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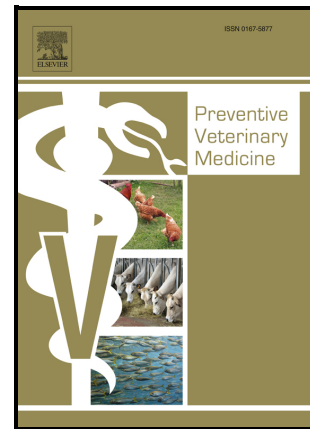
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# **A stochastic modelling study of quarantine strategies against foot-and-mouth disease risks through cattle trades across the Thailand-Myanmar border**

**Short title: Modelling cattle quarantine at Thailand-Myanmar border**

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## **Abstract**

Foot-and-mouth disease (FMD) is an important endemic disease in livestock in Southeast Asia. Transboundary movement of animals may result in the transnational disease spread. A major cattle market is located at the Thailand-Myanmar border, where most cattle imported from Myanmar are traded. In this study, we built a stochastic susceptible-exposed-infectious-recovered (SEIR) model to investigate the effectiveness of a private animal quarantine service center in preventing FMDV from entering the major cattle market. We computed with different parameters and found that, with 50% vaccine effectiveness, the risk of releasing infected cattle to the market per batch was generally low during the quarantine period of 21 and 28 days, with the risk ranging from 0.071 to 0.078 and 0.032 to 0.036, respectively. Despite the best scenario, the zero-risk state is difficult to attain. The sensitivity analysis highlights that the percentage of immune animals before entering the quarantine centers and the vaccine effectiveness are important factors. In conclusion, the 21-day quarantine period mitigates the risk of FMDV introduction into the cattle market. This control measure should be rigorously maintained to sustainably prevent FMDV outbreaks through transboundary animal movements, especially among countries in FMD-endemic regions.

## **Keywords:**

cattle trade, foot-and-mouth disease, quarantine, risk, transboundary

## 1. Introduction

In Southeast Asia, cattle are raised for agricultural purposes, primarily as work animals for rice production and human consumption. According to the Food and Agriculture Organization (FAO), Myanmar has approximately 21 million cattle and buffaloes, of which over 17.2 million are cattle (Roche et al., 2020). While a large portion of beef cattle raised in South Asia and Myanmar may travel across Thailand to destinations with high demand for beef cattle, such as China and Vietnam (Bunmee et al., 2018; Roche et al., 2020), some may remain in the country. The largest gateway that receives cattle across the Thailand-Myanmar border into Thailand is found in Mae Sot District, Tak Province, where the area is geographically separated from the rest of Thailand by the Thanon Thong Chai Mountain Range. According to the official record by the Department of Livestock Development (DLD) of Thailand, over 80,000 registered beef cattle have been introduced through this channel annually, accounting for 68% of all cattle imported from 2015 to 2017 (DLD, Personal communication, 31<sup>st</sup> August 2018). Imported beef cattle subsequently leave Mae Sot District across the mountain range and are distributed to other regions across Thailand (Wiratsudakul and Sekiguchi, 2018).

Foot-and-mouth disease (FMD) has long been a critical transboundary animal disease (TAD) in Southeast Asia. In 2020, 556 FMD outbreaks were notified from half of the countries in Southeast Asia (5/10), including Cambodia, Myanmar, Malaysia, Thailand, and Vietnam in 2020 (WOAH, 2021). Among these outbreaks, 188 were categorized as foot-and-mouth disease virus (FMDV) serotype O, while 368 were unclassified. Cattle were reported as hosts for the virus in 95.3% (530/556) of these outbreaks. Three outbreaks were reported from Myanmar, and 218 other events were reported from Thailand. FMDV serotype O was the leading viral cause of the

outbreaks in Thailand during the past recent years (Arjkumpa et al., 2020; WOAHA, 2021, 2020, 2019). The transboundary cattle movement is deemed a vital contributor to transnational FMDV dissemination through the cattle trade network in this region (Bartels et al., 2017; Blacksell et al., 2019).

Animal quarantine has been considered the first line of defense against cross-border disease transmission through animal trades (Otte et al., 2004). It can be carried out in exporting countries to limit the risk of batch rejection (Knight-Jones et al., 2014), in importing countries to prevent disease transmission to the local animal population (Otte et al., 2004), or on both sides. At the Thailand-Myanmar border in Mae Sot District, the quarantine process of imported beef cattle from Myanmar is regulated by the Tak animal quarantine office of the DLD. By the previously recommended protocol (Dele et al., 2014; Knight-Jones et al., 2014; Paton et al., 2010; Thomson et al., 2009; USDA, 2012), all imported cattle are obliged to stay quarantined at the border area for 21 days before being released into the country. Phylogenetic analysis of FMDV sub-lineages from Myanmar and Thailand isolated in 2016 revealed that the viruses were closely related to those circulated in South Asia in 2015 (Qiu et al., 2018), which corresponded to the cattle trade route from South Asia into Southeast Asia via Myanmar and Thailand. The common FMDV strains found across the trade route, including Thailand, indicated that the virus from the South Asian region can still slip through the recommended 21-day quarantine strategy.

A modeling approach has been increasingly used to evaluate the risk of importing TADs into a country. In Thailand, an import risk assessment study for FMDV has previously estimated that approximately 3% of accepted animals are infected, assuming a constant quarantine period of 21 days (Wongsathapornchai et al., 2008). To date, the effectiveness of quarantine strategies for preventing the transboundary introduction of FMDV into the importing country located in an

endemic area has never been evaluated. The present study aimed to evaluate the effectiveness of different quarantine periods in limiting the FMDV importation risk from beef cattle trade across the Thailand-Myanmar border.

## **2. Materials and Methods**

### **2.1. Site visit and observation**

The Tak animal quarantine office of the DLD, located in Mae Sot District, Tak Province, Thailand (Figure 1A), was visited in August 2018 to gain insight into the processes of animal quarantine for the cross-border cattle movement at the Thailand-Myanmar border. The primary objective of the office is to prevent the introduction of transboundary diseases into Thailand by implementing different control measures, such as animal quarantine, before moving to the market. This animal quarantine office was chosen because Mae Sot District is the most important hub for cattle importation into Thailand. The quarantine strategy implemented by the Tak animal quarantine at Mae Sot District in Thailand was described by local veterinary authorities during a field visit. Following that, a mechanistic stochastic disease dynamics framework was developed to investigate the effectiveness of the quarantine practices.

### **2.2. Disease dynamics model**

A disease dynamics model was constructed to evaluate the risk of releasing FMDV-infected cattle to the cattle market through quarantine processes. The model represented the transmission of FMDV within an animal quarantine center in Mae Sot District, which operated following the protocol provided by the Tak animal quarantine station. The cattle were housed in batches, but individual animals within each batch were tethered within the same housing structure. This

limited direct contact primarily to cattle in close proximity to each other. While the transmission rate represents an average risk across all potential routes, the tethering arrangement likely makes aerosol transmission the dominant mode of spread. The dynamics of viral transmission were described by a susceptible-exposed-infectious-recovered (SEIR) compartmental modeling framework. Besides, the dynamics of the cattle population describing the flows of different cattle herds within the quarantine center were also considered. Our dynamic model was mainly based on the ‘time course of infection’ (Real and Biek, 2007) in which the compartment ‘E’ represented the latent period where the cattle were ‘infected’ but not yet ‘infectious’. In contrast, our ‘I’ was the status in which the animals were already infected and infectious, ready to transmit the virus to others. The disease transmission dynamics within the quarantine center were described by a susceptible-exposed-infectious-recovered (SEIR) compartmental modeling framework (Figure 2).

### **2.2.1. Dynamics of cattle population**

The cattle population dynamics were modeled following the management procedures of private animal quarantine centers. At the beginning of each week (every seven days), a new cattle batch  $b$  was introduced into the quarantine center, and the animals needed to stay quarantined for a period of  $t_{max}$  week(s) before being released. Batch-week, denoted as  $i \in \{1, \dots, t_{max}\}$ , indicates the number of weeks upon arrival for each cattle batch. For example, a newly introduced cattle batch is assigned a batch-week of  $i = 1$ , signifying that this is their first week in the quarantine center. Then, the batch-week of a cattle batch shifted from  $i$  to  $i + 1$  after the model run for seven days. All cattle were then released from the quarantine center after staying for  $t_{max}$  week(s), equivalent to  $7 \times t_{max}$  days, either through removal following physical



examination or being released to the cattle market if no clinical signs were detected. Cattle that exhibited clinical signs were not allowed to enter the quarantine center.

Local veterinarians reported that, on a weekly basis, from 1 to 9 cattle herds were imported into a quarantine center with an average of 3 herds. An average number of cattle imported from each herd comprises 10 – 30 cattle. To model the number of cattle herds within a batch  $b$  (denoted as  $h_b$ ), we employed a discrete triangular distribution, represented as  $h_b \sim \mathcal{T}(1, 3, 9)$ . The number of cattle within each herd (denoted as  $n_{k,b}$ ) within batch  $b$ , where  $k \in \{1, \dots, h_b\}$ , was simulated using a Poisson distribution with an average cattle number that ranged from 10 to 30 per herd. Thus, number of cattle in a heard  $n_{k,b}$  can be expressed as  $n_{k,b} \sim \mathcal{P}(\mathcal{U}[10, 30])$ . Ultimately, the total number of cattle imported into the quarantine center each week within the same batch ( $N_b$ ) was calculated as the sum of cattle number  $n_{k,b}$  across  $h_b$  herds in the same batch, expressed as  $N_b = \sum_{k=1}^{h_b} n_{k,b}$ .”

### 2.2.2. Dynamics of FMDV transmission

The disease dynamics model classified the cattle population within the quarantine center according to the epidemiological status (compartments) as susceptible ( $S$ ), exposed ( $E$ ), infectious ( $I$ ), and recovered ( $R$ ). Following the disease management protocol, all cattle were vaccinated upon being introduced into the quarantine center. Cattle that were no longer susceptible to FMDV infection, either through recovering from infection or vaccine-induced immunity, were considered “recovered” ( $R$ ) in this study. Furthermore, the model allowed us to consider asymptomatic FMDV infections by dividing compartment “infectious” ( $I$ ) into three following compartments: 1) Asymptomatic individuals that would never develop symptoms of infection,  $I^{a_1}$ ; 2) Asymptomatic individuals that would develop symptoms during infection,  $I^{a_2}$ ;

and 3) Symptomatic individuals that were currently showing symptoms of infection,  $I^S$ . Thus,  $I = \{I^{a_1}, I^{a_2}, I^S\}$  and  $I^a = \{I^{a_1}, I^{a_2}\}$  (Figure 2).

According to population management procedures, cattle from different batches may coexist in shared spaces and share time within the quarantine center. Consequently, the potential for FMDV transmission across batches exists due to this overlapping management framework. To account for this scenario, we employed a meta-population SEIR compartmental model, which allows for the spread of FMDV among cattle from different batches within the quarantine center (between-batch transmission). In our modeling context, since cattle batches are imported on a weekly basis, transmission between cattle batches (referred to as between-batch transmission) is equivalent to transmission between cattle at different batch-weeks.

In addition, as the disease dynamics system involved a small cattle population size, this study employed a stochastic process over a discrete time (1-day) to describe the transition processes between the two compartments, including immunization, infection, latency, symptomatic infection, and recovery processes. The stochastic approach avoids the uncertainty caused by non-integer cattle numbers, which can occur when using deterministic ordinary differential equations with a small cattle population. As a result, the dynamics system for FMDV transmission within a quarantine center was described as a meta-population stochastic SEIR model as expressed in Eqs. (1) to (6). (Figure 2), where  $X_i(t)$  and  $X_i(t + 1)$  denote the number of cattle in compartment  $X$  at batch-week  $i$  at time  $t$  and  $t + 1$ , respectively.

$$S_i(t + 1) = S_i(t) - N_i^{S \rightarrow R}(t) - N_i^{S \rightarrow E}(t), \quad (1)$$

$$E_i(t + 1) = E_i(t) + N_i^{S \rightarrow E}(t) - N_i^{E \rightarrow I^{a_1}}(t) - N_i^{E \rightarrow I^{a_2}}(t), \quad (2)$$

$$I_i^{a_1}(t+1) = I_i^{a_1}(t) + N_i^{E \rightarrow I^{a_1}}(t) - N_i^{I^{a_1} \rightarrow R}(t), \quad (3)$$

$$I_i^{a_2}(t+1) = I_i^{a_2}(t) + N_i^{E \rightarrow I^{a_2}}(t) - N_i^{I^{a_2} \rightarrow I^S}(t), \quad (4)$$

$$I_i^S(t+1) = I_i^S(t) + N_i^{I^{a_2} \rightarrow I^S}(t) - N_i^{I^S \rightarrow R}(t), \quad (5)$$

$$R_i(t+1) = R_i(t) + N_i^{S \rightarrow R}(t) + N_i^{I^{a_1} \rightarrow R}(t) + N_i^{I^S \rightarrow R}(t), \quad (6)$$

$\forall i \in \{1, \dots, t_{max}\}$ .

$N_i^{X_I \rightarrow X_F}(t)$  denotes the number of cattle at batch-week  $i$  transitioning from initial state  $X_I \in \{S, E, I^{a_1}, I^{a_2}, I^S, R\}$  at time  $t$  to final state  $X_F \in \{S, E, I^{a_1}, I^{a_2}, I^S, R\}$  at time  $t+1$ . For example,  $N_i^{S \rightarrow E}(t)$  denotes the number of susceptible cattle at batch-week  $i$  at time  $t$  to exposed cattle at time  $t+1$ . At each time step, all transitional processes were simulated as stochastic processes that followed binomial distributions and were executed in the following order: 1) Immunization:  $N_i^{S \rightarrow R}(t)$ ; 2) Infection:  $N_i^{S \rightarrow E}(t)$ ; 3) Latency:  $N_i^{E \rightarrow I^{a_1}}(t)$ , and  $N_i^{E \rightarrow I^{a_2}}(t)$ ; 4) Symptomatic infection:  $N_i^{I^{a_2} \rightarrow I^S}(t)$ ; and 5) Recovery:  $N_i^{I^{a_1} \rightarrow R}(t)$ , and  $N_i^{I^S \rightarrow R}(t)$ , respectively.

In this model, the mortality due to infection and the loss of immunity, which causes recovered individuals to be susceptible, were omitted as we focus on a short quarantine period (a few weeks) to mimic the actual quarantine process practiced by Thai DLD. Additionally, airborne FMDV transmission from outside of the quarantine center was also disregarded in this model.

### 2.2.2.1. Immunization process

As stated earlier, all cattle were immunized upon arrival at the quarantine center. The proportion of beef cattle developing vaccination-induced immunity was reported to increase linearly from 4 days post-vaccination to 11 days, with a maximum protection of 100% (Backer et al., 2012).

Therefore, the time-to-immunity of vaccinated beef cattle was assumed to follow a uniform distribution with minimum time-to-immunity ( $\tau_{min}$ ) of 4 days and maximum time-to-immunity ( $\tau_{max}$ ) of 11 days, respectively. At 100% vaccine effectiveness, the probability of cattle developing protective immunity between time  $t$  and  $t + 1$ , denoted as  $p_i^{S \rightarrow R}(t)$ , was calculated from a probability density function of the uniform distribution  $f(x)$  and expressed as in Eqs. (7) to (8).

$$p_i^{S \rightarrow R}(t) = \begin{cases} \frac{\int_t^{t+1} f(x) dx}{1 - \int_0^t f(x) dx} & \text{if } \int_0^t f(x) dx < 1, \\ 0 & \text{if } \int_0^t f(x) dx \geq 1 \end{cases} \quad (7)$$

$$f(x) = \begin{cases} \frac{1}{\tau_{max} - \tau_{min}} & \text{for } x \in [\tau_{min}, \tau_{max}], \tau_{min} < \tau_{max}, \\ 0 & \text{otherwise} \end{cases} \quad (8)$$

Let  $e_v \in [0, 1]$  represent the vaccine effectiveness. The value of  $e_v = 1$  indicates that 100% of vaccinated cattle would successfully develop protective immunity against FMDV infections, while the value of  $e_v = 0$  indicates that none of the vaccinated cattle develop protective immunity. The number of susceptible cattle developing protective immunity against the infection at time  $t$  was generated through a stochastic binomial process following Eq. (9).

$$N_i^{S \rightarrow R}(t) \sim \mathcal{B}(S_i(t), e_v \cdot p_i^{S \rightarrow R}(t)) \quad (9)$$

#### 2.2.2.2. Infection process

In our context, the disease dynamics system occurred within a confined area of a quarantine center, where cattle were not allowed to move freely. Thus, direct contacts were limited even

between cattle from the same batch, and therefore, airborne transmission within the quarantine center becomes the primary mode of transmission. As a result, the infection process was parameterized based on the assumption of density-dependent transmission, where the reproductive number depends on the population density within a given space, and this approach has been widely used to describe the transmission dynamics of airborne diseases (Li et al., 2009). Let  $\beta_{ij}$  be a transmission coefficient between the cattle at batch weeks  $i \in \{1, \dots, t_{max}\}$  and  $j \in \{1, \dots, t_{max}\}$ . The value of  $\beta_{ij}$  when  $i = j$ , reflecting the viral transmission among cattle with the same batch (within-batch), equals  $\beta$ . While the coefficient for the between-batch transmission was expressed as  $\beta_{ij} = r \cdot \beta$  when  $i \neq j$ , where  $r \in [0,1]$  was the reduction factor that indicates the relative strength of between-batch transmission compared to within-batch transmission. For example, the value of  $r = 1$  indicates that the transmission within and between batches were not different, while  $r = 0$  indicates that no transmission between batches occurs. Furthermore, let  $\delta \in [0, 1]$  be a parameter describing the proportional reduction of infectiousness of asymptomatic cattle relative to symptomatic cattle ( $I^a$  in relative to  $I^s$ ). As a result, the overall per capita transmission rate at time  $t$  of the cattle at batch-week  $i$ , denoted as  $\lambda_i(t)$ , was expressed as a sum of the transmission rates from various infectious individual types based on their batch-weeks and clinical symptoms as shown in Eq. (10).

$$\lambda_i(t) = \sum_{j=1}^{t_{max}} \beta_{i,j} \left[ I_j^s(t) + \delta \left( I_j^{a1}(t) + I_j^{a2}(t) \right) \right] \quad (10)$$

Consequently, the number of susceptible cattle becoming exposed to infection during time  $t$  and  $t + 1$ , denoted as  $N_i^{S \rightarrow E}(t)$ , was expressed as in Eq. (11).

$$N_i^{S \rightarrow E}(t) \sim \mathcal{B}(S_i(t) - N_i^{S \rightarrow R}, 1 - \exp(-\lambda_i(t))) \quad (11)$$

### 2.2.2.3. Latency process

Exposed cattle would then become pre-clinical infectious ( $E \rightarrow I^a$ ) at a rate  $\sigma$ , which was the inverse of the average latent period ( $t_{lat}$ ) as in Eq. (12). However, this model assumed that only a fraction  $\pi$  of infected cattle would eventually develop clinical symptoms. As a result, the number of infectious cattle that would not and would develop clinical signs during the infection, denoted as  $N_i^{E \rightarrow I^{a1}}(t)$  and  $N_i^{E \rightarrow I^{a2}}(t)$ , and was expressed as in Eqs. (13) and (14), respectively.

$$N_i^{E \rightarrow I^a}(t) \sim \mathcal{B}(E_i(t), 1 - \exp(-\sigma)) \quad (12)$$

$$N_i^{E \rightarrow I^{a1}}(t) \sim \mathcal{B}(N_i^{E \rightarrow I^a}(t), 1 - \pi) \quad (13)$$

$$N_i^{E \rightarrow I^{a2}}(t) = N_i^{E \rightarrow I^a}(t) - N_i^{E \rightarrow I^{a1}}(t) \quad (14)$$

### 2.2.2.4. Symptomatic infection process

If the infection was symptomatic, clinical signs appear at a rate  $\gamma_1$ , which was the inverse of the average subclinical period ( $t_{sub}$ ). Therefore, the number of infectious cattle exhibiting some clinical symptoms during time  $t$  and  $t + 1$ , denoted as  $N_i^{I^{a2} \rightarrow I^s}(t)$ , is described as in Eq. (15).

$$N_i^{I^{a2} \rightarrow I^s}(t) \sim \mathcal{B}(N_i^{E \rightarrow I^{a2}}(t), 1 - \exp(-\gamma_1)) \quad (15)$$

### 2.2.2.5. Recovery process

Finally, let the recovery rates of asymptomatic and symptomatic infectious cattle be denoted as  $\gamma_2$  and  $\gamma_3$ , which equal the inverses of the average infectious period ( $t_{inf}$ ) and the average recovery period ( $t_{rec}$ ), respectively. As a result, the numbers of asymptomatic and symptomatic

infectious cattle recovering from an infection during time  $t$  and  $t + 1$ , denoted as  $N_i^{I^{a_1} \rightarrow R}(t)$  and  $N_i^{I^s \rightarrow R}(t)$ , can be expressed as in Eqs. (16) and (17), respectively.

$$N_i^{I^{a_1} \rightarrow R}(t) \sim \mathcal{B}(I_i^{a_1}(t), 1 - \exp(-\gamma_2)) \quad (16)$$

$$N_i^{I^s \rightarrow R}(t) \sim \mathcal{B}(I_i^s(t), 1 - \exp(-\gamma_3)) \quad (17)$$

### 2.2.3. Initial state of newly imported cattle

At the beginning of each week, a total of  $N_b$  new cattle of batch  $b$  were introduced into the quarantine center as described in Section 2.2.1, where  $N_b = S_1(0) + E_1(0) + I_1^{a_1}(0) + I_1^{a_2}(0) + I_1^s(0) + R_1(0)$ . The number of imported infected cattle  $Inf_1(0) = E_1(0) + I_1^{a_1}(0) + I_1^{a_2}(0) + I_1^s(0)$  was generated following a binomial distribution as  $Inf_1(0) \sim \mathcal{B}(N_b, P_{Inf})$ , where  $P_{Inf}$  denotes a probability of imported cattle being infected with FMDV upon arrival. Besides, the number of non-infected imported cattle in the “recovered” compartment, denoted as  $R_1(0)$ , either having protected immunity from vaccination or natural infections, was generated from a binomial distribution as  $R_1(0) \sim \mathcal{B}(N_b - Inf_1(0), P_{R(0)})$ , where  $P_{R(0)}$  denotes a proportion of non-infected imported cattle having protective immunity against FMDV-infection/reinfection. Additional details on how the initial states for all newly imported cattle were assigned are described in Additional file 1. All cattle were examined for clinical signs upon arrival. The total number of cattle permitted to stay at the quarantine center was  $N_b - I_1^s(0)$ .

### 2.2.4. Model parameters

The values of the model parameters used in the model are summarized in Table . The durations of latent period ( $t_{lat}$ ), incubation period ( $t_{inc}$ ), and infectious period ( $t_{inf}$ ) for the FMDV

infection in cattle used in the model were derived 1.5, 3.6, and 10.8 days, respectively (Yadav et al., 2019). The density-dependent transmission coefficient  $\beta$  and the proportional infectiousness of asymptomatic individuals relative to symptomatic individuals  $\delta$  have been reported at 0.010 and 0.99, respectively (Hayer et al., 2018). An expert elicitation study suggested that the proportion of infectious cattle becoming symptomatic  $\pi$  is 0.68 (Cabezas et al., 2018). Besides, the probability of imported cattle of each batch being FMDV infected was suggested to be approximately 10% by local veterinarians during the site visit  $P_{Inf}$ . Since the data on the proportion of immunized cattle (vaccine/infection-induced) in Myanmar was not publicly available, we explored the scenarios where the proportion of non-infected newly imported cattle having immunity at arrival ( $P_{R(0)}$ ) of 0% to 100%. In addition, we also explored the effects of vaccine effectiveness  $e_v$  in the range of 0% to 100%. It should be noted that even though all the parameters in Table 1 are displayed as single values, our stochastic model captures the variability of these parameters through the randomness in the binomial process at each time step and iteration. For example, the average infectious period  $t_{inf}$  of 3.6 days indicates that 95% of infectious cattle stay infectious between 0.09 to 13.3 days, centered at 3.6 days. Finally, we evaluated the risks in different scenarios where cattle stay quarantined for the periods  $t_{max}$  of 1, 2, 3, and 4 weeks.

### **2.2.5. Simulating the stochastic SEIR model**

The solutions for the stochastic SEIR model were solved together for  $\forall i \in \{1, \dots, t_{max}\}$  on a weekly basis. The model is run in daily discrete time steps at  $0 \leq t \leq 7$  days. After seven days, the batch-week changed from  $i$  to  $i + 1$ , and the current state of the present week was used as the initial state for the following week. The new cattle batch was subsequently introduced into the



quarantine center as described in Sections 2.2.1 and 2.2.3. The model repeated the weekly cycle for 52 weeks per iteration. Furthermore, the process was repeated for 100 iterations per each analyzed scenario to deal with uncertainty. The stochastic model was constructed with the programming language R version 4.3.0 (R Core Team, 2023), using the “*odin*” package version 1.2.4 (FitzJohn, 2022).

### 2.2.6. Risk estimates

After finishing the quarantine process at the end of week  $t_{max}$ , all cattle were physically examined before releasing to the market. Cattle showing clinical signs upon examination were removed from their herds. The risk of releasing infected cattle to the market was evaluated using the following estimates: 1) The risk of released cattle being infected, denoted as  $P_{cattle}$ ; 2) The risk of infected weeks, denoted as  $P_{week}$ . The risk of released cattle being infected ( $P_{cattle}$ ) was calculated for each cattle batch as in Eq. (18).

$$P_{cattle} = \frac{E_{t_{max}}(7) + I_{t_{max}}^{a_1}(7) + I_{t_{max}}^{a_2}(7)}{S_{t_{max}}(7) + E_{t_{max}}(7) + I_{t_{max}}^{a_1}(7) + I_{t_{max}}^{a_2}(7) + R_{t_{max}}(7)} \quad (18)$$

While the risk of infected weeks ( $P_{week}$ ) of each iteration was defined as the proportion of weeks in which at least one infected cattle was exported to the market divided by the total weeks. In addition, the proportion of symptomatic cattle removed from the cattle batch, denoted as ( $P_{remove}$ ), was also evaluated as an indicator of economic loss and expressed as in Eq. (19).

$$P_{remove} = \frac{I_{t_{max}}^S(7)}{S_{t_{max}}(7) + E_{t_{max}}(7) + I_{t_{max}}^{a_1}(7) + I_{t_{max}}^{a_2}(7) + I_{t_{max}}^S(7) + R_{t_{max}}(7)} \quad (19)$$

Finally, the proportion of cattle with protective immunity released to the market  $P_{immunized}$  was calculated using Eq. (20). As the cattle population cycles in the quarantine center were incomplete during the first few weeks of model initiation, all risk estimates were calculated after the cattle population dynamics had stabilized by disregarding the first five weeks in all model iterations.

$$P_{immunized} = \frac{R_{t_{max}}(7)}{S_{t_{max}}(7) + E_{t_{max}}(7) + I_{t_{max}}^{a_1}(7) + I_{t_{max}}^{a_2}(7) + R_{t_{max}}(7)} \quad (20)$$

### 2.2.7. Sensitivity analysis

The sensitivity analysis of model parameters on the risk estimates ( $P_{cattle}$ ,  $P_{week}$ ,  $P_{remove}$ , and  $P_{immunized}$ ) was performed with a Latin Hypercube Sampling (LHS) method and the Partial Rank Correlation Coefficient (PRCC) (Marino et al., 2008), including a total of 5,000 LHS samples for each parameter. Model parameters incorporated in the sensitivity analysis included 1) Within-herd transmission coefficient,  $\beta$ ; 2) The reduction factor of between-batch transmission,  $r$ ; 3) The proportional infectiousness of asymptomatic individuals,  $\delta$ ; 4) Vaccine effectiveness,  $e_v$ ; 5) Minimum time-to-immunity,  $\tau_{min}$ ; 6) Difference between maximum and minimum time-to-immunity,  $\tau_{max} - \tau_{min}$ ; 6) Probability of imported cattle being FMDV infected,  $P_{Inf}$ ; 7) Proportion of non-infected newly imported cattle having immunity at arrival,  $P_{R(0)}$ ; 8) Proportion of infectious individuals becoming symptomatic,  $\pi$ ; 9) Recovery rate of asymptomatic individuals,  $\gamma_1$ ; 10) Transition rate from asymptomatic to symptomatic individuals,  $\gamma_2$ ; 11) Recovery rate of symptomatic individuals,  $\gamma_3$ . The PRCC statistics were calculated for the risk estimates after a quarantine period  $t_{max}$  of 3 weeks using “*epiR*” package version 2.0.63 (Stevenson and Sergeant, 2023).

### **3. Results**

#### **3.1. Quarantine processes at the Thailand-Myanmar border**

At the Thailand-Myanmar border, cattle were moved to small boats across the Moei River, which flows along Myawaddy District, Myanmar, and Mae Sot District, Thailand (Figure 1B). Once the cattle arrived in Thailand, they were placed in one of the private animal quarantine service centers near the river. These centers were operated by the private sector under the supervision of Thai DLD, and the centers must be verified annually. In the center, cattle were vaccinated with a monovalent vaccine against FMDV serotype O at arrival (Day 0), and the animals were provided with shelter and fed throughout the quarantine period, which was 21 days. The cattle were moved in and out of the centers in batches during the quarantine process, different batches of cattle keep flowing and overlapping with other batches until completing the quarantine period. The cattle were then moved to the cattle market in Mae Sot District (Figure 1B). This main cattle market was where all imported cattle from different private animal quarantine service centers were sold. At the market, cattle were traded under the supervision of the local veterinary authority. Veterinary officers examine cattle individually for clinical signs of FMD (fever, inappetence, recumbency, and vesiculo-erosive lesions on the tongue, interdigital regions, and teats) before releasing them out of the market. Before cattle were moved out of Tak Province, they were rechecked for FMD clinical signs at the Tak animal quarantine station, a DLD office responsible for animal quarantine and movement. From arrival until departure, imported cattle were examined for FMD four times: twice at the private quarantine center (days 0 and 21), once at the cattle market, and again at the official animal quarantine station. Cattle presenting FMD signs at any checkpoints were not allowed to be traded. If the animal had symptoms, it would be isolated at the isolated barn available at the animal quarantine centers. If they were confirmed,

they were quarantined until symptoms resolved and returned to their origins. The overall importation and quarantine process are depicted in Figure 3.

### 3.2. Disease dynamics model

All risk estimates derived from the disease dynamics model were profoundly influenced by the duration of quarantine period  $t_{max}$ , the proportion of non-infected newly imported cattle having immunity at arrival  $P_{R(0)}$ , the vaccine effectiveness  $e_v$ , and the reduction factor for the between-batch transmission  $r$ , as shown in Figures 4-5 and Figures S2-S4 of Additional file 2.

The overall estimates of  $P_{cattle}$  and  $P_{week}$  tended to decrease and the proportion of releasing immunized cattle  $P_{immunized}$  tended to increase as the duration of quarantine period  $t_{max}$  and the proportion of non-infected cattle with immunity at arrival  $P_{R(0)}$  increased (Figure 4-5, and Figures S2 and S4). The median risk of released cattle getting infected by FMDV  $P_{cattle}$  might remain higher than 0.2 in several situations with a quarantine period of fewer than 14 days, particularly when the vaccine effectiveness  $e_v$  was as low as 0. With vaccine effectiveness  $e_v$  of 0.5, the risk  $P_{cattle}$  after 21 days of quarantine was generally low, ranging from 0.078 [95% CI: 0.000; 0.151] to 0.071 [95% CI: 0.000; 0.148] at the reduction factor for the between-batch transmission  $r$  of 0 and 1, respectively (Figure 4A and Figure S2A). While the risk of released cattle being infected  $P_{cattle}$  after 28 days with the vaccine effectiveness  $e_v$  of 0.5 ranged from 0.036 [95% CI: 0.000; 0.087] to 0.032 [95% CI: 0.000; 0.085] at the reduction factor  $r$  of 0 and 1, respectively.

The risk of infected weeks  $P_{week}$  remained high even after 28 days of quarantine with a high vaccine effectiveness ( $e_v = 1$ ), ranging from 0.766 [95% CI: 0.638; 0.872] to 0.894 [95% CI:

0.809; 0.979] at the reduction factor  $r$  of 0 and 1, respectively (Figure 4B and Figure S2B). Besides, in scenarios where there was no between-batch transmission ( $r = 0$ ), the overall transmission within the quarantine center was low (Figure S1), resulting in decreased  $P_{cattle}$  and  $P_{week}$  in most situations, except when vaccine effectiveness  $e_v$  and the proportion of immune cattle at arrival were low  $P_{R(0)}$  (Figures 4-5, and Figures S2-S4). The reduction factor  $r$  may influence the proportion of immunized cattle being released to the market  $P_{immunized}$  with high uncertainty, particularly at a low vaccine effectiveness ( $e_v = 0$ ) (Figure 5B). Furthermore, the risk estimates  $P_{cattle}$  and  $P_{week}$  markedly reduced across all scenarios when the proportion of non-infected cattle with immunity at arrival  $P_{R(0)}$  was as high as 100%.

The worst scenario yielding the highest median  $P_{cattle}$  was the scenario in which none of the cattle have protective immunity before the importation ( $P_{R(0)} = 0$ ), vaccine effectiveness  $e_v$  of 0%, the reduction of between-batch transmission  $r$  of 0.1, and the quarantine process of 14 days (Figure S2A). The risk of released cattle being infected  $P_{cattle}$  and the risk of infected weeks  $P_{week}$  of this worst scenario were estimated at 0.458 [95% CI: 0.255; 0.690] and 1.000 [95% CI: 1.000; 1.000], respectively.

The sensitivity analysis revealed the important parameter influencing  $P_{cattle}$ ,  $P_{week}$ , and  $P_{remove}$  was the proportion of non-infected cattle with immunity at arrival  $P_{R(0)}$ , along with other parameters that yielded  $|PRCC| > 0.25$ , including the transition rate from asymptomatic to symptomatic individuals  $\gamma_2$ , vaccine effectiveness  $e_v$ , and the probability of imported cattle being FMDV infected  $P_{inf}$  (Figure 6 and Table S1). The rank-transformed values of the proportion of non-infected cattle with immunity at arrival  $P_{R(0)}$ , followed by vaccine effectiveness  $e_v$  and the transition rate from asymptomatic to symptomatic individuals  $\gamma_2$ , and

the probability of imported cattle being FMDV infected  $P_{inf}$  were all negatively correlated with the risk of released cattle being infected  $P_{cattle}$  (PRCC of  $P_{R(0)} = -0.55$ ; PRCC of  $e_v = -0.28$ ; PRCC of  $\gamma_2 = -0.39$ ; PRCC of  $P_{inf} = -0.27$ ), the risk of infected weeks  $P_{week}$  (PRCC of  $P_{R(0)} = -0.48$ ; PRCC of  $e_v = -0.28$ ; PRCC of  $\gamma_2 = -0.25$ ; PRCC of  $P_{inf} = -0.28$ ), and the proportion of removing symptomatic cattle  $P_{remove}$  (PRCC of  $P_{R(0)} = -0.53$ ; PRCC of  $e_v = -0.23$ ; PRCC of  $\gamma_2 = -0.29$ ; PRCC of  $P_{inf} = -0.31$ ). The PRCC statistics between the reduction factor for the between-batch transmission  $r$  and the risk of released cattle being infected  $P_{cattle}$  and the risk of infected weeks  $P_{week}$  were 0.07 and 0.08, respectively. In addition, the most important parameters influencing  $P_{immunized}$  were the probability of imported cattle being FMDV infected  $P_{inf}$ , followed by vaccine effectiveness  $e_v$ , and the proportion of non-infected cattle with immunity at arrival  $P_{R(0)}$ , respectively (Figure 6 and Table S1). Besides,  $P_{immunized}$  was positively correlated with the reduction of between-batch transmission  $r$ .

#### 4. Discussion

The quarantine protocols were primarily intended to reduce the risk of FMDV-infected cattle being introduced into importing countries. In Thailand, newly imported cattle are obliged to receive a vaccination and are repeatedly examined for signs of FMDV infection during a 21-day quarantine period before entering the main market and leaving the border area. This three-week quarantine regulation is in accordance with the recommendations of prior studies (Dele et al., 2014; Knight-Jones et al., 2014; Paton et al., 2010; Thomson et al., 2009; USDA, 2012), which should minimize the risk of releasing FMD-infected cattle from the quarantine sites. Therefore, the present study used a modelling approach to explore the dynamics of FMDV circulation

within an animal quarantine center and assess its effectiveness in reducing the risk of FMDV introduction through cross-border cattle trade in an endemic setting.

As Thailand and Myanmar are both FMD endemic areas (WOAH, 2021), the crossed-border cattle movements between the two countries are expected to continuously involve active infectious and immune cattle, either through natural infection or vaccination. As FMDV is highly contagious within a cattle herd (Hayer et al., 2018), our disease dynamics model suggests that there is always an active spread of FMDV within the quarantine center, particularly when the proportion of cattle with preexisting immunity is low. As a result, protective immunity against FMDV infections acquired during the quarantine period is competitive due to either vaccination or spontaneous infection within the quarantine center. A higher proportion of infectious cattle arriving at the quarantine center may reduce the risk of releasing infected cattle and increase the likelihood of releasing immune cattle to the market. Introducing infectious animals into the quarantine center may help increase the overall herd immunity. Nonetheless, it also produces different negative consequences on animal health and welfare, production loss, and maintaining the virus in the area. Therefore, mass vaccination is a more desirable way to improve the immunity status and the welfare of the cattle herd before release, even though the success rate still depends on different factors, such as vaccination strategies (Sharma et al., 2017), and vaccine effectiveness against circulating virus strains.

According to our disease dynamics model, a quarantine period of less than or equal to 14 days yields a high risk of releasing FMDV-infected cattle to the market at any level of vaccine effectiveness, with the highest median risk of  $\sim 0.46$ . Nevertheless, when highly effective vaccines were used ( $e_v \geq 0.5$ ), the risk would be reduced substantially after a 21-day quarantine period, where up to 91.0% to 96.0% of released cattle developed protective immunity. In

accordance with a previous import risk assessment study in Southern Thailand (Wongsathapornchai et al., 2008), the proportion of asymptomatic infected cattle released into the country was estimated as low as  $\sim 0.07$ , assuming vaccine effectiveness of 0.5. The model also suggested that an additional extension of the quarantine period from 21 to 28 days ensures that the median probability of releasing asymptomatic cattle was  $\sim 0.03$ . These findings consistently suggest that the 21-day quarantine protocol, which has been widely used in several countries (Dele et al., 2014; Knight-Jones et al., 2014; Paton et al., 2010; Thomson et al., 2009; USDA, 2012), effectively reduced the proportion of infected cattle being released into the country. Nonetheless, it does not achieve a zero-risk state, even with 100% vaccine effectiveness. Extending the quarantine period to 28 days could not successfully achieve a zero risk of releasing infected cattle every week, where the risk of releasing at least one infected cattle to the market each week could still be as high as  $\sim 0.8$ . Besides, a previous livestock movement network analysis study at Mae Sot district suggested that a proper market closure strategy may help mitigate the risk once an outbreak occurs in the market (Wiratsudakul and Sekiguchi, 2018).

The sensitivity analysis revealed that a high proportion of cattle with pre-existing immunity upon arrival  $P_{R(0)}$  was the most sensitive factor that could reduce the risk of releasing infected cattle to the market. To introduce such a high proportion of cattle with preexisting immunity into the quarantine center in the importing country, cattle should be initially vaccinated and quarantined in the exporting country prior to the cross-border movement. Besides, animals that show clinical signs of FMD after the initial quarantine should not be allowed to cross the border. However, the policymakers of the two countries must agree on this bilateral quarantine practice, which would require strong collaboration and a diplomatic process to implement this framework successfully.



Moreover, the vaccine effectiveness  $e_v$  ranked the second highest sensitive factor that could reduce the risk. This highlights the necessity of mass vaccination programs upon arrival, using vaccines with high effectiveness against circulating viral strains. From 2018 to 2020, the most frequently reported serotype causing FMDV outbreaks in Southeast Asia was serotype O, followed by serotype A (Arjkumpa et al., 2020; WOA, 2021, 2020, 2019). Currently, the DLD of Thailand actively produces trivalent (serotypes O, A, and Asia-1), bivalent (serotypes O and A), and monovalent (serotype O) vaccines for field usage, using the serotype O/189/87, serotype A/Lopburi/2012, and serotype Asia-1/Thailand/85 lineages (Arjkumpa et al., 2020). In addition, serotype A/TAI/Sakon Nakhon/1997 is also still being used. However, a recent study showed that the endemic FMDV serotype A in Thailand undergoes antigenic drift every few years, affecting the vaccine effectiveness circulating strains over time (Seeyo et al., 2020). As a result, regular antigenic characterization studies of field FMDV strains are critical in identifying an appropriate vaccine for usage and a suitable strain for vaccine production that potentially reduces the risk of releasing infected cattle into the country.

The overlapping population management governed by private quarantine centers in Mae Sot District facilitates viral transmission among cattle arriving at different weeks. According to the disease dynamics model, any efforts to limit the transmission between cattle batches globally lessen the risk of releasing diseased cattle to the market, albeit not drastically. A complete blockage of between-batches transmission ( $r = 0$ ) slows down the outbreak within the quarantine station. As a result, when the proportion of susceptible individuals within the herd was high, more infected cattle with a complete blockage of between batches were predicted to be observed than in the scenarios with incomplete or no blockage ( $r > 0$ ) after 14 to 28 days of quarantine. Furthermore, when cattle receive ineffective vaccines, restricting the between-batch infection

may result in a large proportion of susceptible individuals being released to the market, where they may become infected with FMDV and trigger outbreaks shortly after being distributed across the country. This result also underlines the importance of using vaccines with high effectiveness against FMDV infection for all cattle upon arrival at the border.

The repeated disease screening practices implemented by The Tak animal quarantine office may help minimize the risk of FMDV-infected cattle being released into the country. Throughout the importation process, all cattle are examined for FMDV infection solely based on clinical symptoms four times: twice at the quarantine center, once at the market, and once more before leaving the Mae Sot District. However, our disease dynamics model suggests that, even if all symptomatic cattle are identified and removed from the herd, the quarantine process could not attain a zero-risk level due to asymptomatic infection, which is consistent with a prior risk assessment study (Wongsathapornchai et al., 2008). Therefore, implementing a more sensitive laboratory-based tool during the quarantine process should be implemented, allowing asymptomatic infected cattle to be detected and removed from the herd, which is critical to reducing FMDV importing risk.

Nonetheless, adjusting the quarantine protocol to lessen the risk, such as extending the quarantine period, implementing a bilateral quarantine practice, improving a diagnostic tool, or completely blocking transmission between batches, could result in considerable additional costs, labor, and time, whether for the government or directly for the farmers. Given that Thailand and Myanmar are both FMD endemic areas with limited resources, as both are developing countries, some of these measures could be economically impractical. Therefore, the cost-effectiveness of these adjusted control measures should be evaluated and optimized for the greatest benefit,

epidemiologically, economically, and practically, before they are officially implemented (Mushayabasa and Tapedzesa, 2015).

Our disease dynamics model neglected the possibility of infection from outside of the quarantine center, as well as the infections from environmental contamination. Besides, all model parameters, such as FMDV prevalence, the proportion of immune cattle, transmission coefficient, and the number of cattle arriving at the border, are assumed to stay constant throughout the year. Therefore, incorporating these additional sources of infections and seasonal effects could improve the accuracy of risk estimates. Furthermore, we acknowledge that some empirical data are currently unavailable, such as the actual FMD infection prevalence in cattle in Thailand and Myanmar, the observed initial FMD immunity of cattle entering the quarantine centers, the vaccine effectiveness, and protective antibody titer in 50% of vaccinated animals ( $PA_{50}$ ). The lack of such data was handled in the dynamics model by evaluating the risk estimates across various combinations of the possible range of these parameters. We recommend conducting a field study to estimate FMD prevalence in both nations and a survey of the actual initial immunological statuses of cattle entering quarantine centers to create a more accurate conclusion. Incorporating these data into our disease dynamics model could create a more realistic result.

Additionally, our model did not incorporate various FMDV strains with different strain-specific parameters, which is worth exploring in future studies. However, the results from our sensitivity analysis could help to interpret how the effectiveness of the quarantine process (after a 21-day quarantine period) might respond to FMDV strains with different average state transition rates. An FMDV strain with a longer average infectious period  $t_{inf}$  (reduced average recovery rates  $\gamma_2$  and  $\gamma_3$ ) would greatly increase the risk of exporting infected cattle to the market from having

more asymptomatic infectious cattle upon release (Figure 6). On the other hand, an FMDV strain with a more extended average incubation period  $t_{inc}$  (reduced average rate of showing clinical signs  $\gamma_1$ ) may not affect the risk of exporting infected cattle to the market with more symptomatic cattle are expected upon release (Figure 6).

In addition, the disease dynamics model developed in our study could be adjusted to evaluate the effectiveness of quarantine processes for various diseases and animal species. As an emergence, animal diseases involving livestock trade have become increasingly reported in Thailand in recent years, such as lumpy skin disease in cattle (Arjkumpa et al., 2021), African horse sickness in horses (Bunpaong et al., 2021), and African swine fever in pigs (WOAH, 2022). However, the models for other emerging diseases with different infectious dynamic structures like vector-borne diseases should be redesigned to fit with the nature of those diseases (Wiratsudakul et al., 2018). Evaluating the effectiveness of quarantine processes to prevent these diseases could be beneficial. Finally, our model can be developed into a web-based or mobile application, like one being developed for African swine fever (Thanapongtharm et al., 2022), for the veterinary authority to use in routine FMD monitoring and surveillance activities that help protect animal health within the country.

## **5. Conclusion**

This study mathematically evaluated the effectiveness of quarantine strategies to prevent the importation of FMDV-infected cattle implemented at the Thailand-Myanmar border in Mae Sot District, Thailand. The 21-day quarantine period is theoretically effective in mitigating the risk of FMDV introduction into the country. However, it is difficult to attain a zero-risk level even with a more extended quarantine period. Strengthening the immunity level in the cattle herds

before arrival, along with mass vaccination with a highly effective vaccine upon arrival, could warrant a lower risk of releasing infected cattle into the country. Before optimizing the costs and benefits of adjusting quarantine strategies, this 21-day protocol should be rigorously maintained to sustainably prevent FMDV outbreaks through transboundary animal movement, particularly among countries located in FMD-endemic regions. Our findings may aid decision-makers and stakeholders in gaining a deeper understanding of how quarantine strategies assist in reducing risks associated with international livestock trade, particularly in endemic areas.

## **Ethical statement**

This study does not require ethical approval as neither samples nor questionnaires were collected from humans/animals.

## **Data availability statement**

R codes related to the stochastic SEIR model and sensitivity analysis are available at [https://github.com/pwongnak/FMD\\_quarantine](https://github.com/pwongnak/FMD_quarantine).

## **Conflict of interest**

None.

## **References**

Arjkumpa, O., Suwannaboon, M., Boonrawd, M., Punyawan, I., Laobannu, P., Yantaphan, S., Bungwai, A., Ponyium, V., Suwankitwat, N., Boonpornprasert, P., Nuansrichay, B., Kaewkalong, S., Ounpomma, D., Charoenlarp, W., Pamaranon, N., Prakotcheo, R., Buameetooop, N., Punyapornwithaya, V., Songkasupa, T., 2021. First emergence of lumpy skin disease in cattle in Thailand, 2021. *Transboundary and Emerging Diseases* 68, 3002–3004. <https://doi.org/10.1111/tbed.14246>

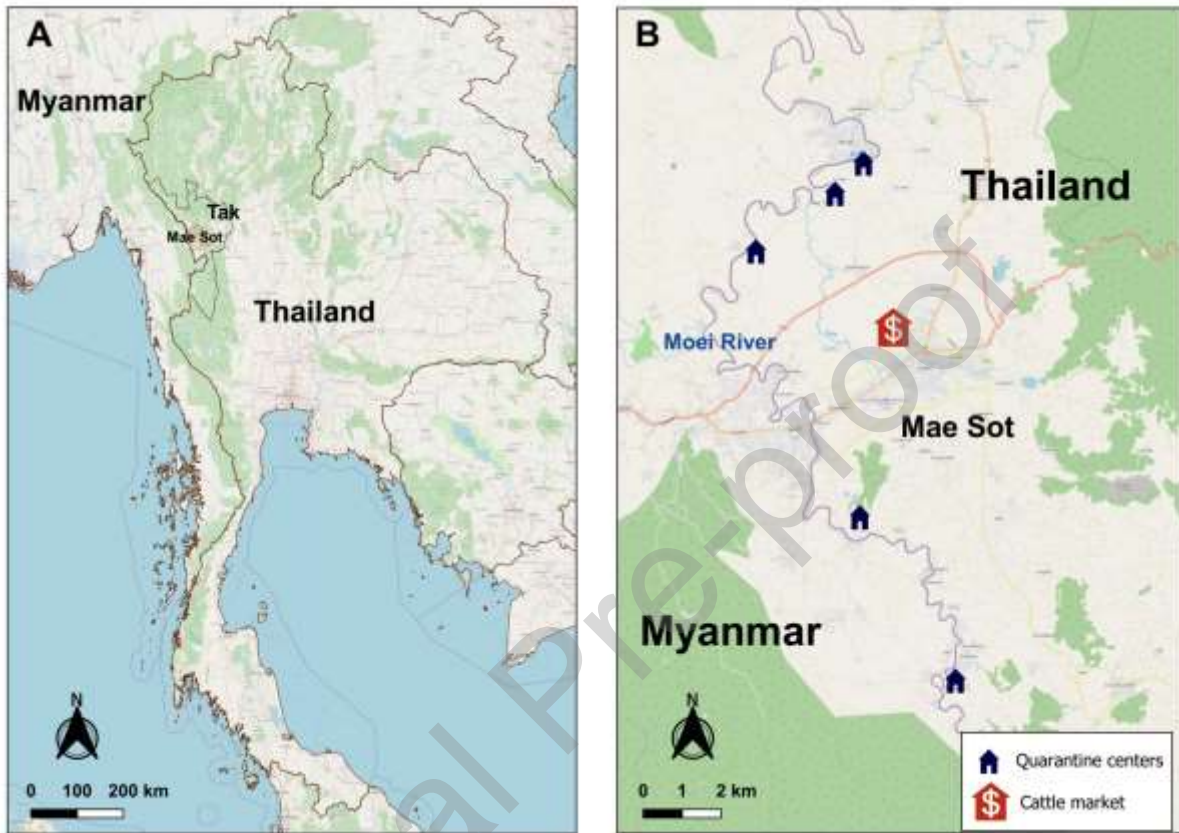
- Arjkumpa, O., Yano, T., Prakotcheo, R., Sansamur, C., Punyapornwithaya, V., 2020. Epidemiology and National Surveillance System for Foot and Mouth Disease in Cattle in Thailand during 2008–2019. *Veterinary Sciences* 7, 99. <https://doi.org/10.3390/vetsci7030099>
- Backer, J.A., Hagenaars, T.J., Nodelijk, G., Van Roermund, H.J.W., 2012. Vaccination against foot-and-mouth disease I: Epidemiological consequences. *Preventive Veterinary Medicine* 107, 27–40. <https://doi.org/10.1016/j.prevetmed.2012.05.012>
- Bartels, C., Afonso, J., Sieng, S., McLaws, M., 2017. Risk analysis on incursion of exotic FMD viruses into South-East Asia.
- Blacksell, S.D., Siengsan-Lamont, J., Kamolsiripichaiorn, S., Gleeson, L.J., Windsor, P.A., 2019. A history of FMD research and control programmes in Southeast Asia: lessons from the past informing the future. *Epidemiology & Infection* 147, e171. <https://doi.org/10.1017/S0950268819000578>
- Bunmee, T., Chaiwang, N., Kaewkot, C., Jaturasitha, S., 2018. Current situation and future prospects for beef production in Thailand — A review. *Asian-Australas J Anim Sci* 31, 968–975. <https://doi.org/10.5713/ajas.18.0201>
- Bunpapong, N., Charoenkul, K., Nasamran, C., Chamsai, E., Udom, K., Boonyapisitsopa, S., Tantilertcharoen, R., Kedsangsakonwut, S., Techakriengkrai, N., Suradhat, S., Thanawongnuwech, R., Amonsin, A., 2021. African Horse Sickness Virus Serotype 1 on Horse Farm, Thailand, 2020. *Emerg Infect Dis* 27, 2208–2211. <https://doi.org/10.3201/eid2708.210004>
- Cabezas, A.H., Sanderson, M.W., Jaber-Douraki, M., Volkova, V.V., 2018. Clinical and infection dynamics of foot-and-mouth disease in beef feedlot cattle: An expert survey. *Preventive Veterinary Medicine* 158, 160–168. <https://doi.org/10.1016/j.prevetmed.2018.08.007>
- Dele, E., Afera, B., Kebede, E., Awol, N., Hadush, B., 2014. Seroprevalence of Trade Hampering Livestock Diseases in Animals Originated from Borana at Export Quarantine Centers in Adama, Central Ethiopia.
- FitzJohn, R., 2022. *odin: ODE Generation and Integration*.
- Hayar, S.S., VanderWaal, K., Ranjan, R., Biswal, J.K., Subramaniam, S., Mohapatra, J.K., Sharma, G.K., Rout, M., Dash, B.B., Das, B., Prusty, B.R., Sharma, A.K., Stenfeldt, C., Perez, A., Delgado, A.H., Sharma, M.K., Rodriguez, L.L., Pattnaik, B., Arzt, J., 2018. Foot-and-mouth disease virus transmission dynamics and persistence in a herd of vaccinated dairy cattle in India. *Transboundary and Emerging Diseases* 65, e404–e415. <https://doi.org/10.1111/tbed.12774>
- Knight-Jones, T.J.D., Njeumi, F., Elsalwaly, A., Wabacha, J., Rushton, J., 2014. Risk assessment and cost-effectiveness of animal health certification methods for livestock export in Somalia. *Preventive Veterinary Medicine* 113, 469–483. <https://doi.org/10.1016/j.prevetmed.2014.01.003>
- Li, S., Eisenberg, J.N.S., Spicknall, I.H., Koopman, J.S., 2009. Dynamics and Control of Infections Transmitted From Person to Person Through the Environment. *American Journal of Epidemiology* 170, 257–265. <https://doi.org/10.1093/aje/kwp116>
- Marino, S., Hogue, I.B., Ray, C.J., Kirschner, D.E., 2008. A methodology for performing global uncertainty and sensitivity analysis in systems biology. *Journal of Theoretical Biology* 254, 178–196. <https://doi.org/10.1016/j.jtbi.2008.04.011>

- Mushayabasa, S., Tapedzesa, G., 2015. Modeling the Effects of Multiple Intervention Strategies on Controlling Foot-and-Mouth Disease. *Biomed Res Int* 2015, 584234. <https://doi.org/10.1155/2015/584234>
- Otte, M.J., Nugent, R., McLeod, A., 2004. Transboundary animal diseases: assessment of socio-economic impacts and institutional responses. *FAO Livestock Policy Discussion Paper* (FAO).
- Paton, D.J., Sinclair, M., Rodríguez, R., 2010. Qualitative Assessment of the Commodity Risk for Spread of Foot-and-Mouth Disease Associated with International Trade in Deboned Beef. *Transboundary and Emerging Diseases* 57, 115–134. <https://doi.org/10.1111/j.1865-1682.2010.01137.x>
- Qiu, Y., Abila, R., Rodtian, P., King, D.P., Knowles, N.J., Ngo, L.T., Le, V.T., Khounsy, S., Bounma, P., Lwin, S., Verin, B.C., Widders, P., 2018. Emergence of an exotic strain of serotype O foot-and-mouth disease virus O/ME-SA/Ind-2001d in South-East Asia in 2015. *Transboundary and Emerging Diseases* 65, e104–e112. <https://doi.org/10.1111/tbed.12687>
- R Core Team, 2023. *R: A Language and Environment for Statistical Computing*.
- Real, L.A., Biek, R., 2007. Infectious Disease Modeling and the Dynamics of Transmission, in: Childs, J.E., Mackenzie, J.S., Richt, J.A. (Eds.), *Wildlife and Emerging Zoonotic Diseases: The Biology, Circumstances and Consequences of Cross-Species Transmission, Current Topics in Microbiology and Immunology*. Springer, Berlin, Heidelberg, pp. 33–49. [https://doi.org/10.1007/978-3-540-70962-6\\_2](https://doi.org/10.1007/978-3-540-70962-6_2)
- Roche, X., Rozstalnyy, A., TagoPacheco, D., Pittiglio, C., Kamata, A., Beltran Alcrudo, D., Bisht, K., Karki, S., Kayamori, J., Larfaoui, F., Raizman, E., VonDobschuetz, S., Dhingra, M.S., Sumption, K., 2020. Introduction and spread of lumpy skin disease in South, East and Southeast Asia: Qualitative risk assessment and management. *FAO*, Rome, Italy. <https://doi.org/10.4060/cb1892en>
- Seeyo, K.B., Nishi, T., Kawaguchi, R., Ungvanijban, S., Udon, R., Fukai, K., Yamakawa, M., Rukkamsuk, T., 2020. Evolution of antigenic and genetic characteristics of foot-and-mouth disease virus serotype A circulating in Thailand, 2007–2019. *Virus Research* 290, 198166. <https://doi.org/10.1016/j.virusres.2020.198166>
- Sharma, G.K., Mahajan, S., Matura, R., Biswal, J.K., Ranjan, R., Subramaniam, S., Misri, J., Bambal, R.G., Pattnaik, B., 2017. Herd Immunity Against Foot-and-Mouth Disease Under Different Vaccination Practices in India. *Transboundary and Emerging Diseases* 64, 1133–1147. <https://doi.org/10.1111/tbed.12478>
- Stevenson, M., Sergeant, E., 2023. *epiR: Tools for the Analysis of Epidemiological Data*.
- Thanapongtharm, W., Wongphruksasoong, V., Sangrat, W., Thongsrimoung, K., Ratanavanichrojn, N., Kasemsuwan, S., Khamsiriwatchara, A., Kaewkungwal, J., Leelahapongsathon, K., 2022. Application of Spatial Risk Assessment Integrated With a Mobile App in Fighting Against the Introduction of African Swine Fever in Pig Farms in Thailand: Development Study. *JMIR Formative Research* 6, e34279. <https://doi.org/10.2196/34279>
- Thomson, G.R., Leyland, T.J., Donaldson, A.I., 2009. De-Boned Beef – An Example of a Commodity for which Specific Standards could be Developed to Ensure an Appropriate Level of Protection for International Trade. *Transboundary and Emerging Diseases* 56, 9–17. <https://doi.org/10.1111/j.1865-1682.2008.01054.x>
- USDA, 2012. *Biosecurity in Small-scale U.S. Livestock Operations*.

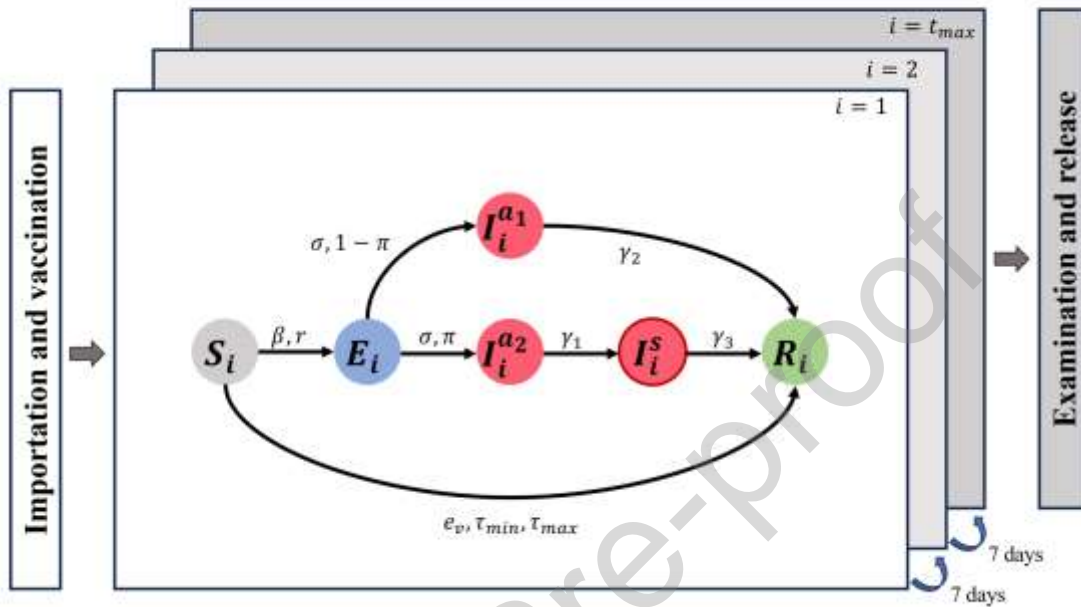
- Wiratsudakul, A., Sekiguchi, S., 2018. The implementation of cattle market closure strategies to mitigate the foot-and-mouth disease epidemics: A contact modeling approach. *Research in Veterinary Science* 121, 76–84. <https://doi.org/10.1016/j.rvsc.2018.10.007>
- Wiratsudakul, A., Suparit, P., Modchang, C., 2018. Dynamics of Zika virus outbreaks: an overview of mathematical modeling approaches. *PeerJ* 6, e4526. <https://doi.org/10.7717/peerj.4526>
- WOAH, 2022. African swine fever (ASF) – Situation report 6. WOA.
- WOAH, 2021. SEACFMD Bulletin: Foot and Mouth Disease Situation January to December 2020. WOA, Bangkok.
- WOAH, 2020. SEACFMD Bulletin: Foot and Mouth Disease Situation January to December 2019. WOA, Bangkok.
- WOAH, 2019. SEACFMD Bulletin: Foot and Mouth Disease Situation January to December 2018. WOA, Bangkok.
- Wongsathapornchai, K., Salman, M.D., Edwards, J.R., Morley, P.S., Keefe, T.J., Campen, H.V., Weber, S., 2008. Assessment of the likelihood of the introduction of foot-and-mouth disease through importation of live animals into the Malaysia-Thailand-Myanmar peninsula. *American Journal of Veterinary Research* 69, 252–260. <https://doi.org/10.2460/ajvr.69.2.252>
- Yadav, S., Stenfeldt, C., Branan, M.A., Moreno-Torres, K.I., Holmstrom, L.K., Delgado, A.H., Arzt, J., 2019. Parameterization of the Durations of Phases of Foot-And-Mouth Disease in Cattle. *Front. Vet. Sci.* 6, 263. <https://doi.org/10.3389/fvets.2019.00263>



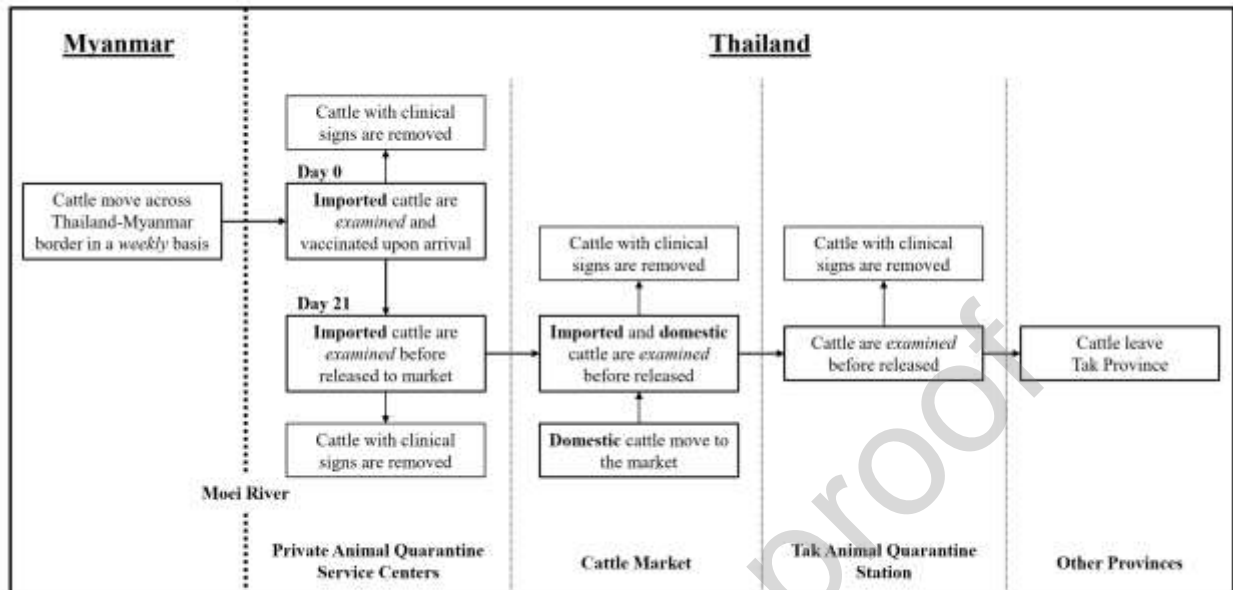
## Figures



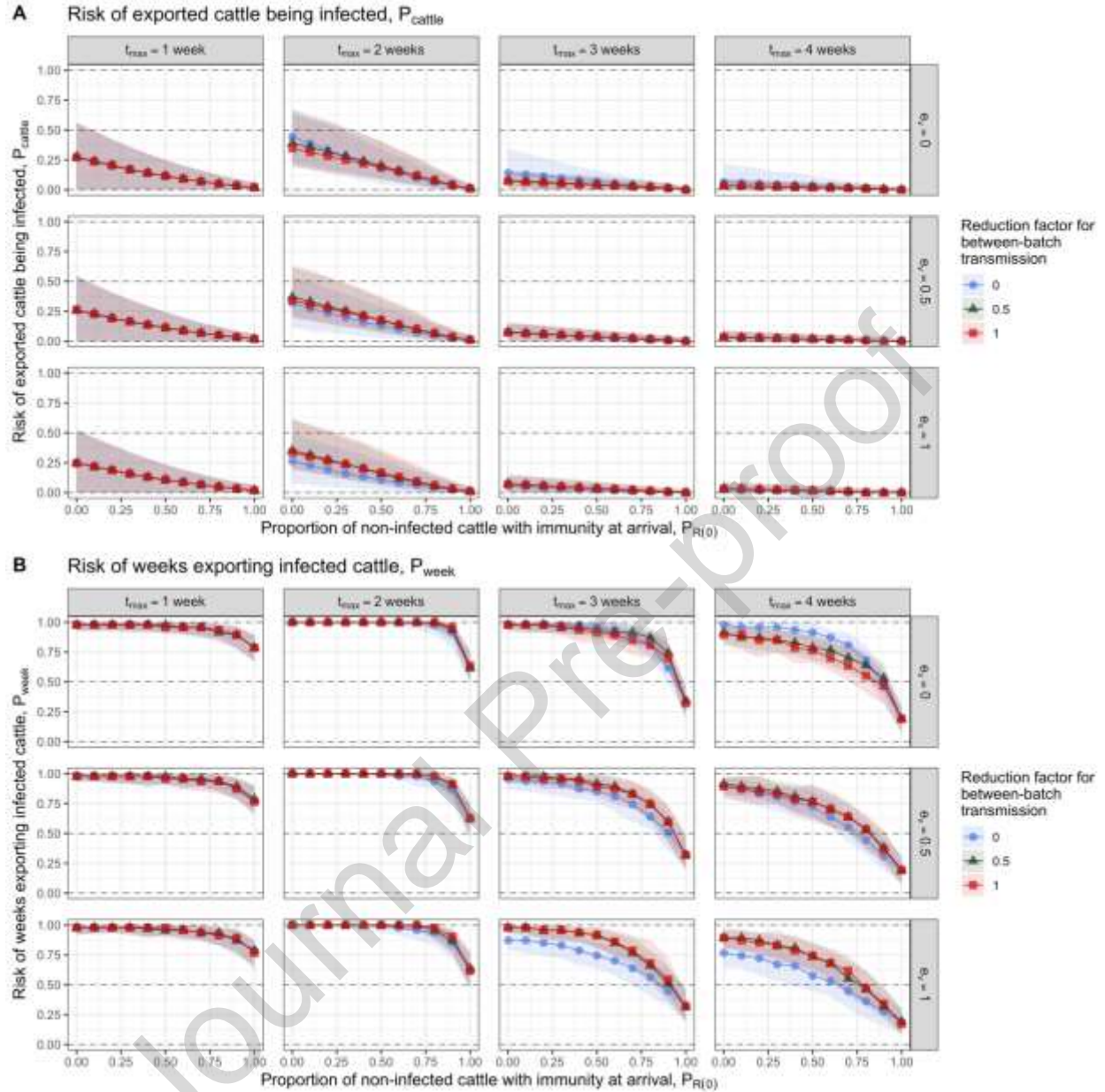
**Figure 1** Locations of study areas: A) The location of Mae Sot District, Tak Province, Thailand (highlighted in red); B) Locations of private animal quarantine centers and the main cattle market. Before entering the cattle market and being released into other regions of Thailand, cattle are required to stay quarantined at one of the private animal quarantine centers near the Myanmar-Thailand border (Moei River). The map was created using QGIS version 3.8, Zanzibar (<https://www.qgis.org>).



**Figure 2** A conceptual framework for disease dynamics model. Cattle are classified according to the epidemiological statuses as susceptible ( $S$ ), exposed ( $E$ ), asymptomatic infectious ( $I^{a1}$  and  $I^{a2}$ ), symptomatic infectious ( $I^s$ ), and recovered ( $R$ ). New cattle are imported across the border into the quarantine center every seven days. FMDV transmission could occur among the cattle from different batch-weeks  $i \in \{1, 2, \dots, t_{max}\}$ . Cattle are examined and released once they stay quarantined for  $t_{max}$  weeks. The compartment transition processes were mathematically described in Eqs. (1) to (17). Parameters indicated in the diagram included 1) Within-herd transmission coefficient,  $\beta$ ; 2) The reduction factor of between-batch transmission,  $r$ ; 3) The proportional infectiousness of asymptomatic individuals,  $\delta$ ; 4) Vaccine effectiveness,  $e_v$ ; 5) Minimum time-to-immunity,  $\tau_{min}$ ; 6) Maximum time-to-immunity,  $\tau_{max}$ ; 7) Proportion of infectious individuals becoming symptomatic,  $\pi$ ; 8) Recovery rate of asymptomatic individuals,  $\gamma_1$ ; 9) Transition rate from asymptomatic to symptomatic individuals,  $\gamma_2$ ; 10) Recovery rate of symptomatic individuals,  $\gamma_3$ .

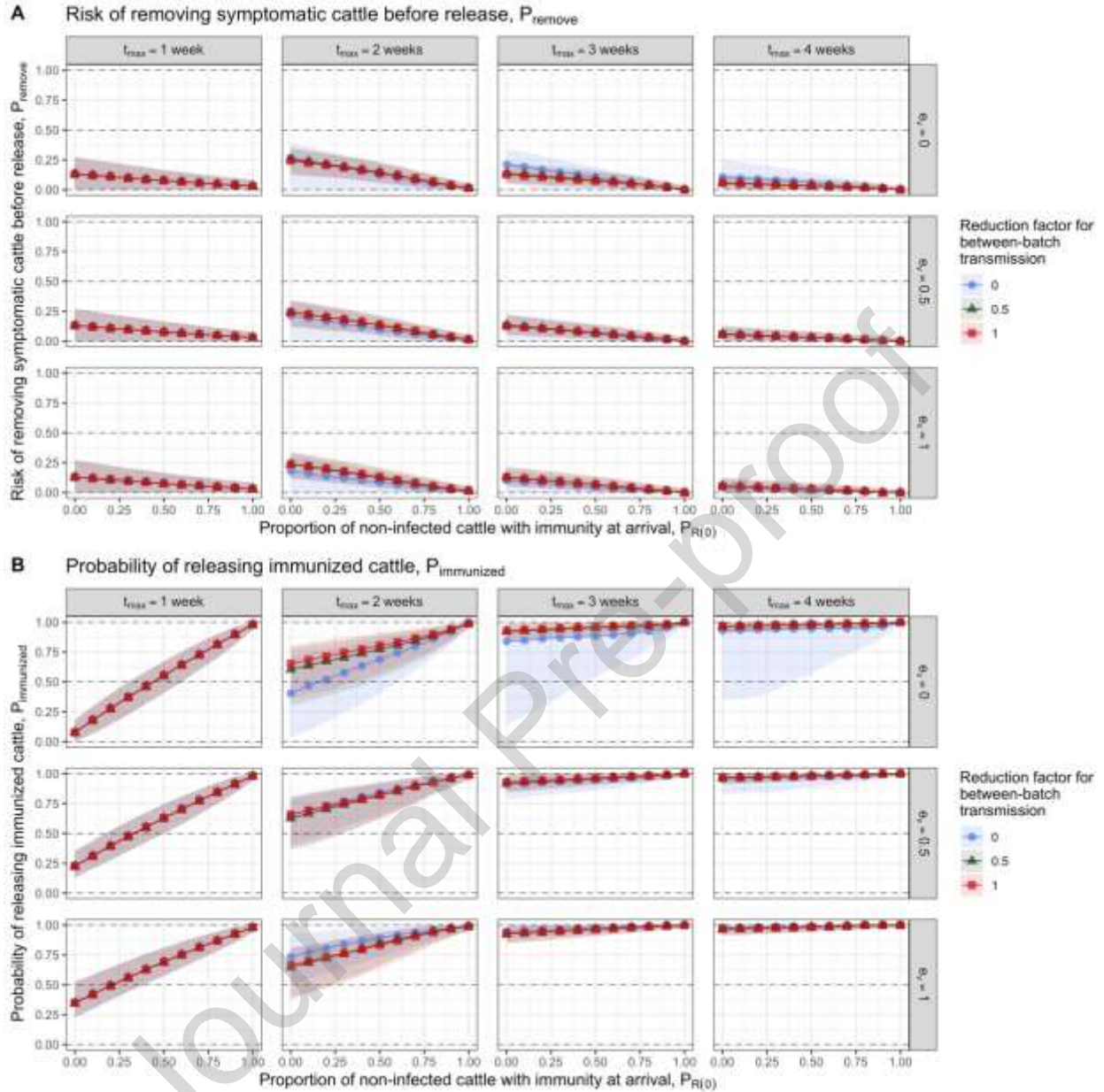


**Figure 3** Overview of control measures for cattle importations through the Thailand-Myanmar border at Mae Sot District, Tak Province, Thailand. Cattle are all vaccinated against FMDV infections upon arriving at the quarantine service center. Before releasing to other regions of Thailand, cattle are examined for clinical signs four times: 1) upon arrival; 2) before releasing from the quarantine centers; 3) at the cattle market; 4) at Tak Animal Quarantine Station.



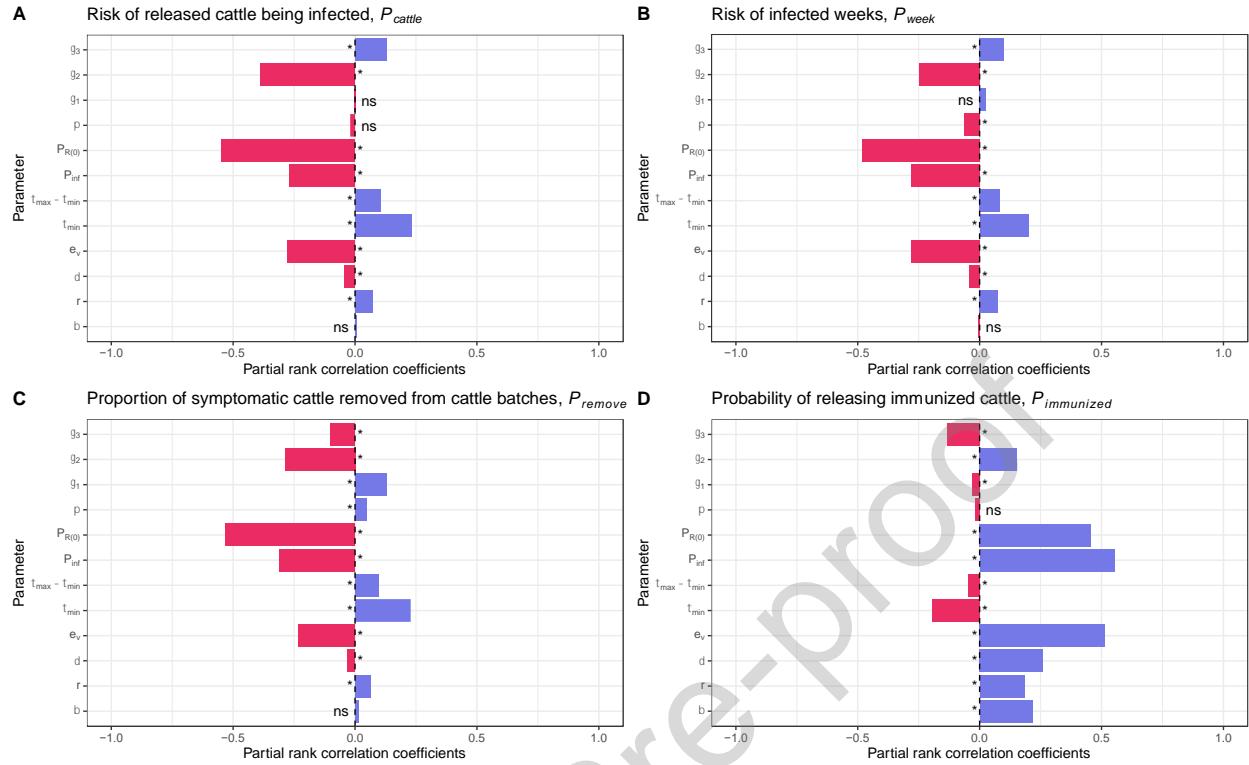
**Figure 4** Risks of releasing infected cattle to the market per batch; A) Risk of released cattle being infected,  $P_{cattle}$ ; B) Risk of infected weeks,  $P_{week}$ . Risk estimates on the Y-axis were evaluated across various combinations of the following model parameters: 1) The proportion of non-infected cattle with immunity at arrival,  $P_{R(0)}$ , displayed on the X-axis; 2); The reduction factor of the between-batch transmission,  $r$ . Colors and shapes indicate different levels of the reduction factor:  $r = 0$ , no between-batch transmission (dark blue circle);  $r = 0.5$ , the between-batch transmission is reduced by 50% (green triangle);  $r = 1$ , no reduction on the between-batch transmission (red square); 3) Vaccine effectiveness,  $e_v$  of 0.0, 0.5, and 1.0; 4) Quarantine period,  $t_{max}$  of 1, 2, 3, and 4 week(s). Risk estimates shown in this figure were the median (symbols) and the 95% CI (shaded areas) across 100 iterations.





**Figure 5** Risks of releasing infected cattle to the market per batch; A) Risk of symptomatic cattle removed from the cattle batch,  $P_{remove}$ ; B) Probability of releasing immunized cattle,  $P_{immunized}$ . Risk estimates on the Y-axis were evaluated across various combinations of the following model parameters: 1) The proportion of non-infected cattle with immunity at arrival,  $P_{R(0)}$ , displayed on the X-axis; 2) The reduction factor of the between-batch transmission,  $r$ . Colors and shapes indicate different levels of the reduction factor:  $r = 0$ , no between-batch transmission (dark blue circle);  $r = 0.5$ , the between-batch transmission is reduced by 50% (green triangle);  $r = 1$ , no reduction on the between-batch transmission (red square); 3) Vaccine effectiveness,  $e_v$  of 0.0, 0.5, and 1.0; 4) Quarantine period,  $t_{max}$  of 1, 2, 3, and 4 week(s). Risk estimates shown in this figure were the median (symbols) and the 95% CI (shaded areas) across 100 iterations.

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**Figure 6** Tornado plots of the partial rank correlation coefficients (PRCC) between the rank-transformed model parameters and rank-transformed risk estimates: A) The risk of released cattle being infected,  $P_{cattle}$ ; B) The risk of infected weeks,  $P_{week}$ ; C) The proportion of symptomatic cattle removed from cattle batches,  $P_{remove}$ ; D) Probability of releasing immunized cattle,  $P_{immunized}$ . Asterisks (\*) indicate that the PRCC statistics are significantly different from 0 ( $p < 0.05$ ), while “ns” indicates the non-significant PRCC statistics. Model parameters shown in the X-axis were following (from bottom to top): 1) Within-herd transmission coefficient,  $\beta$ ; 2) The reduction factor of between-batch transmission,  $r$ ; 3) The proportional infectiousness of asymptomatic individuals,  $\delta$ ; 4) Vaccine effectiveness,  $e_v$ ; 5) Minimum time-to-immunity,  $\tau_{min}$ ; 6) Difference between maximum and minimum time-to-immunity,  $\tau_{max} - \tau_{min}$ ; 6) Probability of imported cattle being FMDV infected,  $P_{Inf}$ ; 7) Proportion of non-infected newly imported cattle having immunity at arrival,  $P_{R(0)}$ ; 8) Proportion of infectious individuals becoming symptomatic,  $\pi$ ; 9) Recovery rate of asymptomatic individuals,  $\gamma_1$ ; 10) Transition rate from asymptomatic to symptomatic individuals,  $\gamma_2$ ; 11) Recovery rate of symptomatic individuals,  $\gamma_3$ .

## Tables

**Table 1** Summary of parameters used in the disease dynamics model.

Parameter	Description	Value/Model	Source
$t_{lat}$	Average latent period (days)	1.5	(Yadav et al., 2019).
$t_{inc}$	Average incubation period (days)	3.6	(Yadav et al., 2019).
$t_{inf}$	Average infectious period (days)	10.8	(Yadav et al., 2019).
$t_{sub}$	Average subclinical period (days)	$t_{inc} - t_{lat}$	
$t_{rec}$	Average time to recovery of symptomatic individuals (days)	$t_{inf} - t_{sub}$	
$\beta$	Within-herd transmission coefficient (Density-dependent)	0.010	(Hayer et al., 2018)
$\delta$	Proportional infectiousness of asymptomatic individuals relative to symptomatic individuals	0.99	(Hayer et al., 2018)
$\sigma$	Average transition rate from exposed to infectious individuals	$1/t_{lat}$	
$\gamma_1$	Average transition rate from asymptomatic to symptomatic individuals	$1/t_{sub}$	
$\gamma_2$	Average recovery rate of asymptomatic individuals	$1/t_{inf}$	
$\gamma_3$	Recovery rate of symptomatic individuals	$1/t_{rec}$	
$\pi$	Proportion of infectious individuals becoming symptomatic	0.68	(Cabezas et al., 2018)
$P_{inf}$	Probability of imported cattle being FMDV infected	0.1	Local veterinarians
$r$	Reduction factor for between-batch transmission	[0.0, 1.0]	
$P_{R(0)}$	Proportion of non-infected newly imported cattle having immunity at arrival	[0.0, 1.0]	
$e_v$	Vaccine effectiveness	[0.0, 1.0]	
$\tau_{max}$	Maximum time-to-immunity (days)	11	(Backer et al., 2012)
$\tau_{min}$	Minimum time-to-immunity (days)	4	(Backer et al., 2012)

## Additional files

### Additional file 1 Assignment of initial states to newly imported cattle

This document provides the details of how the initial states of newly imported cattle are assigned.

### Additional file 2 Additional figures and tables

This document includes Figure S1-S4 and Table S1.



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## **Conflict of interest**

None.

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