. This approach is widely used in economic dynamics (e.g. Hopenhayn and Prescott 1992; Epanchin-Niell *et al.* 2012).

For each optimisation problem, we use a simple search algorithm to find the optimal value of BMT interval k and then compare the minimised total cost with its corresponding cost when BMT is not implemented.

3.3 Model parameterisation

Model parameters and their values are presented in Table 1. Parameters of the epidemiological model are estimated based on simulation outcomes from AusSpread, a separate FMD spatial model referred to above (Garner and Beckett 2005). Briefly, AusSpread is a Markov chain state-transition susceptible-latent-infected-recovered (SLIR) model, modified to include stochastic elements. It is based on real farm point location data and contains detailed information about each farm such as the number and type of animal species and the production type. AusSpread simulates disease spread in daily time steps, allowing for interactions between herds or flocks of different animal species and production types. It accommodates the spread of disease by way of animal movements through saleyards, wind-borne spread and local spread, as well as by direct and indirect farm-to-farm contact. Since the model is run in a series of random iterations, their simulation outcomes form a set of random data, which can be used to estimate parameters for an epidemic.

Estimates for FMD local transmission rates (β^{ii} and β^{ij}), the long-distance transmission rate (g) and the maximum carrying capacity of colonies ($q_{\max}$) are obtained by fitting equations (1) and (2) to the AusSpread simulation data using nonlinear methods (details on estimations are available upon request). All transmission rate estimates, save for the ones from *non-pig* farms to *pig* farms, are statistically different from zero at 1 per cent level and positive as expected. The transmission rate estimates of *non-pig* farms to *pig* farms have high variances, are very small and of wrong sign since *pig* farms are less than one per cent of total farms in Victoria, albeit accounting for as much as 21 per cent of the total number of pigs in Australia (ABS 2011b). As

Table 1 Table of parameter values and descriptions

Parameter	Description	Dairy subregion		Nondairy subregion		Unit
		Pig farm	Non-pig farm	Pig farm	Non-pig farm	
β^{ij}	FMD local transmission rate from Pig farm to:†	0.109	0.0013	0.0852	0.0010	Per day
	FMD local transmission rate from Non-pig farm to:†	~0.00	0.0455	~0.00	0.0369	Per day
N	Maximum number of farms in a colony†	6	859	11	1347	Farm
c_e	Unit cost of eradication per farm‡	0.439	0.194	0.456	0.149	$ Mil
π^s	Probability of being a seed farm†	0.607	0.393	0.607	0.393	—

		From dairy subregion		From nondairy subregion		
		→ dairy	→ nondairy	→ dairy	→ nondairy	
κ	Probability of the location of a 'child' colony generated by a 'mother' colony†,††	0.702	0.298	0.332	0.668	—

		Dairy subregion	Nondairy subregion	
η^{1l}	Probability of the location of the 1st colony†	0.352	0.648	—
Φ	Detection time by passive surveillance†	21	23	Day
$\mathcal{T}$	Detection time by active†	16	21	Day

		For the whole outbreak	
λ	FMD arrival probability§	~0.000055 per day	—
θ	The culling ratio†	3.74	—
g	Colony growth rate†	0.0709	Per day
q_{max}	Maximum number of colonies in an outbreak†	19	Colony
δ	Unit cost per bulk milk test¶	36	$
c_m	Daily operating cost of an FMD disease control centre(s)‡	0.475	$ Mil
c_{r1}	Daily revenue loss in the first year§	$5.4 billion/ 365 days = $14.8 million	$ Mil
c_{r2}	Daily revenue loss in the 9 following year§	$0.807 billion/ (9 years × 365 days) = $0.246 million	$ Mil

Table 1 (*Continued*)

	Description	For the whole outbreak	
h	Number of farms visited by a milk tanker in one trip‡‡	5	Farm
ϵ	Testing equipment set-up time¶	7	Day
M_{df}	Number of dairy farms†	7,590	Farm
E_{daily}	Daily amortised cost of testing equipment/factory¶	\$50,000/365 days	\$
$E_{\text{one-off}}$	One-off cost of testing equipment/factory¶	\$500,000	\$
M_{fac}	Number of milk factories§§	25	Factory

Values are in Australian Dollar 2014.
†Estimated from AusSpread simulations, available upon request.
‡The eradication cost per farm is calculated based on the actual farm size and type in the AusSpread, and various unit cost items from Garner *et al.* (2012) and Abdalla *et al.* (2005).
§About two outbreaks/100 years, based on Productivity Commission (2002) and Buetre *et al.* (2013).
¶Peter Kirkland, Elizabeth Macarthur Agricultural Institute (Personal Communication).
††$\eta^l = \sum_m \eta^{1m}\kappa^{lm}$ where $m, l \in L$.
‡‡Garner *et al.* (2016).
§§ABS (2011a).

using these relatively poor estimates would affect the prediction of our model against the simulation data, we set their values to zero and re-estimate other transmission parameters conditional on this restriction in our model. Our model outcomes are comparable with those of AusSpread.

Other parameters for an epidemic including detection time, the culling ratio, the probability of being a seed farm and the location probabilities of colonies are drawn from the average values of the simulation data. Last, but not least, the FMD arrival probability, λ, is estimated using the information on the past FMD incursions in Australia. Since there were four FMD incursions and establishments over the last 200 years (Productivity Commission, 2002), we assume the FMD arrival and establishment probability is two outbreaks/100 years, which is a very conservative estimate given the massive increase in mobility and trade over the last 50 years. Approach rates alone are thought to be much higher. The benefit of using this conservative estimate in our analysis is that we get results for the most 'optimistically preventative' case of an FMD incursion and establishment likelihood. More precautionary risk-based approaches can be based on this benchmark. We discuss this further in the discussion section below.

Estimates for parameter values in the economic model are from the literature, with the exception of BMT cost. In particular, the net present values of revenue losses due to an FMD outbreak are \$5.4 and \$0.81 billion in the first year and the following 9 years, respectively. These estimates are based on the average revenue losses of \$6.21 billion for a small FMD outbreak in Victoria, controlled using a 'stamp-out' policy estimated by Buetre *et al.* (2013), and the assumption of 87 per cent of these revenue losses

being incurred in the first year (Productivity Commission 2002). The eradication cost per farm per region is calculated based on the actual farm size and type in each region in the AusSpread model database, and various unit cost items from Garner *et al*. (2012) and Abdalla *et al*. (2005). The daily operating cost of an FMD disease control centre(s) is also based on Garner *et al*. (2012) and Abdalla *et al*. (2005). Finally, the cost per bulk milk test and testing equipment is estimated based on the combination of ABS (2011a); Garner *et al*. (2016) and expert opinion since BMT is yet to be commercially available. Specifically, the unit cost of a bulk milk test and testing equipment is based on personal communication with Peter Kirkland, Elizabeth Macarthur Agricultural Institute (EMAI)[3]. Sample handling cost is based on extensive experience of the authors at Australia's Department of Agriculture and Water Resources. The number of tests required are calculated based on Garner *et al*. (2016). Accordingly, a typical milk tanker of 20,000 L can collect milk from about five farms since the average size of an Australian dairy herd is 225 cows and the average yield is 17 L/cow/day (i.e. $17 \times 225 \times 5 \approx 20{,}000$ L) (ABS 2011a). With 7590 dairy farms in Victoria (ABS 2011a), and tankers visiting five farms/trip, there will be 552,552 (i.e. $(7590/5) \times 52$(weeks) $\times$ 7(days)) milk samples to test on a daily basis.

3.4 Sensitivity analysis

Our sensitivity analysis is based on a standard combination of Latin hypercube sampling (LHS) for efficient sampling of the parameter space (McKay *et al*. 1979), and the multivariate partial rank correlation coefficient (PRCC) analysis (Campolongo *et al*. 2000; Marino *et al*. 2008), following Blower and Dowlatabadi (1994), and as used in Thomas *et al*. (2011); Nguyen *et al*. (2015). LHS, a type of stratified Monte Carlo sampling, is an extremely efficient sampling design (McKay *et al*. 1979). In LHS, each input parameter is treated as a random variable with a defined probability distribution function (PDF). In our case, the PDFs of the input parameters of interest are triangle distributions, since we have no other information on their underlying PDFs. PRCC coefficients are then calculated for each input and the outcome variable while holding all other input variables constant. The sign of PRCC represents the qualitative relationship between each input variable and the model outcome, while its absolute value, being the range of [0,1], reflects the strength of this relationship.

Regarding the range of variation, estimated coefficients in Table 1 are varied within $\pm$ of their standard deviations. Since the culling rate, θ, can be

[3] Dr Peter Kirkland is a senior principal research scientist and leader of the animal virology team at EMAI, Menangle. He is the designated OIE expert for bovine viral diarrhoea virus (BVDV) in the OIE (World) reference laboratory for BVDV, and has a special interest and expertise in the development of rapid diagnostic tests for viral diseases of animals, studies of the epidemiology and control of insect vector-borne infections of livestock and research related to the diagnosis, pathogenesis and control of infections of livestock.

high due to a possible delay in the culling process which, in turn, can increase the number of contiguous and infected premises as well as dangerous contact farms, we let it vary in the range [−10 per cent, +30 per cent] of its value. We vary the number of farms that a tanker can visit per day (h) by ±20 per cent of its value. The unit cost per bulk milk test could fall substantially when it becomes commercially available; we, therefore, vary its value in the range [−90 per cent, +10 per cent]. Since the main difference in revenue losses under BMT-post and passive surveillance alone rests on the differences in the corresponding outbreak durations to avoid the case when the revenue loss dominates other parameters in this exercise. We also exclude from our sensitivity analysis some parameters that are basically fixed, given actual data, such as the number of milk factories, the number of dairy farms and the cost of testing equipment, along with protocols such as the quarantine duration and restrictions on animal movements. All other coefficients are varied within ±10 per cent of their values.

4. Results

4.1 BMT-pre

The expected total cost per day under BMT-pre is presented against that under passive surveillance alone in Figure 1. Given the parameter values in Table 1, costs under BMT-pre is a monotonically diminishing function, having no optimal point. The reason is twofold. First, the BMT cost is very large compared to outbreak costs, given the low FMD arrival probability (λ). Second, the difference in the time it would take for FMD to be detected under BMT-pre compared to passive surveillance is not particularly large, on average, 5 and 2 days for dairy and nondairy regions, respectively (Table 1). Consequently, as the cost of active surveillance falls when bulk milk tests are done less frequently (i.e. the testing interval k increases), more infected farms are likely to be detected by passive surveillance rather than by BMT. To this end, the outbreak cost does not increase quickly enough under BMT-pre to create an optimum, hence resulting in a monotonic fall of the expected total cost as the BMT interval increases. In addition to not having an optimum, the expected total cost under BMT-pre is always higher than that under passive surveillance, making the scenario noneconomic. Due to the lack of an optimal solution, there is no need to do sensitivity analysis for this scenario.

Nonetheless, it is important to know when the BMT-pre would be economically worthwhile to be implemented. Put differently, when does an optimal point exist, or when is the total expected cost under BMT-pre smaller than that under passive surveillance? Such optimal points are represented in Figure 2, obtained by varying values of the two key economic parameters, namely the unit cost per bulk milk test and the FMD arrival probability. In particular, we vary FMD arrival probability around the baseline value of two outbreaks per 100 years (discussed earlier) in the range from 1 to 30

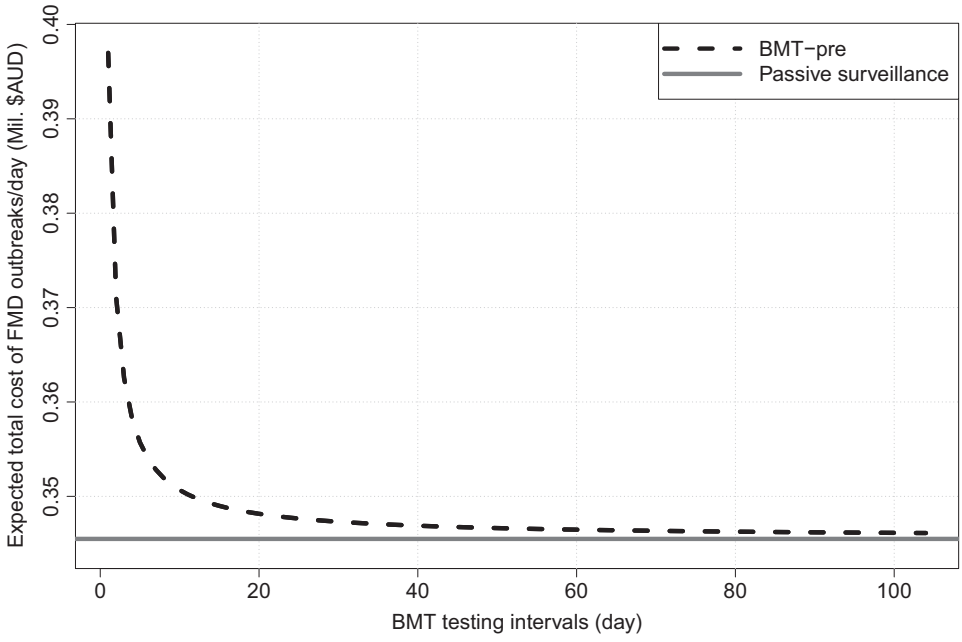

Figure 1 Bulk milk testing-pre: expected total cost of an FMD outbreak versus bulk milk testing intervals. Notes: BMT-pre is an active surveillance program that implements regular bulk milk tests to detect FMD disease before there is a known or suspected incursion of FMD.

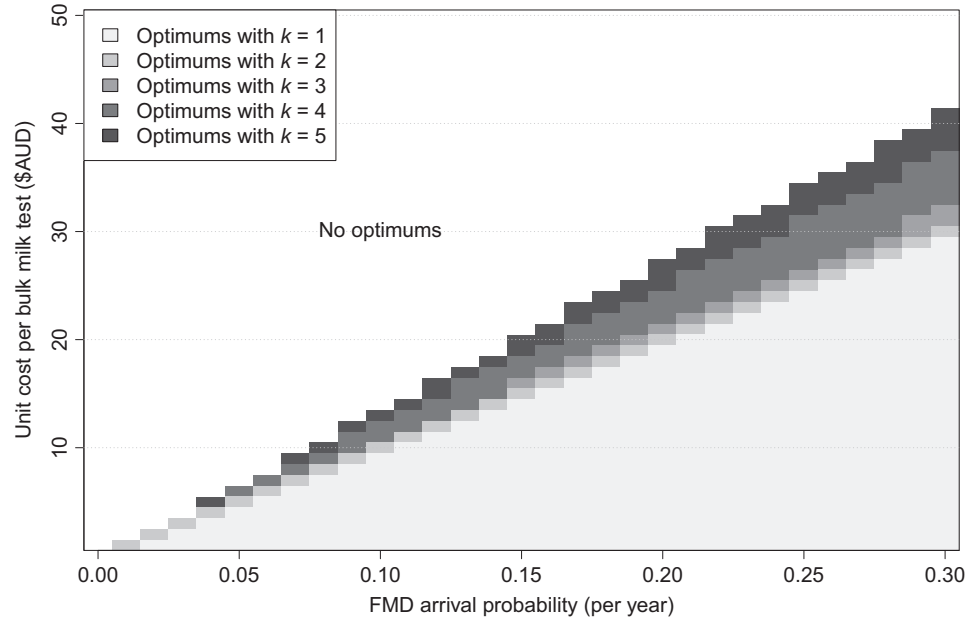

Figure 2 Bulk milk testing-pre: surveillance frontier. Notes: k is the bulk milk testing interval; step sizes for y-axis and x-axis are \$1 and 0.01, respectively. BMT-pre is an active surveillance program that implements regular bulk milk tests to detect FMD disease before there is a known or suspected incursion of FMD.

outbreaks per 100 years. We do not reduce the value of FMD arrival probability any further since such values are highly unlikely in the light of increasing globalisation and expert opinion. Likewise, we vary the value of the unit cost per bulk milk test around the baseline value of $36 in the range of $1 to $50 per test which also conforms to expert opinion.

As can be seen in Figure 2, there are no optimal points when the FMD arrival probability is small and the unit cost per bulk milk test is large (the top left region). Furthermore, optimal points exist only for a BMT interval in the range of 1–5 days. This result is plausible since FMD can be detected, on average, 1–5 days earlier by BMT active surveillance than by passive surveillance (Table 1), and FMDV is contained in milk for up to 4 days before clinical signs of the disease become evident (Burrows 1968; Donaldson 1997).

Figure 2 is also revealing in several other ways. First, if the probability of an FMD incursion is two outbreaks/100 years as assumed in this paper, it is not cost-effective to adopt BMT-pre unless the unit cost per bulk milk test is $2 or lower. While our estimated unit cost per bulk milk test is $36, this cost would be much less expensive when it becomes commercially available and efficiently combined with other milk tests for food safety purposes. Of course, the actual cost per bulk milk test would depend on the duration of time over which these tests are needed. For example, bulk milk tests would probably be much cheaper if applied widely as part of an ongoing surveillance effort than being applied for a short period of time or for targeted surveillance purposes. Second, if the unit cost per bulk milk test remains $36, then BMT-pre is not economically justified unless the FMD arrival probability is as high as roughly 25 outbreaks/100 years. While this high arrival rate seems unlikely for Australia given the country's biosecurity measures and good record of preventing FMD, there are good reasons to believe that the FMD arrival probability could be much higher than our assumed two outbreaks/100 years. Indeed, over the last 50 years, FMD has occurred more regularly in FMD previously free countries due to increasing globalisation and international trade. That, combined with the risk that goes with increases in FMD prevalence in now two-thirds of the world (Knight-Jones and Rushton 2013; Kompas *et al.* 2015), suggests that the probability based on data from a century or more ago is no longer truly reliable. The recent outbreak from an unknown source in Japan, also an island country with strict quarantine regulations, serves as a good warning for Australia (Muroga *et al.* 2012).

4.2 BMT-post

Figure 3 shows the total cost under passive surveillance alone is above that under BMT-post for any BMT interval of fewer than 100 days (or more). Furthermore, the optimal point is achieved when bulk milk tests are done every single day. These results are clearly in contrast with those

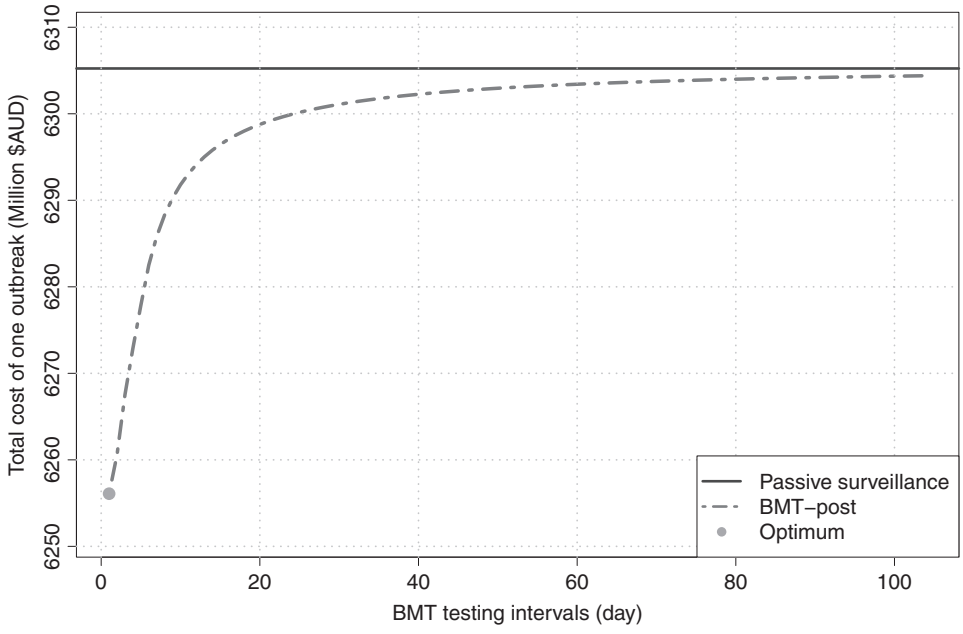

Figure 3 Bulk milk testing-post: total cost of an FMD outbreak versus bulk milk testing intervals. Notes: BMT-post is an active surveillance program that implements bulk milk tests to detect FMD disease after a known FMD incursion.

for BMT-pre. The reason is that the BMT cost ($C_{\text{bmt}}^{\text{post}}$) becomes relatively small in comparison with the outbreak cost, since the latter is no longer considered in conjunction with the FMD arrival probability. In fact, outbreak costs now become very high, with certainty, generating substantial benefits for each extra day that an outbreak is shortened. Overall, our result suggests that using BMT as a means of active surveillance is much more cost-effective that merely relying on passive surveillance.

Since an optimal solution exists in this scenario, we only need to check how sensitive the result is to parameter values. To do so, we focus on the ratio of total cost under BMT-post and the total cost under passive surveillance alone. Starting at the optimal point (when the ratio is much smaller than 1), with all parameter values specified as in Table 1, we vary parameter values as described in the previous section. Based on 3000 simulations, our sensitivity analysis is presented in Figure 4. As can be seen, our model outcome is most sensitive to culling time and detection time, and to a lesser extent, daily revenue loss and the unit cost of a bulk milk test. This makes good sense since culling time and detection time play a pivotal role in determining the size and length of an outbreak, while daily revenue loss and the unit cost of a bulk milk test are key determinants for the potential costs and benefits of a policy intervention.

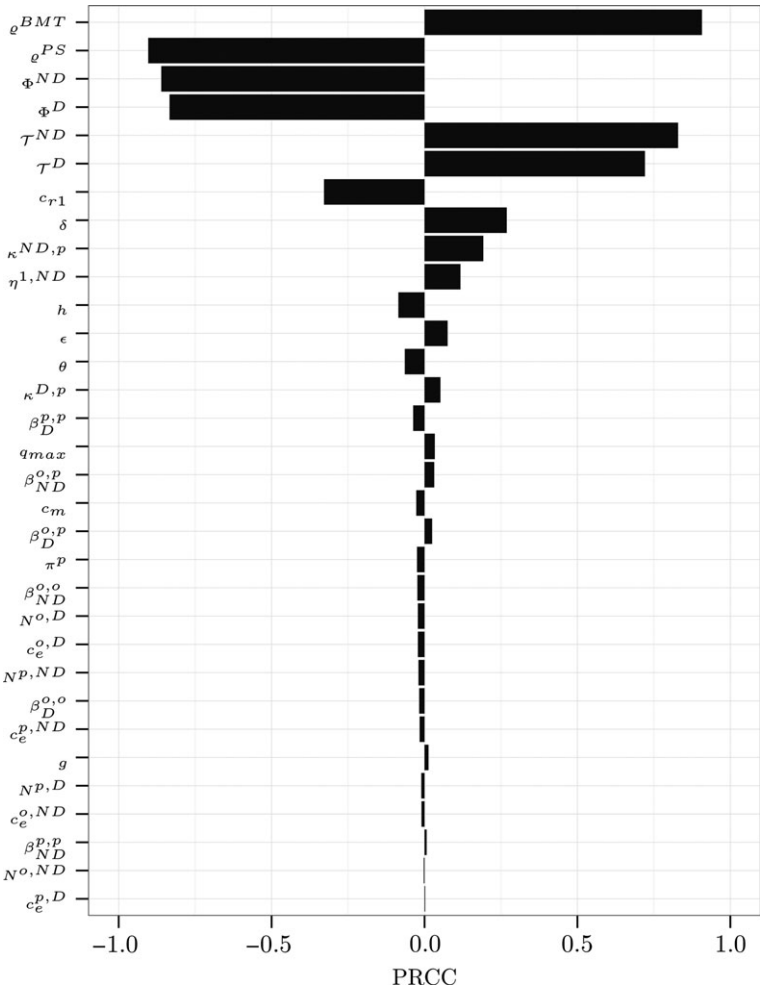

Figure 4 Bulk milk testing-post: sensitivity analysis. Parameters are defined in Table 1. PRCC, partial rank correlation coefficient; D, dairy region; ND, nondairy region; p, pig farms; o, other farms. BMT-post is an active surveillance program that implements bulk milk tests to detect FMD disease after a known FMD incursion.

5. Discussion

In this article, we analyse the possibility of using active surveillance for the early detection of FMD. This animal disease, caused by a viral infection, and often resulting in enormous economic damages, spreads across both time and space and is similar to many other kinds of animal and human diseases. The lack of perfect prevention, coupled with massive damages caused by the disease, makes early detection essential to reduce the potential impact of this disease – a context applicable to many bio-invasions.

Examining the most possible active surveillance measure for early detection, namely BMT, we investigate when its use is economically justified.

We consider the two scenarios typically faced by policymakers. For BMT-pre, active surveillance is aggressive with ongoing BMT regardless of FMD presence while for BMT-post, the testing only starts after FMD is detected.

5.1 Policy implications

We find that BMT-pre is highly contingent on the risk of FMD incursion and the unit cost of the bulk milk test. If the risk of an FMD incursion is too small or the unit cost of bulk milk test is too high, BMT-pre is unlikely to be cost-effective. Applied to Australia, BMT-pre is thus not well justified when the risk of FMD incursion is estimated based on the country's historical record of maintaining FMD-free status, thanks in part to being an island continent with stringent border quarantine and sound biosecurity practices in place. Nonetheless, there are reasons to believe that the FMD arrival rate is much higher now and in the future for Australia given rapid globalisation, mobility and growing FMD prevalence, currently in two-thirds of the world. In such a case, BMT-pre might be cost-effective at some point. With this in mind, our result suggests the need for a more affordable BMT procedure. Given BMT is not yet commercially available, perhaps a partnership between the public and private sectors is worth exploring to reduce the cost of this testing method.

On the other hand, we have shown that BMT is highly suited to active surveillance once FMD is detected. The result is relatively insensitive to model parameter values, except for the parameters especially crucial to the size and the cost of an FMD outbreak. Thus, BMT-post is recommended to shorten the length and size of an epidemic, even at the current estimated cost of the test in Australia. This result is particularly promising since current practices in FMD outbreak management rely mostly on pre-emptive depopulation and/or vaccination. While the former can lead to public outcry and detrimental economy-wide impacts, the latter seriously constrains exporting countries from regaining access to their export markets. It is not unusual to see massive pre-emptive depopulation done to protect export markets as in the UK FMD outbreak in 2001. In contrast, BMT can be used not only to reduce the size of an outbreak but also potentially for postoutbreak proof of FMD-free status to help expedite the process of regaining export markets after an epidemic.

Regarding international comparisons, it is worth noting that there have been no active surveillance programs similar to BMT-pre using either BMT or any other measures implemented in FMD-free countries, at least to the best of our knowledge. That said, and despite the dominant use of quarantine and depopulation to shorten an outbreak in FMD-free countries, to regain official recognition by the OIE of freedom from FMD, active surveillance is required to provide evidence of FMD status (OIE 2016). Measures such as serological testing, for example, are typically recommended by the OIE, but we are not aware of any optimisation analysis of their costs and benefits and therefore cannot compare them directly with our results.

5.2 Contributions, limitations and future work

Analysing policy responses to an incursion, the existing literature largely focuses on the relative effectiveness of various FMD control strategies based on disease and spread simulations. These simulations are performed on epidemiological models developed using farm data, transmission parameters and a spatial transmission kernel (the relative probability of transmission over some distance) (Ferguson *et al.* 2001; Kao 2001; Morris *et al.* 2001; Tomassen *et al.* 2002; Keeling *et al.* 2003; Garner and Beckett 2005; Tildesley *et al.* 2006; Rich and Winter-Nelson 2007; Ward *et al.* 2009; Hayama *et al.* 2013). While these approaches succeed in articulating the spatial–temporal features of an FMD incursion, in an often elaborate way, they do not provide a 'global' optimal solution.

We propose a multihost, multiregion optimisation framework to early detect FMD using BMT. The multiregion dimension in our framework is an extension of the multihost simulation-based optimisation model by Kobayashi *et al.* (2007). As a result, the typical feature of long-distance spread in an FMD outbreak is accounted for in our model, making it applicable at the state, national or cross-country scale. Since the model in Kobayashi *et al.* (2007) is used to evaluate daily FMD control strategies of depopulation and vaccination in the Central Valley of California, while our model is applied to justify the use of BMT for FMD early detection in Victoria, the outcomes of the two models are not directly comparable.

Because of the challenge in optimising over a problem that involves uncertainty and spatial dynamics, we used a simulation-based optimisation approach with a simplified probability tree to enhance tractability. A missing feature and an important future improvement in this work would be to account for farm-level strategies which could alter the outbreak duration at the farm level and colony level. A model framework for such detailed spatial dynamics has been proposed in other bioeconomic applications, but in a deterministic setting (Epanchin-Niell and Wilen 2012; Epanchin-Niell *et al.* 2015). With more computational power, future research could incorporate more spatial defined measures to provide further insights, while retaining the fundamentally stochastic nature of the problem.

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