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Evaluation of foot and mouth disease control measures: Simulating two endemic areas of Thailand

Thanicha Chanchaidechachai [a,b,*], Helmut W. Saatkamp [a], Henk Hogeveen [a], Mart C.M. de Jong [c], Egil A.J. Fischer [d]

[a] Business Economics Group, Wageningen University, Wageningen, the Netherlands
[b] Research Unit of Data Innovation for Livestock, Department of Veterinary Medicine, Faculty of Veterinary Science, Chulalongkorn University, Bangkok, Thailand
[c] Quantitative Veterinary Epidemiology Group, Wageningen University, Wageningen, the Netherlands
[d] Department of Population Health Sciences, Division Farm Animal Health, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands

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ABSTRACT

Foot and mouth disease (FMD) is an important livestock disease in Thailand, with outbreaks occurring every year. However, the effects of FMD control measures in Thailand have received little research attention. Epidemiological models have been widely used to evaluate FMD outbreak control, but such a model has never been developed for Thailand. We constructed a stochastic between-farm transmission model to evaluate FMD control measures. The epidemiological unit of the model was the farm, which could be in different states: susceptible, latent, undetected infectious, detected infectious and recovered. The between-farm transmission was calculated by the sum of distance-dependent transmission and trade network transmission using parameters derived from FMD outbreaks in 2016–2017. We used this model to simulate the outbreaks with and without the implementation of the following control measures: culling all animals on infected farms, ring vaccination, animal movement restrictions and isolation of infected farms. The control measures were evaluated by estimating the number of secondarily infected farms and the outbreak duration for each scenario. The model was simulated in two study areas located in the Lamphaya Klang subdistrict (high farm density) and the Bo Phloi district (low farm density). The effects of control measures differed between the two study areas. When farm density was high, rigid control measures were required to prevent a major outbreak. Among all options, culling the animals on infected farms resulted in the lowest number of infected farms and the shortest outbreak duration. In contrast, for an area with a low farm density, less stringent control measures were sufficient to control the usually minor outbreaks. The results indicate that different areas require a different approach to control an outbreak of FMD.

1. Introduction

Foot and mouth disease (FMD) is the most important livestock disease in the world in terms of economic impact as outbreaks and control and prevention measures cause huge economic losses (James and Rushton, 2002). For this reason, many epidemiological models have been developed to estimate the outcomes of FMD outbreaks and to evaluate different control options. This type of research has been carried out extensively in FMD-free countries, for example, the United Kingdom (Keeling et al., 2001; Morris et al., 2001), the Netherlands (Backer et al., 2012a; 2012b), Japan (Hayama et al., 2013), and Peru (Martínez-López et al., 2014). However, simulation models developed for FMD-free countries are not suitable for application in countries where FMD is endemic because the immunity and transmission dynamics are different (Knight-Jones et al., 2016).

Over the past decades, several models have been developed to study FMD in endemic areas. For example, Lyons et al. (2021) investigated the possibility of establishment of FMD-free zones in Pakistan, Randolph et al. (2002) analysed the cost-benefit of FMD eradication in the Philippines, and similar studies were conducted on FMD control in Cambodia (Young et al., 2016) and in Ethiopia (Jemberu et al., 2016). However, most of these studies were based on population-level incidence rather than focusing on the individual level, and the models were simplified without including spatial information. One study in Vietnam constructed a transmission model at a commune level and incorporated spatial distance between communes (Do et al., 2022). Despite this

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* Corresponding author at: Business Economics Group, Wageningen University, Wageningen, the Netherlands.
E-mail address: thanicha.chanchaidechachai@wur.nl (T. Chanchaidechachai).

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progress, there is still a significant gap in the development of individual-based simulation models that consider spatial elements in endemic situations, especially in comparison to FMD-free countries where such models are commonly used for FMD outbreak control (Backer et al., 2012a; 2012b; Hayama et al., 2013; Keeling, 2005).

FMD is an endemic disease in Thailand with 980 reported outbreaks across the country between 2016 and 2021 (WOAH, 2022). The Thai government established an FMD outbreak control guideline in Animal Epidemics Act B.E. 2558, including multiple measures such as outbreak zone announcement, animal movement restrictions, ring vaccination and sanitary control (Arjkumpa et al., 2020). These control measures are defined as generic regulations for every area. However, we know that FMD transmission is affected by multiple factors, such as farm density (Boender et al., 2010; Keeling et al., 2001) and animal movement (Dubé et al., 2009). Therefore, generic measures may not be equally effective across areas.

The objective of this research was to develop an FMD simulation model, based on the input parameters derived from outbreaks in 2016–2017 in two endemic areas of Thailand with different livestock species and farm densities. With this model, we evaluated the effects of different control measures under various circumstances.

2. Materials and methods

2.1. Data collection

The two study areas were selected in consultation with the Thai Department of Livestock Development. The first study area was located in the Lamphaya Klang subdistrict in the Saraburi province in the central region of Thailand. The area is densely populated, with a density of 7.6 farms per km^2, and 95% of farms are dairy cattle farms (DLD, 2019). The second study area was located in the Bo Phloi district in the Kanchanaburi province in the western region of Thailand. The area consists of multiple livestock species, i.e. beef cattle, goats and pigs. This area is sparsely populated, with a density of 0.5 farms per km^2 (DLD, 2019). In these two areas, FMD outbreaks happened in 2016–2017. According to the official records and verification with local authorities, there were no official outbreak zones in either area. In other words, no specific control measures were implemented during the outbreaks.

The outbreak data were collected by research staff from the Faculty of Veterinary Science at Chulalongkorn University via questionnaires that were administered in October 2017 after the outbreak. The boundaries of the study areas were established by starting at the centre of each area and gradually increasing the radius until approximately 500 farms were included. The census survey included all farms within the defined radius and involved the collection of information on farm location, animal species, farm size, animal trading history, and the occurrence of an FMD outbreak on the farms in 2016–2017.

The study area in the Lamphaya Klang subdistrict was 105 km^2 (12.5 $\times$ 8.4 km^2) covering 502 dairy farms. On average, the distance between two farms was 4 km (min = 0.002 km, max = 12.5 km). The FMD outbreak started from 15 September 2016 and lasted until 8 August 2017, affecting 273 dairy farms. For the Bo Phloi district, the size of the study area was 785.4 km^2 (30.8 $\times$ 25.5 km^2) covering 346 beef cattle farms, 104 goat farms and 51 pig farms. On average, the distance between two farms was 9.9 km (min = 0.002 km, max = 30.1 km). The FMD outbreak lasted from 13 October 2016–15 December 2016 and affected 15 beef farms (Fig. 1). The detailed outbreak data can be found in Supplementary S1.

2.2. Model

The description of the model follows the Overview, Design concepts and Details (ODD) protocol originally used for describing individual and

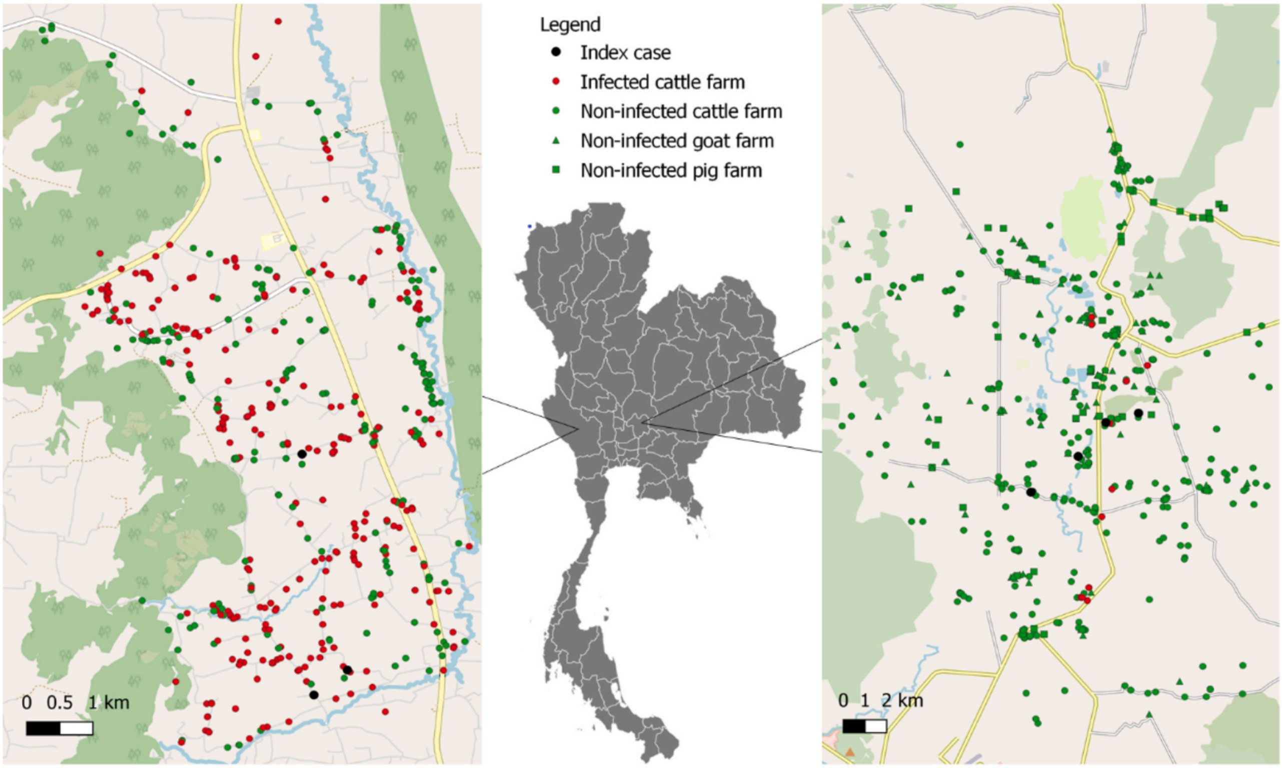

Fig. 1. The study areas located in the Lamphaya Klang subdistrict with an area of 105 km2 (12.5 $\times$ 8.4 km^2) (left) and in the Bo Phloi district with an area of 785.4 km2 (30.8 $\times$ 25.5 km^2) (right). It is to be noted that the scales are different between left and right maps. The circles, squares and triangles represent cattle farms, pig farms and goat farms. The red, green and black colours symbolise the infected status, non-infected status and index cases during the foot and mouth disease outbreaks in 2016–2017, respectively.

agent-based models (Grimm et al., 2020), but was adapted here to explain a stochastic simulation model.

2.2.1. *Purpose*

The model was developed to simulate FMD outbreaks in two study areas in Thailand with different control scenarios. The aim is to assess the effects of FMD control measures taking into account different farm densities and farm types.

2.2.2. *Entities, state variables, and scales*

The entity in the model is a farm. The farm state variable indicates whether the livestock on the farm is susceptible to FMD, latent, undetected infectious, detected infectious or recovered. The model runs at a 1-day time step. For each day, the model is appraised, and the farm states are updated.

2.2.3. *Process overview and scheduling*

The processes of state transition of farms are as follows:

2.2.3.1. Susceptible to latent. The transition from the susceptible state to the latent state is determined by the between-farm transmission rate, which is calculated via two mechanisms. The first is the spatial transmission kernel, which is a function describing the transmission rate between two farms depending on the distance between the farms (Boender et al., 2010) (Eq. 1).

$$k(r_{ij}) = \frac{k_0}{1 + \left(\frac{r_{ij}}{r_0}\right)^{\alpha}} \tag{1}$$

Where $k(r_{ij})$ is the transmission rate exerted by infectious farm j on susceptible farm i, r_{ij} is the Euclidean distance between susceptible farm i and infectious farm j. Parameters k_0, r_0, and α determine the height and shape of the transmission kernel. The force of infection from the transmission kernel of susceptible farm i on day t ($\lambda_{\text{kernel}}(t)$) is the sum of the transmission rate from all infectious farms j to susceptible farm i on day t (Eq. 2).

$$\lambda_{\text{kernel}}(t) = \sum_{j\in \text{infectious}} k(r_{ij}) \tag{2}$$

The second transmission mechanism is a trader-based transmission. When the farms are infectious, they can spread the disease to other susceptible farms that share the same trader with a constant rate δ per day (Eq. 3).

$$\lambda_{\text{trade}}(t) = \sum_{j\in \text{infectious}} \delta_{ij};\ \text{if farm i sharing the same trader with farm j} \tag{3}$$

The force of infection from the trader-based transmission of susceptible farm i on day t ($\lambda_{\text{trade}}(t)$) is the sum of the trader-based transmission rates from the infectious farms j on day t that share the same trader with susceptible farm i (δ_{ij}).

The probability of infection of a susceptible farm i on day t (p_{inf}) was calculated from the sum of the force of infection from the transmission kernel and trader-based transmission as follows:

$$p_{\text{inf}} = 1 - e^{-(\lambda_{\text{kernel}}(t) + \lambda_{\text{trade}}(t))} \tag{4}$$

On each day, the probability of infection (p_{inf}) of each farm is calculated, and it is used to stochastically determine the transition of farms from the susceptible state to the latent state.

2.2.3.2. Latent to undetected infectious. The farm is in the latent state for 3 days (Mardones et al., 2010) and then transitions to the undetected infectious state.

2.2.3.3. Undetected infectious to detected infectious. The undetected infectious farms become detected infectious farms after a constant detection time, which was estimated from a standard SEIR model for within-farm spread. We assumed that an outbreak on a farm was detected when the number of infected animals on the farm was higher than a certain case limit depending on the livestock species (Table 1, Supplementary S2 for the detailed estimation of the detection time). The case limits were estimated by consulting with local veterinary officers. During the undetected and detected infectious state, the farms were able to spread the disease to other susceptible farms.

2.2.3.4. Detected infectious to recovered. After the duration of the infection (Table 1), the infected farms changed to the recovered states until the end of the simulation.

2.2.4. *Initialisation*

The model are scheduled to start at day 0 with all farms being susceptible, except for a set of index cases, which are undetected infectious (3 farms in the Lamphaya Klang subdistrict and 4 farms in the Bo Phloi district based on interview data, see Fig. 1). The model is run until there is no infectious farm in the area.

2.2.5. *Input data*

The input data used in the model include attributes of each farm,

Table 1

Summary of foot and mouth disease outbreak model parameters.

Parameters	Value	Sources
Transmission kernel parameters	$k_0 = 0.0054$ day^{-1} $r_0 = 0.171$ km $\alpha = 1.50$	Estimated from outbreak data using method from (Chanchaidechachai et al., 2021)
Trade transmission rate	$\delta = 0.0006$ day^{-1}	
Latent period	3 days	Mardones et al. (2010)
Farm Infectious period in Lamphaya Klang subdistrict	Gamma(shape =3.02, rate = 0.137), mean = 22	Estimated from outbreak data
Farm Infectious period in Bo PhloiBo Phloi district	Gamma (shape =1.87, rate = 0.126), mean = 15	Estimated from outbreak data
Detection time for dairy cattle farm	5 days	SEIR model with the transmission rate = 0.67 day^{-1} (Bravo de Rueda et al., 2015), the rate from exposed to infectious = 0.33 day^{-1} (Mardones et al., 2010), average dairy cattle farm size = 40 and the number of detection cases = 2
Detection time for beef cattle farm	7 days	SEIR model with the transmission rate = 0.67 day^{-1} (Bravo de Rueda et al., 2015), the rate from exposed to infectious = 0.33 day^{-1} (Mardones et al., 2010), the rate from exposed to infectious = 0.33 day^{-1} (Mardones et al., 2010), average beef cattle farm size = 44, and the number of detection cases = 3
Detection time for pig farm	8 days	SEIR model with the transmission rate = 0.59 day^{-1} (Eblé et al., 2006) the rate from exposed to infectious = 0.33 day^{-1} (Mardones et al., 2010), average pig farm size = 1400 and the number of detection cases = 3
Detection time for goat farm	18 days	SEIR model with the transmission rate = 0.21 day^{-1} (Orsel et al., 2007), the rate from exposed to infectious = 0.33 day^{-1} (Mardones et al., 2010), average goat farm size = 45 and the number of detection cases = 3

such as location, animal type, and trade network with other farms. These data are based on interview data as explained in Section 2.1. The files can be downloaded from Supplementary S1.

2.3. *Parameterisation*

The spatial transmission kernel and the trader-based transmission parameters were estimated from the combined outbreak data in the two study areas using the maximum likelihood method as previously described in Chanchaidechachai et al. (2021). The R code for the estimation of parameters can be found in Supplementary S3. Other model parameters (Table 1) were obtained from the literature, except for the infectious period of farms, which was drawn randomly from a gamma distribution fitted on the outbreak duration data collected during the interviews.

2.4. *Control measures*

The model was run for 5 scenarios: (1) baseline without control measures, (2) culling all animals on infected farms, (3) ring vaccination, (4) animal movement restrictions and (5) isolation of infected farms. The details of the control measures are explained below.

2.4.1. *Culling all animals on infected farms*

Although animals culling is a common control measure during FMD epidemics (European Union, 2016), culling has never been deployed to control an FMD outbreak in Thailand. For this reason, we would like to explore the potential effect of culling in the endemic FMD situation of Thailand. We made three assumptions. First, the livestock on infected farms are culled on the first, seventh or 14th day after detection. Second, the culling process is finished in 1 day, independent of farm size. Third, there is no reintroduction of new animals into the farms during the outbreak. Thus, farms where livestock is culled are not able to spread the disease to other farms nor be susceptible again until the end of the outbreak.

2.4.2. *Ring vaccination*

Ring vaccination is defined as the vaccination of animals on susceptible farms in delineated areas surrounding the infected farms. We assumed that the ring vaccinations are implemented for all animals in farms within a 10-km radius of the detected infected farms with a maximum vaccination rate of 40 farms per day, starting with the farms furthest away from the infected farm. The radius of ring vaccination is adjusted twice. The initial implementation is the area 10-km radius around the index cases. Later, the vaccination area is expanded to a radius of 10 km around newly-detected infected farms 7 days after the detection of index cases. The effect of vaccines starts after immunity onset. Farms with vaccinated livestock are assumed to have a reduced susceptibility, but not complete immunity. Infected farms with vaccinated livestock are assumed to have reduced infectivity. The force of infection experienced by a farm with vaccinated livestock is decreased by the value of relative susceptibility and relative infectivity. To consider the parameter uncertainty, we tested the model with various combinations of immunity onset (7, 14, 21 or 28 days) and vaccine efficacy (0 – 100%). Lastly, we assumed that the immunity from the vaccine lasts for 6 months.

2.4.3. *Animal movement restrictions*

Animal movement restrictions are defined as the prohibition of the movement of animals and animal products within or from the outbreak zone (The Royal Thai Government Gazette, 2015). We assumed that animal movement restrictions are announced 1 day after detection of the index cases, and enforced until the last infected farm was recovered. We assumed that, after the implementation of animal movement restrictions, trade transmission is reduced to zero. To the best of our knowledge, no literature has shown the effect of animal movement restrictions on the FMD transmission kernel. One study in Belgium showed that during the animal transport restrictions, the tail of the transmission kernel for a bluetongue outbreak was flattened, which implies the reduction of long-distance transmission as part of the transmission kernel (de Koeijer et al., 2011). In this model, we assumed that other transmission routes besides animal and animal product movements, such as the movement of people, vehicles and fomites and the over-the-fence transmission between the adjacent farms, are not affected by animal movement restrictions. This kind of transmission is likely to happen between farms close to each other. Therefore, we assumed that the local transmission kernel, below a specific cut-off distance from the infectious farm, remains the same. In contrast, the long-distance transmission kernel, above the cut-off distance from the infectious farm, is assumed to be reduced, resulting from lower animal movement activities, like the effect shown in de Koeijer et al. (2011). We chose a maximum cut-off distance of 1 km based on the nearest neighbour distance. A cut-off distance of 1 km covered an average of 8 nearest neighbours in the Bo Phloi district and 15 nearest neighbours in the Lamphaya Klang subdistrict, which we assumed to be more than enough to represent possible local transmission. We assumed various combinations of cut-off distances from 0 to 1 km and the percentage decrease of long-distance transmission kernel from 0% to 100%.

2.4.4. *Isolation of infected farms*

The costs of animal movement restrictions are enormous (Tildesley et al., 2019). In addition, the prolonged restriction can disrupt the normal flow of animals between units and lead to animal welfare problems (Knight-Jones and Rushton, 2013). Therefore, we proposed the isolation of infected farms as an alternative option. The concept is to restrict animal and animal product movements from detected infected farms exclusively. In this model, we assumed that infected farms were isolated one day after detection until they recovered. During the isolation, the trade transmission from isolated farms became zero. However, the isolation did not completely stop the spatial transmission kernel since people and vehicles still needed to move for farm maintenance. Thus, we used the same effect as animal movement restrictions on the spatial transmission kernel of the isolated farms.

The parameters concerning FMD control measures are summarised in Table 2. A schematic overview of farm-state transitions and the effect of control measures is shown in Fig. 2.

2.5. *Model software and outcomes*

For each scenario, the simulation was run for 500 iterations to account for stochasticity. The outputs from the model were the number of secondary infected farms excluding the index cases and the outbreak duration. The model was programmed in R version 4.2.1 (R Core Team, 2022). The R code can be found in Supplementary S3.

Table 2

Summary of parameters concerning foot and mouth disease control measures.

Control measures	Parameters	Values	Unit
1. Culling animals in infected farms	Delayed culling	1, 7, 14	Days after disease detection on the farms
2. Ring vaccination	Vaccine efficacy	0–100	% Reduction in susceptibility and infectivity
	Immunity onset	7, 14, 21, 28	Days after vaccination
3. Animal movement restriction	Cut-off distance	0–1	Km
	Transmission kernel reduction	0–100	% Kernel reduction
4. Isolation of infected farms	Cut-off distance	0–1	Km
	Transmission kernel reduction	0–100	% Kernel reduction

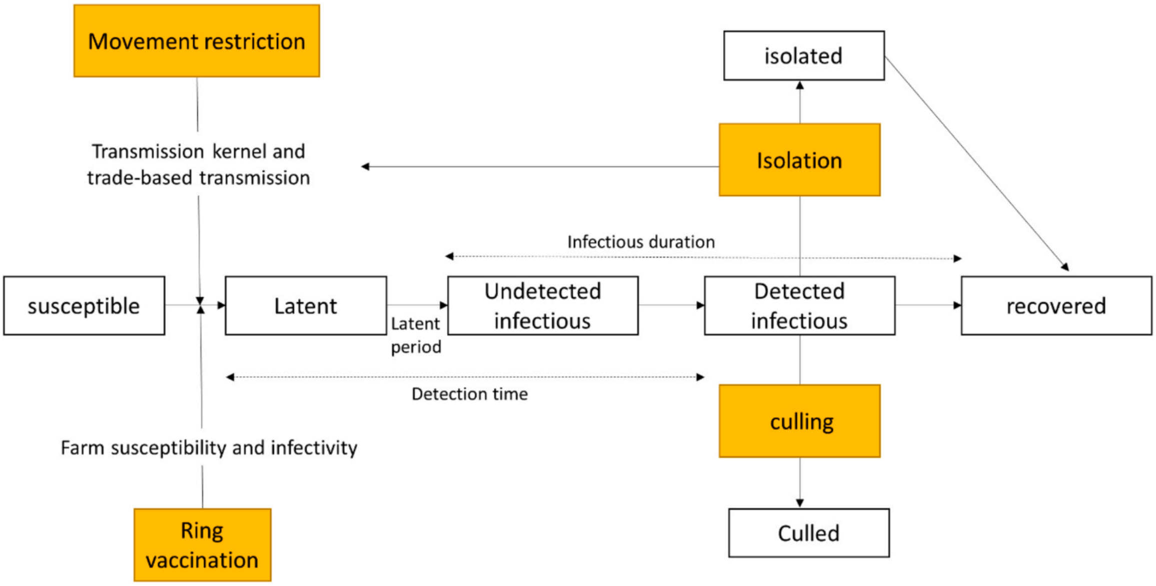

Fig. 2. Diagram of foot and mouth disease outbreak model showing the farm-state transition (white blocks) and the effect of control measures (yellow blocks) on the parameters.

2.6. Sensitivity analysis

A global sensitivity analysis was conducted on the model parameters to assess parameter sensitivity on the number of infected farms and outbreak duration. We sampled 500 parameter sets from the parameter distribution (Table 3) using Latin hypercube sampling. For each parameter set, the model was run for 100 iterations from which the predicted median number of infected farms and outbreak duration were saved. The regression-based method was used to analyse the parameters' variance contributions (Burgers et al., 2010). The regression model was fitted between the outputs and input parameters. Any type of regression model (e.g. linear regression, polynomial regression, spline regression) could be applied, but the fitted regression model needed to explain more than 90% of the output variance. The sensitivity of parameters was presented by the top marginal variance (TMV) and the bottom marginal variance (BMV) which were extracted from the regression model. TMV was defined as the variance reduction that would occur if the parameter became fully known. It was calculated as the variance explained by the regression model with only that parameter. BMV was the variance that the regression model could not be explained without that parameter (Jansen et al., 1994). The sensitivity analysis was performed on 15 input parameters (Table 3) using the simulation outbreaks in the Lamphaya Klang subdistrict. We selected the parameters which have a TMV of more than 25% and made scatter plots to show the effect of selected parameters on the predicted median number of infected farms and outbreak duration.

3. Results

3.1. Baseline model

For the baseline model without control measures for the Lamphaya Klang district, the predicted median number of secondarily infected farms, excluding three index cases, was 293 (95% prediction interval of (0, 361)), and the predicted median outbreak duration was 312 days (95% prediction interval of (24, 469)). The number of infected farms from the real outbreak was 273 farms with an outbreak duration of 335 days. The results from the baseline model were consistent with the real outbreak data in this area. For the Bo Phloi district, the predicted median number of secondarily infected farms, excluding four index cases, was 3 (95% prediction interval of (0, 13)), and the predicted median outbreak duration was 42 days (95% prediction interval of (16, 116)). In comparison, the number of secondarily infected farms from the real outbreak was 11, and the outbreak duration was 68 days.

Table 3
Predicted median and 95% prediction interval of the number of secondarily infected farms (excluding index cases) and the outbreak duration, derived from the foot and mouth disease outbreak model, considering baseline and control measures with the most effective parameters in the Lamphaya Klang and the Bo Phloi districts.

Scenarios	Lamphaya Klang subdistrict		Bo Phloi district	
	Median number of secondarily infected farms (95% prediction interval)	Median outbreak duration (days) (95% prediction interval)	Median number of secondarily infected farms (95% prediction interval)	Median outbreak duration (days) (95% prediction interval)
Baseline	293 (1, 345)	312 (26, 506)	3 (0, 13)	42 (16, 116)
Culling with a delay of 1 day	1 (0, 7)	15 (10, 32)	1 (0, 5)	17 (14, 36)
Ring vaccination with 7 day onset of immunity and 100% vaccine efficacy	4 (0, 11)	54 (27, 85)	2 (0, 7)	39 (17, 73)
Animal movement restriction with cut-off 0 km and 90% kernel reduction	1 (0, 6)	43 (21, 100)	1 (0, 4)	33 (15, 65)
Isolation of infected farms with cut-off 0 km and 90% kernel reduction	1 (0, 6)	43 (21, 92)	1 (0,5)	35 (15, 68)

3.2. Control measures

All four control measures could reduce the number of secondarily infected farms and outbreak duration from the baseline. In the Bo Phloi district, the effect of control measures was limited, and the differences between control measures were small due to the small baseline outbreak. However, in the Lamphaya Klang subdistrict, all four control measures can potentially control the outbreak, but culling was the most effective in reducing both the number of infected farms and the duration of the outbreak (Table 3).

The outputs from the simulation with control measures using different parameters are displayed in Fig. 3. Due to the small baseline outbreak in the Bo Phloi district, we have only presented the outputs for the Lamphaya Klang subdistrict. However, the outputs for the Bo Phloi district are available in Supplementary S4.

A longer culling delay resulted in more infected farms and a longer outbreak duration. The outcomes of ring vaccination were highly affected by the combination of vaccine efficacy and the onset of immunity after vaccination. Higher vaccine efficacy and shorter onset of immunity resulted in fewer infected farms and shorter outbreak. A vaccine efficacy of 60% or more could limit the median number of secondarily infected farms to fewer than 21, equivalent to the outcome of culling with a delay of 14 days (Fig. 3). Regarding animal movement restrictions and isolation, a higher reduction of the transmission kernel and a smaller cut-off distance resulted in fewer infected farms and a shorter outbreak duration. For a transmission kernel reduction of 60% or greater, both animal movement restrictions and isolation could limit the median number of secondary infected farms to fewer than 21, comparable to the outcome of culling with a delay of 14 days. If the reduction of the transmission kernel was 90% or greater, animal movement restrictions could limit the median number of secondarily infected farms to fewer than 4, which was comparable to culling with a delay of 7 days. The outbreak was smaller with animal movement restrictions rather than with isolation of the infected farms given the same parameters.

3.3. Sensitivity analysis

Because the outbreak in the Bo Phloi district was small, the sensitivity analysis was only performed on the models for the Lamphaya Klanag subdistrict. The sensitivity analysis showed that kernel parameters k_0 and r_0 explained most of the outcome variance in the baseline model (Table 4), while transmission via the trade network (δ) barely explained outcome variance. For ring vaccination, outcome variance was mainly explained by the vaccine efficacy. For animal movement

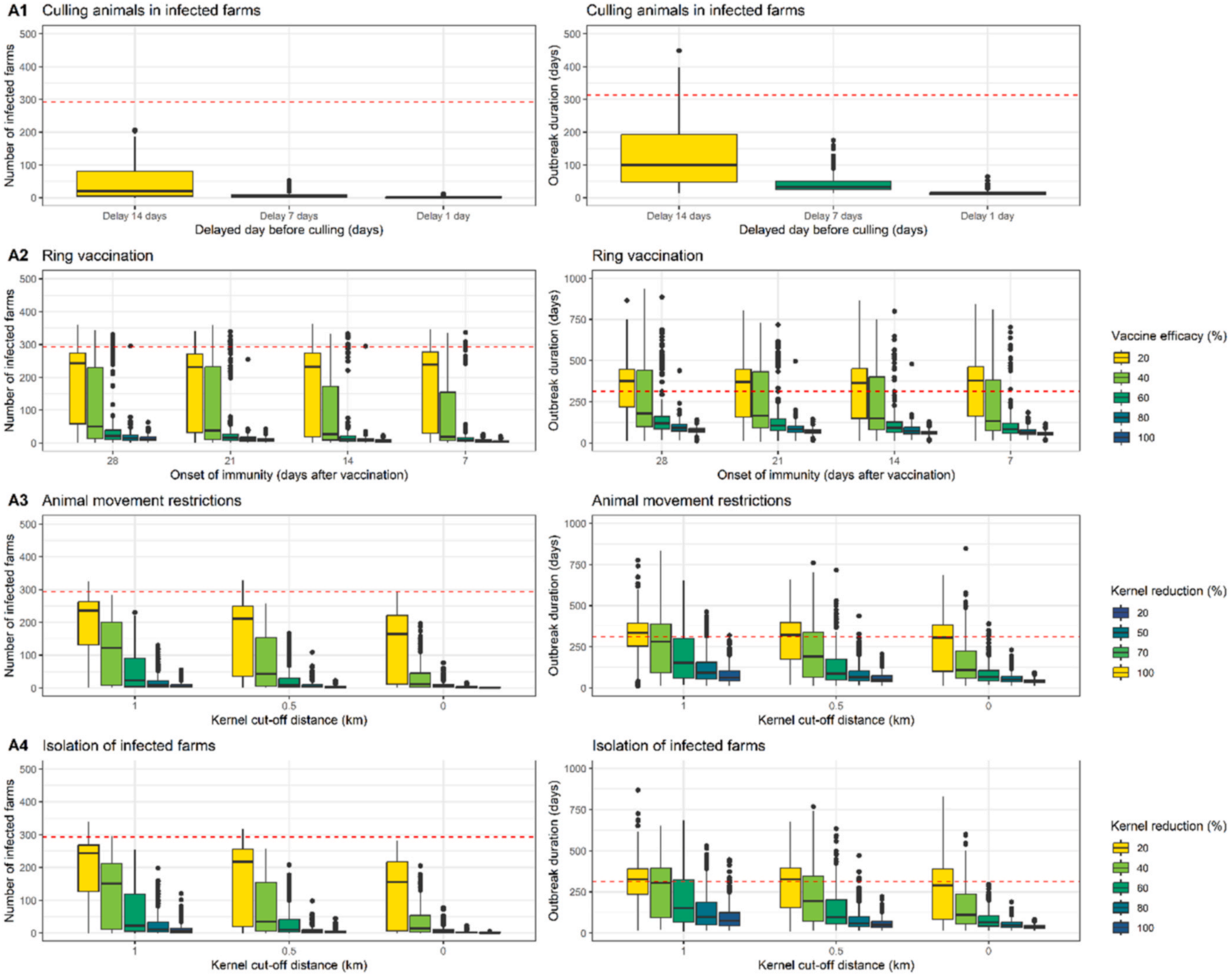

Fig. 3. Median number of secondary infected farms (excluding index cases) and outbreak duration from the foot and mouth disease outbreak model. A1, A2, A3 and A4 graphs represent culling animals in infected farms, ring vaccination, animal movement restrictions and isolation of infected farms in the Lamphaya Klang subdistrict. The dashed red lines represent median predictions from the baseline scenario.

Table 4
Sensitivity analysis of parameters from the foot and mouth disease outbreak model in the Lamphaya Klang subdistrict. Top Marginal Variance (TMV) is the variance reduction if the parameter is fully known. Bottom Marginal Variance (BMV) is the variance not explained by the parameter.

Control Measures	Parameters	Distribution	Median number of infected farms		Median outbreak duration (days)	
			Top marginal variance (%)	Bottom marginal variance (%)	Top marginal variance (%)	Bottom marginal variance (%)
Baseline	k_0	Gamma(shape = 5.25, scale =0.001)	30.7	42.7	10.4	55.6
	r_0	Gamma(shape = 5.63, scale = 0.03)	39.8	53.6	23.2	71.8
	α	Gamma(shape = 118.97, scale =0.012)	9.6	7.8	3.1	28.6
	δ	Gamma(shape =2.18, scale = 0.0002)	1.1	0.1	0.8	0
Ring vaccination	Vaccine efficacy (%)	Uniform(min = 0, max = 100)	86.6	87.2	93.2	90.3
	Vaccination rate (farm per day)	Uniform(min = 20, max = 80)	0	0.2	0	0.3
	onset of immunity (day after vaccination)	Uniform(min = 7, max = 28)	0	0.1	3.3	0.4
	Immunity protection duration (day)	Uniform(min = 90, max = 240)	2.1	2.1	0.9	0.4
Animal movement restrictions	Transmission kernel cut-off distance (km)	Uniform(min = 0, max = 1)	0.5	2.9	1.8	4.8
	Percentage decrease of transmission kernel (%)	Uniform(min = 0, max = 100)	91.9	94.5	81.2	85.9
	Delay animal movement restrictions (day after detection)	Uniform(min = 1, max = 30)	0.5	0.5	1.9	1.8
Isolation of infected farms	Transmission kernel cut-off distance (km)	Uniform(min = 0, max = 1)	2.6	4.1	4.1	8.9
	Percentage decrease of transmission kernel (%)	Uniform(min = 0, max = 100)	70.8	75.2	59.8	65.6
	Delay isolation (day after detection)	Uniform(min = 1, max = 14)	12.6	13.0	14.1	21.5

restrictions and isolation measures, outcome variance was mostly explained by the reduction of the transmission kernel.

The scatter plots in Fig. 4 show the effect of the parameters on the simulated outcomes of FMD outbreaks. The increase of k_0 and r_0 resulted in a higher number of infected farms and longer outbreak duration, but at a certain point, the outbreak duration shortened again. This is caused by the high transmission rate parameter (k_0) that rapidly accelerated the transmission, leading to shorter outbreaks due to the depletion of the susceptible farms. It should be noted that the outcome variance for isolation of infected farms was much larger than that for animal movement restrictions given the same parameters (Fig. 4). The scatter plot of ring vaccination shows that low vaccine efficacy ($\leq$ 50%) increased the duration of the outbreak compared to zero-vaccine efficacy because it did not prevent transmission completely and did not fully protect the vaccinated farms. Thus, the virus continued to spread but at a lower pace.

4. Discussion

In this study, a transmission model was constructed and parameterised based on FMD outbreak data for two different areas of Thailand. To our knowledge, this is the first FMD simulation model in Thailand that incorporates the spatial distance between farms and animal trade data. The comparison between simulation outcomes and outbreak data shows that the baseline results are in accordance with what happened in reality. Despite the slightly underestimated outbreak in the Bo Phloi district, the real outbreak was in the 95% prediction interval. Thus, we argue that the observed outbreak was likely according to the model prediction, and the baseline model is valid for this area. The model could be used to assess the effect of control measures.

Based on this study's findings, culling all animals on infected farms without delay is the most effective control measure in terms of shortening the outbreak and number of infected farms. However, the decision on culling should consider the trade-off between costs and benefits. In FMD-free countries that export livestock and animal products, culling strategies demonstrate positive returns (Boklund et al., 2013; Tildesley et al., 2009). In an endemic country like Thailand with no export benefit and a high probability of outbreak recurrence, culling may not offer positive economic benefits. Further research is needed to explore this issue. It should be noted that this model assumed unlimited culling capacity and a minimum delay of 1 day. In reality, these assumptions are rarely valid, especially during large outbreaks. Therefore, the effects of culling might be overestimated in this model.

Ring vaccination using a standard vaccine with an efficacy of 75% at 4 weeks after vaccination (WOAH, 2021) could control an FMD outbreak. However, multiple extrinsic factors, such as vaccine matching, vaccine logistics, vaccination schedule and vaccine coverage, could lower the efficacy of vaccination in the field (Ferrari et al., 2016a, 2016b). In the case of outbreaks in high-risk areas or with unknown FMD viral strains, we recommend using high potency FMD vaccine for ring vaccination since these can induce protection at 3–5 days post-vaccination and provide better protection against heterologous strains (Barnett and Carabin, 2002; Cox and Barnett, 2009). It should be noted that this model assumed that all animals on the farms are vaccinated, resulting in a vaccination coverage of 100% among susceptible animals. In reality, there may be ineligible populations, such as animals that are too young or those that were not present during vaccination (Ferrari et al., 2016a, 2016b). Therefore, vaccine coverage should also be taken into consideration.

Modelling the effect of animal movement restrictions on the spatial transmission kernel is a big challenge. Since the spatial transmission kernel does not specify the transmission rate by individual transmission routes, we could not quantify how much animal movement contributed to the transmission rate. In this study, we modelled the effect of animal movement restrictions by defining a cut-off distance from infected farms, in which the local transmission kernel below the cut-off remained

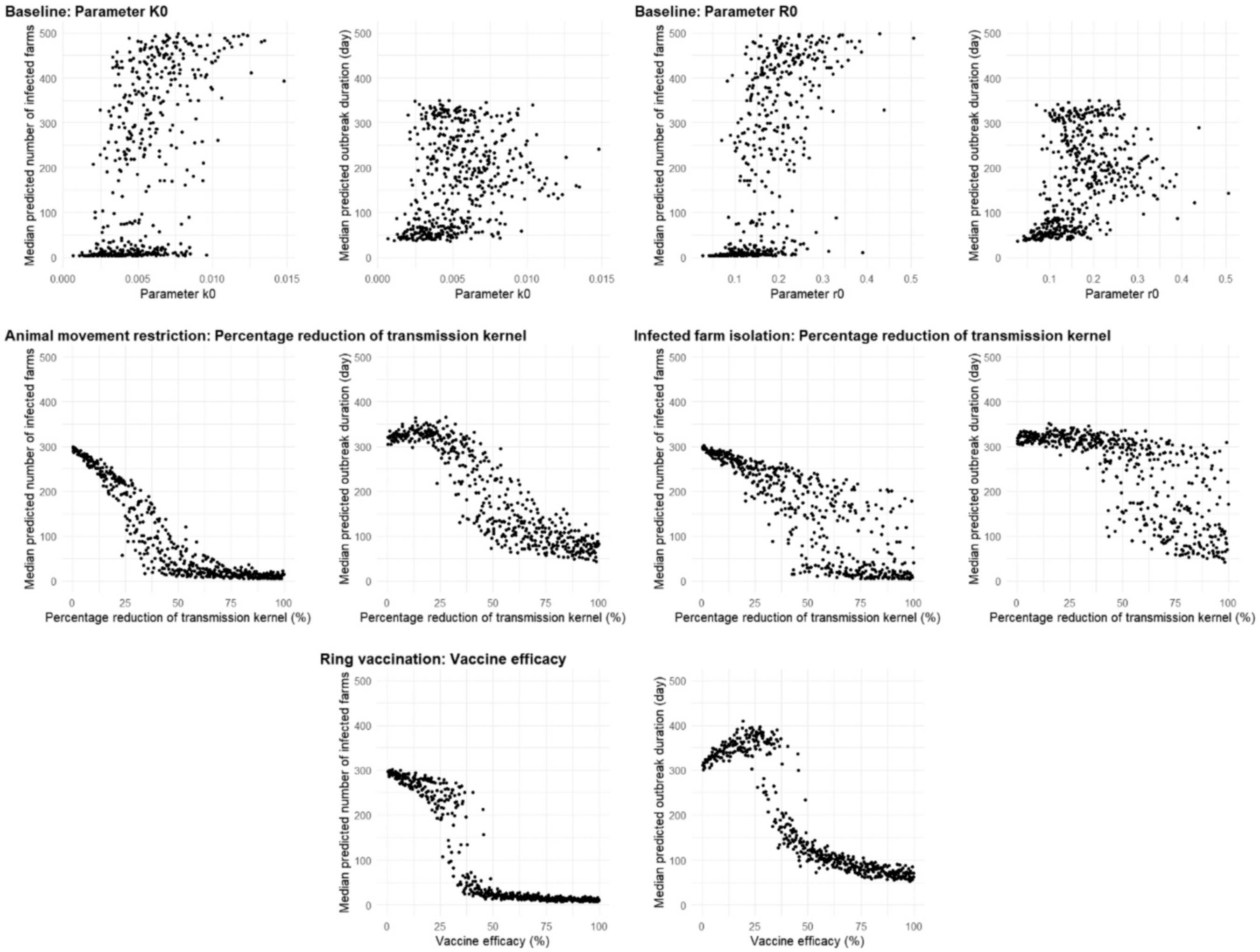

Fig. 4. Scatter plots of the predicted median number of infected farms (left) and predicted median outbreak duration (right) against the parameters from the foot and mouth disease outbreak model in the Lamphaya Klang subdistrict.

the same, and the transmission kernel above the cut-off decreased. The cut-off distance and the kernel reduction are affected by multiple factors, for example, the farm type and management. Extensive farms are expected to have more contact with their neighbouring farms than from intensive farms with strict biosecurity. The reduction of the transmission kernel depended on the contribution of animal movement to the overall transmission. For example, animal movement restrictions in an area with high animal movement should decrease the transmission kernel considerably and vice versa. The results were presented in various combinations of cut-off distance and transmission kernel reduction to let local authorities choose the parameters that are most relevant for their area and interpret the result to reflect their situation.

In our simulation model, animal movement restrictions and isolation of infected farms both affected the transmission by reducing the spatial transmission kernel and stopping the trade transmission. However, animal movement restrictions were assumed to be implemented for all infectious farms (detected and undetected) in the whole area. In contrast, isolation was only applied to the detected infectious farms. Based on the median number of infected farms and the duration of the outbreak, isolation of infected farms was found to be slightly inferior to implementing animal movement restrictions (Fig. 3), but the variance for the former was much larger than for the latter (Fig. 4). This result suggests that there was a higher risk of large outbreaks in the scenario of infected farm isolation compared to the animal movement restriction scenario. It is worth noting that for the sake of simplicity, the cut-off distance and kernel reduction were the same on every farm. In reality, the effect of animal movement restrictions and isolation might be heterogenous depending on multiple underlying factors, such as farm types, biosecurity and farm contact.

Despite our best effort to collect trade network data, this information could only be partially obtained. This resulted in a small trade transmission parameter ($\delta = 0.0006\ \text{day}^{-1}$). However, the spatial transmission kernel and trade transmission parameters were combined in the maximum likelihood estimation. The missing transmission rate from trade was captured by the spatial transmission kernel instead. The underestimated trade transmission might affect the results from control measures associated with trade, such as animal movement restrictions and isolation. Even with an incomplete trade network, it was still worthwhile to separate the partial trade transmission from the spatial transmission kernel because this was more realistic than using the spatial transmission kernel alone.

The findings from a similar FMD simulation model in the Netherlands (Backer et al., 2012a; 2012b), were comparable to ours, as they also indicated that outbreaks were easier to control in more sparsely populated livestock areas. Furthermore, the effect of emergency vaccination could be on par with culling, provided that the ring radius was sufficiently large. In Thailand, no study using a similar model to ours has been conducted. However, one study used a compartment model to evaluate FMD control measures in Southern Thailand (Wongsathapornchai et al., 2008). The results of that study demonstrated that culling infected animals led to a 98% reduction in annual cumulative incidence, which aligns with the high effectiveness of culling in this study.

Overall, our results indicate that all simulated measures can control the outbreak, but their relative effectivity is different between distinct areas. For the area with high farm density, i.e. the Lamphaya Klang subdistrict, the control measures needed to be more rigid to effectively control the outbreak compared to the area with low farm density like the Bo Phloi district. These results suggest that decision-makers should tailor control measure to the local context.

The model could be improved in various ways in further studies. Firstly, we assumed a homogenous baseline immunity, where all farms started with the same susceptibility level. In an endemic situation, some farms possibly have higher immunity levels from earlier vaccination or natural immunity from a previous outbreak. This heterogeneous baseline immunity might increase the spatial transmission kernel parameters, as shown by our previous study (Chanchaidechachai et al., 2021). Secondly, the detection time is estimated simplistically using an SEIR model based on the average population size and a constant number of case detections. Our assumption does not take into account asymptomatic infections, which could result in longer detection times. Thirdly, the model only focused on the transmission between the farms in the study areas without considering the probability of transmission from a farm outside this area and the probability of transmission from a farm inside the study areas to those outside. The effect of transmission from outside on the transmission kernel was comprehensively discussed in our previous study (Chanchaidechachai et al., 2021). This probability should be included in further studies.

5. Conclusion

We developed a simulation model for FMD transmission in endemic areas incorporating spatial features and animal trade data. In a high farm density area, stringent control measures were required to prevent a major outbreak. In contrast, less stringent control measures might be sufficient in areas with low farm density where outbreaks are usually small. These results highlight the need for area-specific control measures.

Declaration of Competing Interest

The authors declare that there is no conflict of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prevetmed.2023.106045.

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