



Spatial model of foot-and-mouth disease outbreak in an endemic area of Thailand

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ABSTRACT

Foot-and-mouth disease (FMD) is a disease of cloven-hoofed animals with high costs in animal welfare and animal production. Up to now, transmission between farms in FMD-endemic areas has been given little attention. Between farm transmission can be quantified by distance independent transmission parameters and a spatial transmission kernel indicating the rate of transmission of an infected farm to susceptible farms depending on the distance. The spatial transmission kernel and distance-independent transmission parameters were estimated from data of an FMD outbreak in Lamphaya Klang subdistrict in Thailand between 2016 and 2017. The spatial between-farm transmission rate in Lamphaya Klang subdistrict was higher compared with the spatial between-farm transmission rate from FMDV in epidemic areas. The result can be explained by the larger size of the within-farm outbreak in the endemic area due to no culling. The inclusion of distance-independent transmission parameters improved the model fit, which suggests the presence of transmission sources from outside the area and spread within the area independent of the distance between farms. The remaining distance-dependent transmission was mainly local and could be due to over-the-fence transmission or other forms of contact between nearby farms. Farm size on the kernel positively affects the transmission rate, by increasing both infectivity and susceptibility with increasing farm size. The results showed that both distance-dependent transmission and distance-independent transmission were contributed to FMDV transmission in Lamphaya Klang outbreak. These transmission parameters help to gain knowledge about FMD transmission dynamic in the endemic area.

1. Introduction

Foot-and-mouth disease (FMD) is an infectious disease in cloven-hoofed animals. The morbidity can reach 100 % in naive populations (Davies, 2002). Foot-and-mouth disease virus (FMDV) infection can occur via multiple routes, including inhalation of the aerosolised virus, contact with FMDV in the environment, eating FMDV contaminated food, direct contact with an infected animal, via skin abrasions and mucous membrane (Bravo De Rueda et al., 2015; Grubman and Baxt, 2004).

Due to high contagiousness and the wide host range, FMDV can instigate massive outbreaks, especially in FMD free areas. During the 2001 FMD epidemic in the United Kingdom and The Netherlands, more than 6.7 million animals were slaughtered. The loss of the agricultural sector was about 3.2 billion euros and additional costs to other sectors, such as tourism, with the sum of expenditure of about 2.7–3.2 billion

euro (Bouma et al., 2003; Thompson et al., 2002). This outbreak triggered the inquiry into FMDV outbreak management. It is also the first time that the mathematical models were introduced to manage the outbreak instead of empirical 'tried and tested' policies (Haydon et al., 2004).

The spatial features of FMDV transmission are crucial factors of its dynamics (Ostfeld et al., 2005; Wilesmith et al., 2003). Models that neglect spatial factors are oversimplified and insufficient to describe the dynamics (Riley et al., 2015). In the UK FMDV epidemic 2001, multiple studies attempted to use integrated spatial models for predicting the disease (Ferguson et al., 2001; Keeling et al., 2001; Morris et al., 2001). Morris et al. (2001) proposed is a large complex stochastic spatial simulation model. This model is initialised with the data from the latest census included farm size, type of livestock, farm location in the UK, and parameterised with a large range of transmission-related factors. Such a complex model thus required a vast number of parameters. This model

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was computationally intensive, and parameter estimation is limited by data availability. Moreover, the accuracy of predictions depends entirely on the validity of estimated parameters and the robustness of assumptions.

Keeling et al. (2001) proposed a simpler model that subsumed all transmission routes into a simple function called "transmission kernel". The transmission kernel is the transmission rate between farms depended on the distance between farms. The results from the model were in agreement with the spatio-temporal pattern of the 2001 UK outbreak and correctly predicted the long tail of the epidemic. Aside from distance dependence, other heterogeneous factors can also influence the kernel, for example, animal species, farm size, weather, biosecurity and management. These factors could all lead to the change of the spatio-temporal pattern of the transmission kernel and can be incorporated in the transmission kernel (Boender et al., 2014; Ster et al., 2009).

The concept of transmission kernel has been applied to FMDV models (Backer et al., 2012; Hayama et al., 2013) as well as other animal infectious disease models, e.g., risk mapping of the spread of highly pathogenic avian influenza (Bonney et al., 2018), modelling the effectiveness of vaccination strategies in classical swine fever epidemic (Backer et al., 2009), analysis of the spatio-temporal pattern of bluetongue in Western Europe (De Koeijer et al., 2011). Even though numerous FMDV models have been developed over the past years, the majority of the models were applied to epidemic areas, in particular, the United Kingdom. Only a few studies were conducted in endemic areas

where most of the FMD outbreaks have happened (Pomeroy et al., 2017). Modelling FMDV outbreak in endemic area assists local governments in designing efficient control strategies.

FMD is endemic in Thailand. Thai Government has been supported routine FMD vaccination two times a year in ruminants. However, the outbreaks were reported in multiple areas of Thailand every year (Blacksell et al., 2019). In 2016, the FMD outbreaks in Lamphaya Klang subdistrict, Thailand was reported to the Department of Livestock Development. The serotyping showed that FMDV from samples belonged to serotype A. In 2017, the FMD Thailand project had conducted an outbreak investigation in this area to collect additional data on farm size and the duration of outbreak in farm.

In this paper, we used the data of outbreak investigation to estimate the transmission kernel and the influence of farm size on the transmission kernel and introductions from outside the study area for the endemic situation from Lamphaya Klang subdistrict in Thailand between 2016 and 2017.

2. Materials and methods

2.1. Data collection

The study area is Lamphaya Klang subdistrict located in Saraburi province, the central region of Thailand. Saraburi province has the highest density of dairy cattle; therefore, it is a good representation of

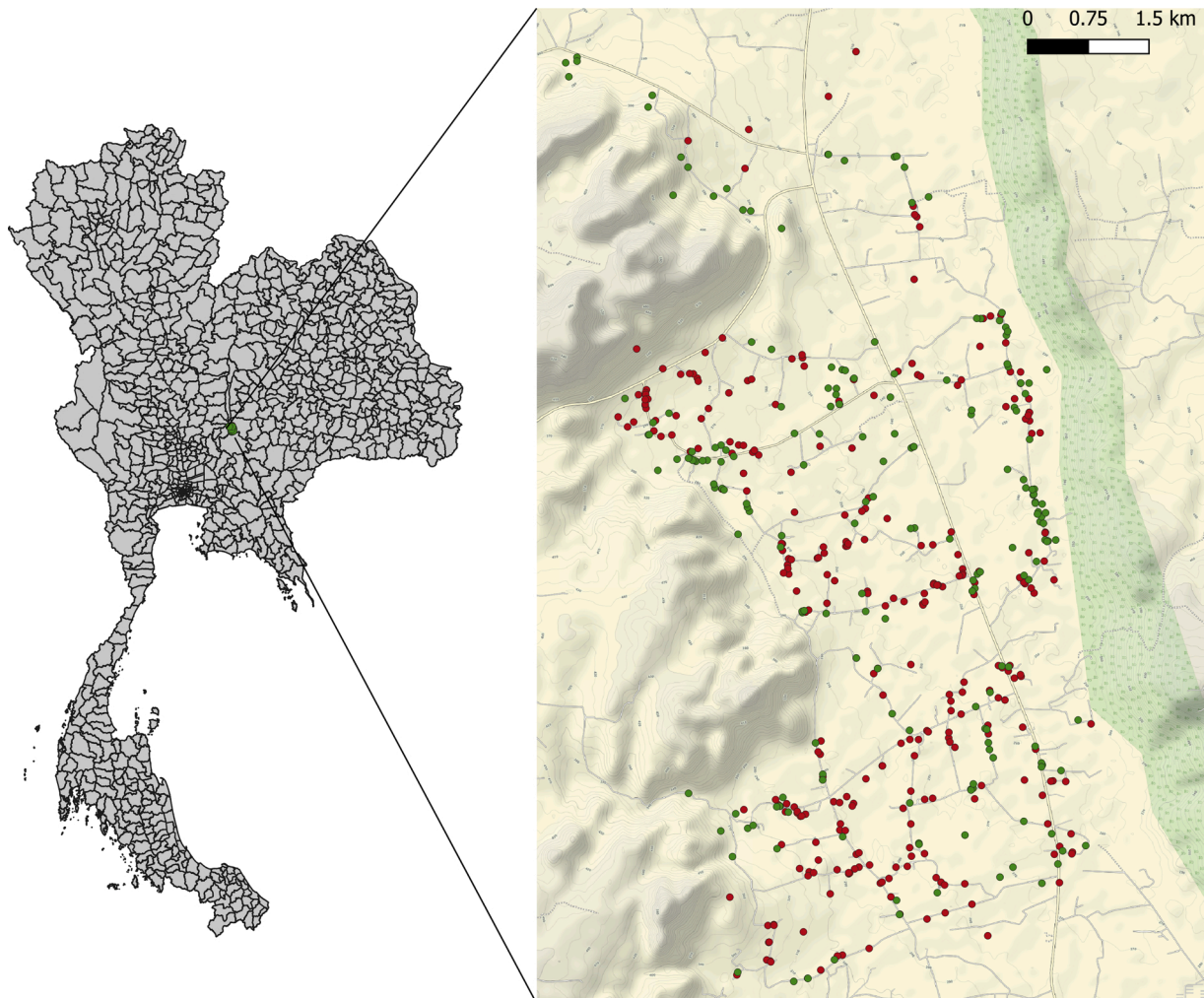


Fig. 1. Map of the outbreak in Lamphaya Klang subdistrict in Thailand. The green dots represent the farms without FMD infection, and the red dots represent the farms with FMD infection from 15 September 2016 to 8 August 2017. The greenish area on the right side of the map represents the forest area.

FMDV outbreak in a high-density cattle area. FMDV incidences were reported in dairy farms in this area between 2016 and 2017 (Fig. 1). We obtained the outbreak data by interviewing dairy farmer using questionnaires in the Thai language (Appendix). The farm data included the geographical coordinates, the total number of animals, the number of animals with clinical signs of FMD, the date that the first animal was showing clinical signs and the date that the last animal was showing clinical signs. The farms were selected starting at the centre of the study area at the milk collection centre in Lamphaya Klang subdistrict. We expanded the study area around the milk collection centre, and collected data from every farm within the area until we reached 500 farms. This method ensured that we had data of all farms in a defined area. The study area was 12.5 by 8.4 km. In total, the dataset includes 500 dairy farms with 273 infected farms in 15 villages of Lamphaya Klang subdistrict. Other FMD susceptible livestock species besides dairy cattle were not presented in the study area. The cases were identified by clinical signs. The numbers of the farm that newly detected with FMD in each month of the outbreak started from 15 September 2016 to 8 August 2017 were plotted (Fig. 2). The total duration of the outbreak is 335 days. The average farm size in the study is 39.5, with the average infected farm size of 44.6 and the average uninfected farm size of 33.4.

2.2. Data categorisation

The farm is the epidemiological unit in this study. Each day, the state of all farms was scored by the method described below as either susceptible, latently infected (thus not being infectious yet), asymptomatic infectious, symptomatic infectious or recovered and being immunised (Fig. 3). The infectious period during, which a farm can infect another farm, is the sum of the asymptomatic infectious and symptomatic infectious period.

All farms start having a susceptible state and become infected five days before the date that the first animals showing clinical signs. The first three days after infection are a latent period followed by two days of asymptomatic infectiousness. The symptomatic infectious period continues from the date that the first animal was showing clinical signs until two days after the last animals showing clinical signs (Mardones et al., 2010). After that, farms remain in the recovered state and we assumed that the farm being immune up to 224 days (32 weeks). The waning immunity duration referred from the study of FMD immunity waning after natural infection in individual animals (El-Sayed et al., 2012). After 32 weeks, the natural immunity wanes and farms resume a susceptible state. The assumptions of our model are somewhat different from previous studies. In Boender et al. (2010) and Hayama et al. (2013) the

farms stay infectious until the culling day. However, FMDV control strategies in Thailand do not include culling. We assume that the farm outbreaks are self-limiting due to a lack of susceptible animals at the farm. After the last symptomatic infections are recovery, these farms are protected against a new outbreak because of herd immunity within the farm.

The study period starts at the date that the first farms were infected ($t_0 = 15$ September 2016), which is five days before the first symptomatic farm was observed, to the date that the last farms stopped being infectious ($t_{max} = 8$ August 2017), which was two days after the last symptoms were observed.

2.3. Transmission kernel estimation

2.3.1. Baseline model

We used the kernel formula presented in Eq. (1) in the analysis. We compared this kernel formula with other formulas (Hayama et al., 2013; Ster et al., 2009). The results did not show statistical difference between kernel formulas (Appendix). Therefore, we selected this kernel formula because it was widely used in the livestock disease studies such as FMDV, avian influenza virus, and bluetongue virus (Boender et al., 2010; De Koeijer et al., 2011; Dorigatti et al., 2010).

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

The $k(r_{ij})$ is the transmission rate from infectious farm j to susceptible farm i which related to the distance between these two farms (r_{ij}). The shape of the kernel is expressed by three parameters: the k_0 parameter represents the transmission rate per day at distance zero; r_0 represents the distance for which the transmission rate is half k_0 ; α represents the slope at which the transmission rate decreases as a function of distance. The force of infection acting on the susceptible farm i on day t can be calculated by the sum of the kernel from all infectious farms on day t (Eq. (2)).

$$\lambda_i(t) = \sum_{j \in \text{infectious}} k(r_{ij}) \quad (2)$$

2.3.2. The distance-independent transmission

In the previous sections, the kernel was estimated under the assumption that the transmission only caused by the infectious farms inside the study area and the transmission rate depends on the distance between farms. Nevertheless, in an endemic situation like Thailand,

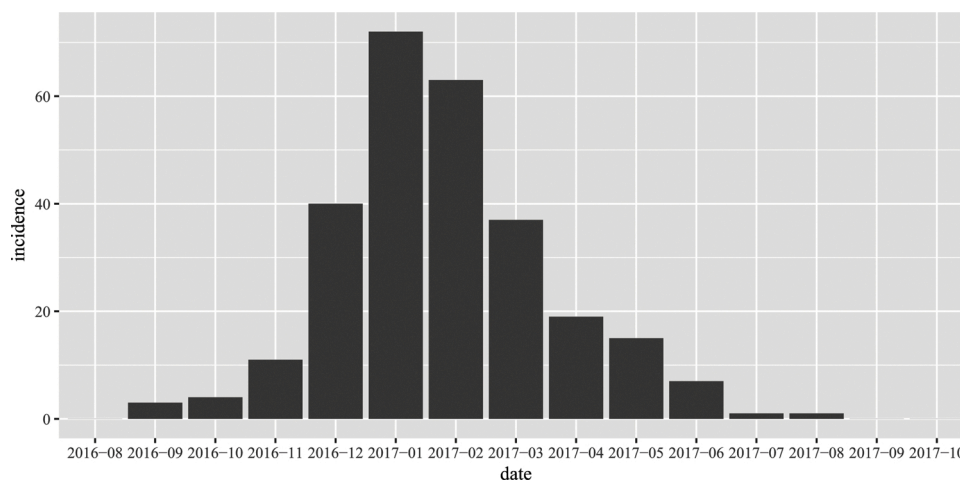


Fig. 2. The number of newly detected FMD farms during the outbreak in Lamphaya Klang subdistrict in Thailand. The first case in this study area was reported in September 2016. The last case was reported in August 2017. In September and October 2017, no new cases were reported in this study area.

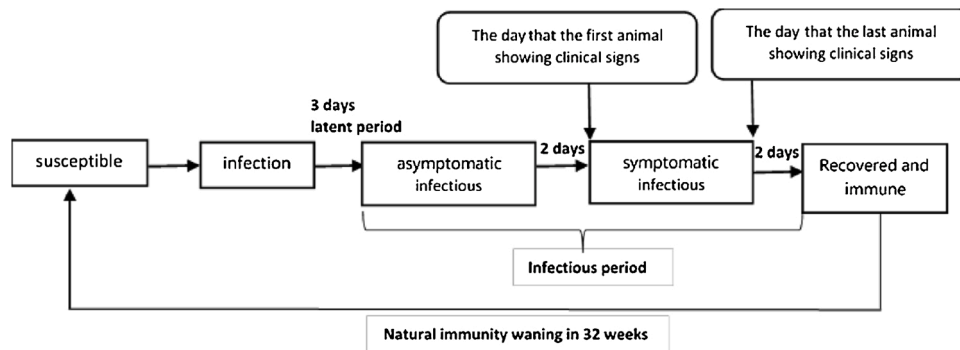


Fig. 3. The state transition of farms during the outbreaks. The square boxes represent the state of farms being susceptible, infection, asymptomatic infectious, symptomatic infectious, recovered and immune state. The date which each farm changes state can be estimated from the date that the first and the last animal was showing clinical signs.

there might be a possibility that the transmission originated from other sources besides the infected farms in the study area. Therefore, the h and δ parameters were introduced into the model to capture the distance-independent transmission (Eq. (3)).

$$\lambda_i(t) = \left(\sum_{j \in \text{infectious}} (k(r_{ij}) + \delta) \right) + h \tag{3}$$

The h parameter is a constant force of infection that is independent of the number of infectious farms and the distance between farms on the susceptible farm i at day t . It can be interpreted as the force of infection from the outside area.

The δ parameter is a distance independent transmission rate to take into account infectious farm contacts that are not determined by inter-farm distance inside the study area. The δ parameter times the number of infectious farms is a distance independent force of infection for each of the susceptible farms.

2.3.3. The influence of farm size on transmission

The heterogeneity of farm size affects the transmission rate; therefore, we tested the influence of farm size on the kernel by multiplying the farm size function ($f^c(N_i, N_j)$) with the kernel in Eq. (4).

$$\lambda_i(t) = \sum_{j \in \text{infectious}} f^c(N_i, N_j)k(r_{ij}) \tag{4}$$

We evaluated six different farm size functions (Boender et al., 2014)

$$f^c(N_i, N_j) = \begin{cases} \left(\frac{N_i N_j}{\bar{N}^2}\right)^c & \text{for (1)} \\ \left(\frac{N_i}{\bar{N}}\right)^{c_i} \left(\frac{N_j}{\bar{N}}\right)^{c_j} & \text{for (2)} \\ 1 + a \left(\frac{N_i}{\bar{N}} - 1\right) \left(\frac{N_j}{\bar{N}} - 1\right) & \text{for (3)} \\ \left[1 + a_i \left(\frac{N_i}{\bar{N}} - 1\right)\right] \left[1 + a_j \left(\frac{N_j}{\bar{N}} - 1\right)\right] & \text{for (4)} \\ \left[1 - \exp\left(-\frac{N_i}{d\bar{N}}\right)\right] \left[1 - \exp\left(-\frac{N_j}{d\bar{N}}\right)\right] & \text{for (5)} \\ \left[1 - \exp\left(-\frac{N_i}{d_i\bar{N}}\right)\right] \left[1 - \exp\left(-\frac{N_j}{d_j\bar{N}}\right)\right] & \text{for (6)} \end{cases} \tag{5}$$

N_i denotes the number of animals in susceptible farm i . N_j denotes the number of animals in infectious farm j . \bar{N} denotes the average number of animals in all farms. The c , a and d are the farm size parameters. In (1),

(3) and (5), the farm size parameters (c , a , d) are the same between infectious and susceptible farms, while in (2), (4) and (6), the farm size parameters are distinct between infectious (c_j , a_j , d_j) and susceptible farms (c_i , a_i , d_i).

2.3.4. The effect of an immune population

The baseline model assumes all farms start with susceptible state. However, this assumption is uncertain in FMD endemic area. Some of the farms might have had the infection before, resulting in herd immunity. Some farms were vaccinated since routine FMD vaccination program in dairy farms is common in Thailand. The analysis was performed to determine the sensitivity of the kernel estimation to the baseline number of immune farms. We randomly assigned 25 %, 50 % and 75 % of the susceptible farms, that remained uninfected during the study period, to be immune from the start of the outbreak. The model for each immune percentage was simulated 100 times to account for uncertainty. For each iteration, the transmission kernel parameters were estimated, and the kernels were calculated and plotted in Fig. 7.

In this model, we estimated the waning immunity at 32 weeks. This assumption was referred from the experiment of natural immunity waning in individual calves (El-Sayed et al., 2012), which is almost as long as the length of the study period. For herd immunity also needs to be considered the heterogeneity among animals of immune level and population turnover. To test the uncertainty of immune waning, we analysed an additional kernel given that the recovered farms did not become susceptible again during the outbreak time frame.

2.4. Parameter estimation

The kernel parameters are estimated by maximising the likelihood function (L), which is the product of probabilities of escaping infection until the infected time of infected farms, the probabilities of escaping infection the whole study period of farms that do not become infected and the probabilities of escaping the infection after waning of immunity until the end of the study period of recovered farms (Eq. (6)).

$$L = \prod_{m \in M} P_{esc,m}(t_{inf,m-1}, t_{start}) P_{inf,m}(t_{inf,m}) \tag{6}$$

Prob. escaping until and infection at t_{inf}
* $\prod_{n \in N} P_{esc,n}(t_{max}, t_{start})$
Prob. escaping until end of study period
* $\prod_{w \in W} P_{esc,w}(t_{max}, t_{waning,w})$
Prob. escaping from waning until end of study period

The set M contains all farms that are infected at times $t_{inf,m}$. The set N contains the susceptible farms that remain uninfected until time t_{max} . The set W contains the farms that are susceptible again after immunity waning at time $t_{waning,w}$ and these farms remain uninfected until time t_{max} .

Reinfection after waning of immunity was not observed. The start of the study period is indicated by t_{start} . P_{esc} denotes the probability of farm escaping infection until time t_{inf} , and P_{inf} denotes the probability of the farm being infected at time t_{inf} . The probability of escaping and the probability of infection follows from the force of infection Eq. (2) assuming a Poisson process:

$$P_{esc,i}(t_{end-1}, t_0) = \exp\left(-\sum_{t=t_0}^{t_{end,i}-1} \lambda(t)\right) \tag{7}$$

$$P_{inf}(t_{inf}) = 1 - \exp(-\lambda(t_{inf})) \tag{8}$$

The log-likelihood ($\ln(L)$) was used for calculation to reduce computational complexity.

The confidence interval for each parameter was obtained by the profile likelihood. The 95 % confidence interval will be reported between brackets in the result. The parameter estimates and confidence interval calculation were done in R version 3.6.2 using package “optimx” and “bbmle2”. The fit of alternative models was evaluated based on the Akaike information criterion (AIC). The model with lower AIC has a better fit, but if the AIC did not differ more than two, the models are considered to be equivalent.

2.5. Reproduction number

The reproduction number of each farm i (R_i) can be calculated by the sum of probability of infection from infected farm i to all susceptible farms j with each their own distance to farm i during infectious period T_i of that farm (Eq. (9)).

$$R_i = \sum_{j \neq i} (1 - E[e^{-k(r_{ij})T_i}]) \tag{9}$$

We used the actual infectious period as T_i for infectious farm i . For susceptible farms, we used a median infectious period estimated from the outbreak data as T_i (15 days).

If farm i has reproduction number above 1, the farm i will on average infected more than one other farms, thus increasing the outbreak size. As the outbreak progresses, more farms get infected, and the number of susceptible farms is depleted. To investigate whether the outbreak was limited because of the depletion of susceptible farms, we calculated the reproduction number (R_i) of remaining susceptible farms after removing the infected farms. If the R_i of remaining susceptible farms below 1, it means that the number of remaining susceptible farms are not enough for outbreak to continue, and the outbreak indeed limited due to the depletion of susceptible farms. We created a map of reproduction number (Fig. 8).

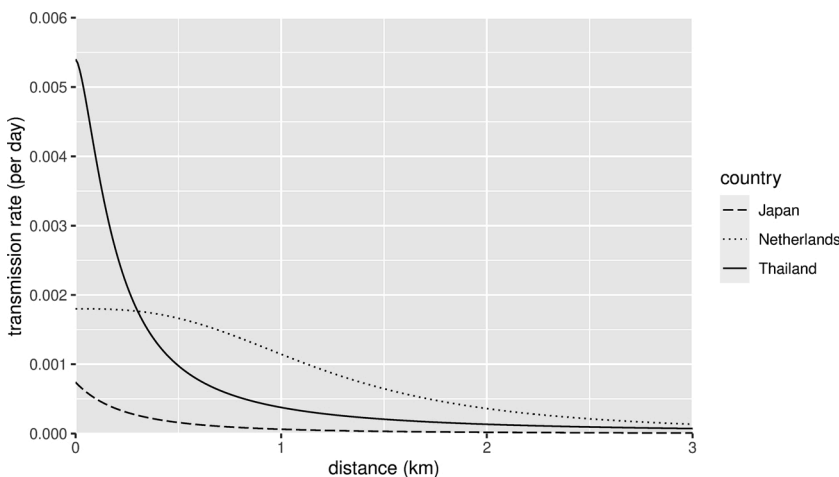


Fig. 4. The Lamphaya Klang subdistrict 2016, Japan 2010 (Hayama et al., 2013) and the Netherlands 2001 (Boender et al., 2010) FMD transmission kernels comparison. The transmission rate (day^{-1}) experienced by one recipient farm from one infectious farm was plotted against the distance (km) between the two. The solid line represents the baseline kernel from the 2016 Lamphayaklang subdistrict outbreak ($k_0 = 0.0054 \text{ day}^{-1}$ (0.0023–0.012), $r_0 = 0.19$ (0.07–0.35) km, $\alpha = 1.56$ (1.29–1.84)). The dotted line represents the baseline kernel of the 2001 Dutch FMD outbreak ($k_0 = 0.0018$ (0.0004–0.0063) day^{-1} , $r_0 = 1.22$ (0.67–3.35) km, $\alpha = 2.8$ (2.3–4.1)). The dashed line the 2010 Japan FMD outbreak ($k_0 = 0.00074 \text{ day}^{-1}$, $r_0 = 0.58$ km, $\alpha = 2.47$).

3. Results

3.1. Transmission kernel estimation

The transmission rate at zero distance (k_0) was estimated as 0.0054 (0.0023–0.012) day^{-1} , the distance where the transmission rate reached half of the maximum transmission rate (r_0) was estimated as 0.19 (0.07, 0.35) km, and the shape parameter (α) as 1.56 (1.29–1.84). The transmission kernel of FMD outbreak in the endemic area of Lamphaya Klang subdistrict 2016 with distance independent parameters and function of farm size (1) was compared with the transmission kernels of FMDV outbreak in the epidemic area of the Netherlands 2001 (Boender et al., 2010) and that of the FMDV outbreak in the epidemic area of Japan 2010 (Hayama et al., 2013) (Fig. 4).

3.2. The distance-independent parameters

The inclusion of distance-independent parameter in the transmission kernel model improved the fit of the model. After including h and δ into the model, the height of the kernel reduced, and the shape became more narrow. The kernel indicated less transmission through local contacts. The parameters of spatial transmission kernel with h and δ were $k_0 = 0.003$ (0.002–0.005), $r_0 = 0.40$ (0.23–0.63) and $\alpha = 2.80$ (1.47–4.13) (Table 1, Fig. 5).

3.3. The influence of farm size on kernel

The estimated farm size function parameters (1), (2), (3) and (4) were all positive (Table 2). It indicated that the between-farm transmission rate increased with farm size. In farm size function (5), the scaling parameter of the infectious farms (d) was 0.21, which meant that the infectivity rapidly increases with farm size, such that the transmission rate is 95 % of the maximum transmission rate at a farm size of 25. The model for farm size function (6) did not converge. Therefore, we could not estimate the farm size function parameter.

The model with farm size function (1) had the lowest AIC. However, the differences in AIC between (1) and (2) is lower than two. We conclude that these had a similar fit. Fig. 6 presents the plot of the estimated transmission kernel and the prediction bounds from the baseline model and the best fit model of farm size function (1) with different combinations of susceptible and infectious farm size.

3.4. The effect of an immune population

The inclusion of a fraction of farm being immune increased the transmission rate. The transmission rate at zero distance (k_0) was

Table 1

Estimated parameters, 95% profile-likelihood confidence interval and AIC for the baseline model and the models with distance-independent transmission parameters. The baseline model represents the kernel without distance-independent transmission parameters. Df denotes degree of freedom.

Models	Optimal spatial parameter values			Distance-independent parameters	df	AIC
	k_0 (day ⁻¹)	r_0 (km)	α			
Baseline model	0.005 (0.003–0.012)	0.19 (0.07–0.35)	1.56 (1.29–1.84)	–	3	3428.3
Model with h	0.004 (0.002–0.007)	0.29 (0.10–0.48)	1.94 (1.43–2.45)	$h = 2.4 \times 10^{-4}$ ($0.3 \times 10^{-4} - 4 \times 10^{-4}$)	4	3421.8
Model with δ	0.003 (0.002–0.005)	0.42 (0.21–0.63)	2.74 (1.40–4.01)	$\delta = 3.6 \times 10^{-5}$ ($1.4 \times 10^{-5} - 5.9 \times 10^{-5}$)	4	3421.7
Model with h and δ	0.003 (0.002–0.005)	0.40 (0.23–0.63)	2.80 (1.47–4.13)	$h = 1.8 \times 10^{-4}$ ($4.1 \times 10^{-5} - 3.6 \times 10^{-4}$) $\delta = 2.6 \times 10^{-5}$ ($0.2 \times 10^{-5} - 4.9 \times 10^{-5}$)	5	3418.6

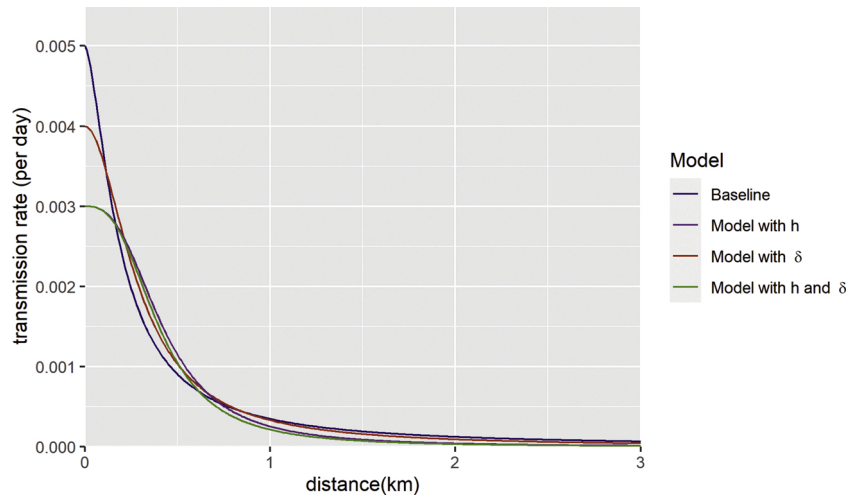


Fig. 5. The comparison transmission kernel plot between the baseline kernel, the kernel with δ parameter, the kernel with h parameter and the kernel with h and δ parameters. The blue line represents the baseline kernel. The purple line represents model with h . The red line represents the kernel with δ . The green line represents the kernel with h and δ .

Table 2

Estimated parameters, 95 % profile-likelihood confidence interval and AIC for each farm size functions. The baseline model represents the kernel without farm size function, i.e., $f^c(N_i, N_j) = 1$. Df denotes degree of freedom. The lower AIC corresponds to a better fit model.

	spatial parameter values					farm size parameter values	AIC
	k_0 (day ⁻¹)	r_0 (km)	α	h	δ		
Baseline model	0.003 (0.002–0.005)	0.40 (0.23–0.63)	2.80 (1.47–4.13)	1.8×10^{-4} ($0-3.6 \times 10^{-4}$)	2.6×10^{-5} ($0.2 \times 10^{-5} - 4.9 \times 10^{-5}$)	–	3418.6
(1)	0.004 (0.002–0.006)	0.38 (0.19–0.56)	2.44 (1.63–3.25)	1.7×10^{-4} ($0-3.4 \times 10^{-4}$)	2.0×10^{-5} ($0.09 \times 10^{-5} - 3.8 \times 10^{-5}$)	$c = 0.60$ (0.40–0.79)	3378.8
(2)	0.004 (0.002–0.006)	0.37 (0.17–0.57)	2.40 (1.58–3.21)	1.7×10^{-4} ($0-3.4 \times 10^{-4}$)	1.9×10^{-5} ($0.04 \times 10^{-5} - 3.8 \times 10^{-5}$)	$c_i = 0.57$ (0.36–0.79) $c_j = 0.71$ (0.22–1.20)	3380.6
(3)	0.004 (0.003–0.005)	0.38 (0.16–0.60)	2.40 (1.34–3.44)	1.8×10^{-4} ($0-3.7 \times 10^{-4}$)	1.9×10^{-5} ($0-4.2 \times 10^{-5}$)	$a = 0.43$ (-0.04–0.90)	3417.7
(4)	0.003 (0.002–0.005)	0.38 (0.18–0.57)	2.41 (1.60–3.22)	1.6×10^{-4} ($0-3.2 \times 10^{-4}$)	2.0×10^{-5} ($0.1 \times 10^{-5} - 3.9 \times 10^{-5}$)	$a_i = 0.64$ (0.41–0.88) $a_j = 0.69$ (0.14–1.24)	3384.0
(5)	0.004 (0.002–0.006)	0.44 (0.25–0.63)	2.99 (1.49–4.48)	1.8×10^{-4} ($0-3.6 \times 10^{-4}$)	2.8×10^{-5} ($0.5 \times 10^{-5} - 5.2 \times 10^{-5}$)	$d = 0.21$ (0–0.47)	3419.6

higher in the model with higher percentage of immune farms, but the distance where the transmission rate reached half of the maximum transmission rate (r_0) and the shape parameter (α) slightly changed (Fig. 7). Assuming a longer immune period did not alter the kernel shape. The kernel of the model assumed that the recovered farms did not lose immunity until the end of the outbreak, had $k_0 = 0.0059$ (0.0031–0.013) day⁻¹; $r_0 = 0.18$ (0.07–0.35) km; $\alpha = 1.56$ (1.30–1.87). The parameters were almost the same as the baseline model, except the k_0 was slightly higher.

3.5. Reproduction number

The risk map (Fig. 8) shows that farms with a reproduction number above one scattered in the centre of study areas, and a number of farms with a reproduction number below 0.5 in the northern part of areas where the farms located sparsely. After removing the infected farms, the reproduction number of remaining farms were below one. The reproduction number of farms at the area border should be carefully interpreted since the data about farm located outside the area was unknown. Therefore, the reproduction number of farms at the area border could be underestimated.

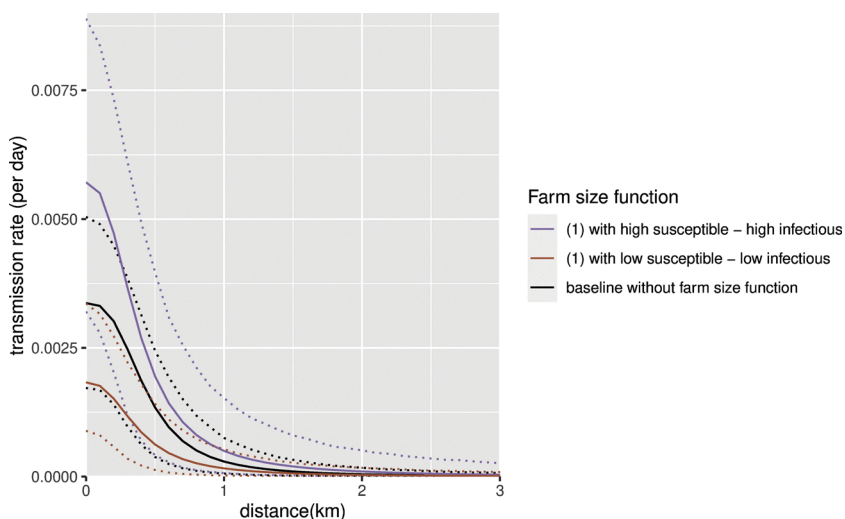


Fig. 6. The estimated transmission kernels of the baseline model and the models with farm size function (1) in different combinations of farm size with the prediction bounds. The solid line represents the kernel from the estimated parameters. The dotted line represents the 95 % prediction bounds of the kernel. The black represents the baseline kernel without farm size function. The purple line represents farm size function (1) with high susceptible farm size and high infectious farm size. High infectious farm size is the third quartile of infectious farm size $N_j = 60$. High susceptible farm size is the third quartile of susceptible farm size $N_i = 50.5$. The orange line represents farm size function (1) with low susceptible farm size and low infectious farm size. Low infectious farm size is the first quartile of infectious farm size $N_j = 25$. Low susceptible farm size is the first quartile of susceptible farm size $N_i = 18$.

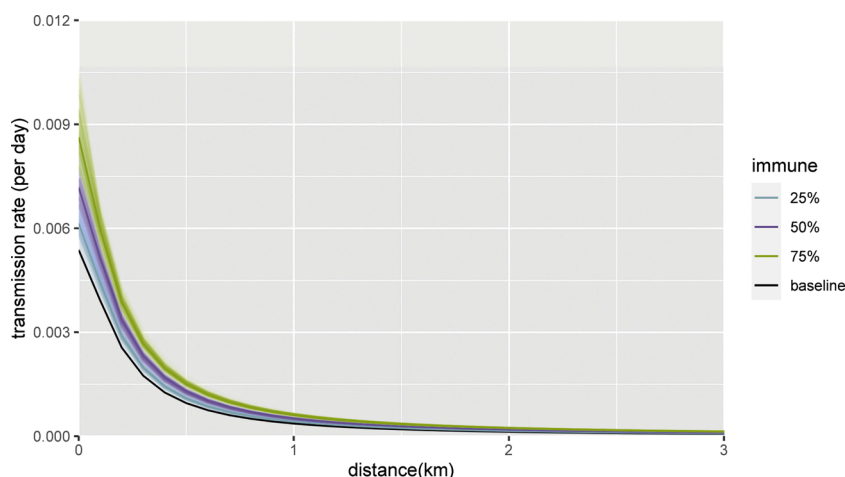


Fig. 7. The estimated transmission kernels for each percentage of the immune farms. The blue lines, purple lines and green lines represent the kernels with the assumptions that 25 %, 50 %, 75 % of the susceptible farms randomly became immune. The black line represents the baseline kernel.

4. Discussion

This study is the first FMDV spatial transmission kernel estimation using the outbreak data from an endemic area. The kernel from Lamphaya Klang subdistrict shows that the transmission rate between farms drastically decreased with distance between farms. This local transmission might be explained by a higher contact rate between nearby farms than farms that locate further. Neighbour farms might share the borders, and the risk of transmission (over-the-fence) between adjacent farms is high. Moreover, neighbour farmers are often relatives, and the contact rate between farms of relatives is likely to be relatively higher than between farms of non-relatives. Risk communication is very important to improve the awareness of farmers about FMD, so these farmers can take action to avoid local transmission. Animals should be kept away from farm border during the outbreak to prevent over-the-fence transmission.

The between-farm transmission rate at the nearest distance (k_0) from Lamphaya Klang subdistrict was higher than the previous FMD studies from the Netherlands 2001 and Japan 2010 FMD outbreak. The higher k_0 might be explained by the size of the within-farm outbreaks in Lumpayaklag subdistrict compared to those in the Netherlands and Japan. In the outbreak of the Netherlands in 2001 and Japan in 2010, outbreak control measures were implemented including immediate culling of all animals at infected farms (Bouma et al., 2003; Muroga

et al., 2012). Although culling might reduce the transmission rate, the adoption of a culling policy in Thailand is controversial because of the widespread occurrence of the disease. Unlike the Netherlands and Japan where regaining the FMDV-free status is the priority of control to enable the export of animals and animal product, an endemic area like Thailand might not gain full benefit from the culling because an FMDV-free status is unlikely to be obtained. Blanket vaccination of all animal in the area might be a more cost-effective intervention in the endemic area since the vaccination significantly reduces the amount of virus excretion in infected animals and also help developing immunity in susceptible animals (Barnett and Carabin, 2002). Vaccination helps to reduce the transmission rate, consequently abating the size of outbreaks with a lower economic cost than culling (Hagerman et al., 2012). According to the Animal Epidemics Act (of Thailand) BE 2558, the authorities can announce an outbreak zone where animal movement restriction and emergency vaccination are implemented. However, the criteria for announcing an outbreak zone is vague, and mostly depends on the discretion of the local authority. We did not find the declaration of outbreak zone during 2016–2017 in our study area, so we cannot confirm the control measures during this outbreak. The outbreak was likely to be self-constrained by the depletion of the susceptible farms because the reproduction numbers of remaining farms after removing all infected farms were below one (Fig. 8).

Some farms in the area might not have been included in the interview

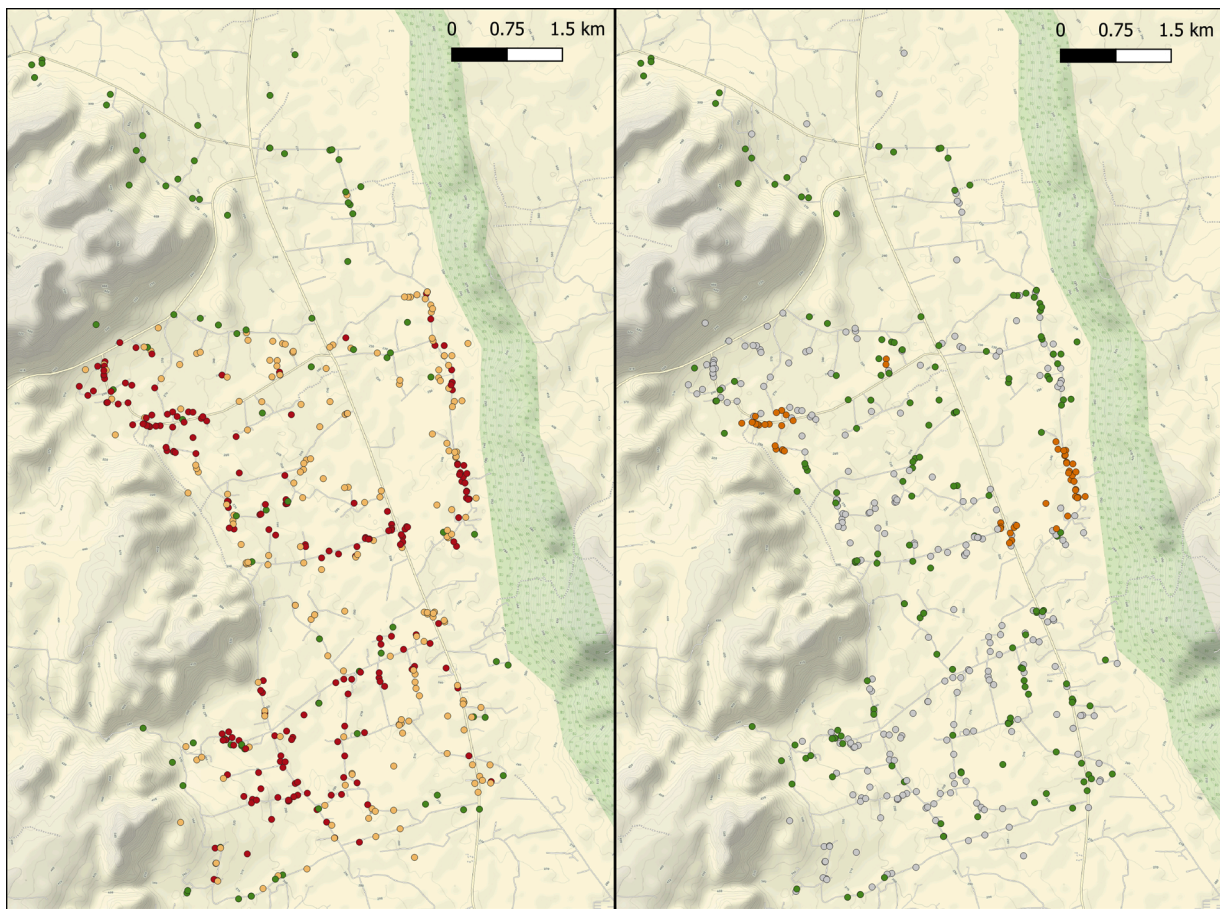


Fig. 8. The effective reproduction number of farms was calculated using the kernel parameters with h and δ . Red dots represent the farms with $R_i \geq 1$; orange dots represent farms with $0.5 \leq R_i < 1$; green dots represent farms with $R_i < 0.5$. The left map shows the effective reproduction number considering all farms. The right map shows the effective reproduction number after removing infectious farms.

leading to selection bias. In case the unobserved farms also were infected, the r_0 and α from the kernel might have been biased. However, we expected that the data covered more than 95% of the farms in the area, the kernel will not noticeably change when including the unobserved farms.

From the effect of immune analysis, Boender the transmission rate k_0 between farm was higher, when we added initially immune farms. The results indicated that the kernel might be underestimated if immune farms were present. Another aspect of immunity is the length of herd immunity depending on heterogeneity in individual animal immunity and population turn-over. We did not observe the reinfection in the study area and period, which is in concordance with previous observations that inter epidemic period in endemic areas are about 2 years (Domenech et al., 2010). Therefore, we tested the robust of kernel estimation with increasing the period of immunity. The result did not substantially change. We conclude that changing the baseline assumptions for immunity did not alter the conclusion.

The inclusion of distance-independent transmission parameters resulted in a kernel being more local spread because the long-distance transmission is covered by the h and δ parameter. For the source of transmission from h , the study of the transmission kernel on the 2015 highly pathogenic avian influenza (HPAI) outbreak in Minnesota interpreted the h parameter as the disease introduction from wild birds (Bonney et al., 2018). It is unlikely that wildlife is the source of introduction due to the absence of cloven-hoofed wildlife in the study area, although the farmers mentioned the free-range beef cattle that sometimes enter the area. Moreover, FMDV might enter the area by vehicles, equipment and people since the movement restriction in the endemic

area is lenient compared to FMD free countries. In our analysis, we assume that h parameter is constant over the outbreak, but in reality the probability of an incursion from outside the sub-district depends on the FMDV situation outside of the sub-district and thus h parameter is likely to change over time. However, we do not have information on the situation outside the outbreak to estimate the change of h parameter. Including time-dependence for example adding monthly values would increase the number of parameters and is likely to cause overfitting of the model.

The δ parameter represents the distance-independent transmission but dependent on the number of infectious farms in the area. Though this δ parameter was small, the inclusion of δ improved the fit of the model and changed other parameter values causing a lower kernel and relatively more local transmission. One of the possible sources of δ are manure traders who buy manure from dairy farms to sell as fertiliser. They always use the same truck to pick up and deliver manure from farms to farms. Another possible source is the feed truck since many farms buy feed from the same sellers.

Including farm size statistically improved the model. The results from five different farm size functions were in agreement with each other that the susceptibility and the infectivity were increased by the higher number of animals on the infectious farms and the susceptible farms. The best fit model was the model (1) that the relative increase in farm size results in a relatively proportional increase the between-farms transmission rate. The susceptibility and infectivity were proportionally increased by the same exponent (c). However, the prediction bounds of the between-farms transmission rate from the model of farm size function (1) with different combinations of susceptible and infectious farm

size overlap with the baseline model without farm size function (Fig. 5). The effect of farm size does not seem to have a relevant affect on the between-farm transmission rate. This could be due to the small variation in farm size in this area with a minimum of 2 and, a maximum of 190 (median = 30). The farm size effect might be more relevant in an area with large variation of farm size.

Our study is one of the few FMDV models in the endemic setting. Moreover, it is also the first FMDV kernel study in the endemic area. However, the kernel result should be meticulously interpreted because the heterogenous factors can affect the kernel, for example, the strain of FMDV. In the 2001 Netherlands outbreak was FMDV serotype O PanAsia lineage (Mason et al., 2003), and the FMDV from the 2010 Japan was caused by FMDV serotype O Mya-98 (Muroga et al., 2012), while the FMD outbreak 2016 Lamphaya Klang subdistrict was caused by FMDV serotype A. The virulence, infectivity and transmission could be diverse between different FMD virus strains. Moreover, the species of animals also affects the transmission (Bravo et al., 2014). The outbreaks in Japan and the Netherlands included the cattle, small ruminants and pigs, but the outbreaks in Lamphaya Klang subdistrict, only the dairy cattle farms are included in the study.

5. Conclusions

FMDV transmission in this outbreak consists of both distance-dependent transmission and distance-independent transmission. The distance-dependent transmission is mainly local and higher compared to the outbreak from the epidemic areas. The significant distance-independent transmission suggested the transmission from outside, and non-local transmission may happen in the outbreak. These transmission parameters help to gain the knowledge about FMD transmission dynamic in the endemic area. Moreover, it could help develop a model for decision-making for outbreak response in further studies.

Ethics statement

Authors have declared that Ethical Statement is not applicable in the current manuscript.

Data availability statement

The data that supports the findings of this study are available in the supplementary material of this article.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.prevetmed.2021.10.5468>.

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