Modeling foot-and-mouth disease dissemination in Brazil and evaluating the effectiveness of control measures

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Running title: Foot-and-mouth disease dissemination across species.

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Summary

Foot-and-mouth disease (FMD) infects multiple food-animal species, thus capable of disseminating among ungulate species with distinct transmission rates. Here present a multilevel compartmental stochastic model, taking into account births and deaths and explicit representation of species-specific transmission dynamics. The model considered two major modes of dissemination, between-farm animal and spatial transmission. Our model outcomes are the number of secondary infected animals and farms, spatial dissemination distances, and effectiveness of depopulation and vaccination along with surveillance and movement restrictions. We demonstrated that after 20 days of FMD dissemination, the median number of infected farms was 8 (IQR: 3-22), of which 7 (IQR: 3-22) were bovine, 3 (IQR: 1-6) swine farms, and 1 (IQR: 1-1) small ruminants. We demonstrate that animal movement dominated dissemination in the first days of epidemics, while at ten days the spatial transmission dominated bovine infections, whilst between-farm led to most swine infections. We have also shown the

median distances between seeded and secondary infections was 5.77 km (IQR: 1-10.29 km), with some long-range dissemination at 695.40 km. We estimated that depopulating 12 and vaccinating 15,000 farms per day faded out 98.3% of the epidemics, however, was insufficient to contain large-scale epidemics (> 248 infected farms). The estimated effectiveness of a baseline control scenario eliminated 93.4% of the epidemics with a median of 9 (IQR: 3-23, max: 221) infected farms. Our results demonstrated that the depopulation alone against epidemics with more than 22 infected farms had limited success, stamping out less than 80% of simulations. The developed transmission model allows for cross-species transmission to be considered in FMD policy-making, and the software implementation facilitates the adaption of scientific-based support to FMD planning and response throughout other Brazilian states.

Keywords: dynamical models, infectious disease control, epidemiology, transmission, targeted control.

1. Introduction

Foot-and-mouth disease (FMD) is an infectious disease in cloven-hoofed animals infecting multiple species, pigs, sheep, goats, and wildlife (Davies, 2002; Paton et al., 2018). During the 2001 FMD epidemic in the U.K. and The Netherlands, together more than 6.7 million animals were slaughtered, including preemptively healthy and infected farms (Bouma et al., 2003; Thompson et al., 2002). The majoring of infected animals in both outbreaks were not unique to one species, infection was detected in goats on a mixed dairy-goat/veal-calf farms (Bouma et al., 2003; Thompson et al., 2002). 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 to 3.2 billion euros (Chanchaidechachai et al., 2021). Meanwhile, the distribution of FMD outbreaks in the South Americas has changed over the years, with the most recent outbreaks being reported in

Colombia in 2017 and 2018 (F. Gómez et al., 2019), while no epidemics have been reported in Latin America since then, despite Venezuela's absence of official international status for FMD (PANAFTOSA-OPS/OMS, 2019).

The official data from OIE of more than 57 thousand outbreaks in 99 counties from 1996 until 2012, 68% of the cases were associated with cattle, 22% with swine, and 21% with small ruminants and other species (Santos et al., 2017). Even with the strong evidence that all susceptible species can drive large FMD epidemics (Bertram et al., 2020; Tildesley et al., 2012), for example, the 2001 UK epidemic has been traced back to an infected Essex swine slaughterhouse (Davies, 2002), control measures and surveillance programs have been developed to target mostly the dissemination within the cattle populations, thus neglecting the role of other species in FMD transmission (Naranjo and Cosivi, 2013; Santos et al., 2017; Seymour et al., 2022; Singanallur et al., 2021).

It is worth noting that FMD pathogenesis and transmission dynamics are different between species, including viral replication, persistence, incubation period, and potential to infect the same and/or different hosts with different transmission probabilities (Alexandersen et al., 2003; Arzt et al., 2011; Moreno-Torres et al., 2022; Stenfeldt et al., 2016), for example, pigs emit more viruses than cattle and sheep which increases the transmission rate when the pigs are the more infectious host when compared with other domestic species (Brown et al., 2022; Donaldson and Alexandersen, 2002; Moreno-Torres et al., 2022). Thus, it is pivotal that such heterogeneity in the transmission dynamics is considered while modeling either within or between-farm transmission dissemination (Seymour et al., 2022). Whilst, between farm transmission, primarily occurs through the direct contact among susceptible and infected animals (Alexandersen et al., 2003; van Andel et al., 2021), field observation and experimental trials

demonstrated the spread of the virus via indirect contact with fomites and long-distance transport of aerosols, a process known as spatial transmission (Chakraborty et al., 2021; Guyver-Fletcher et al., 2021; Sellman et al., 2020; van Andel et al., 2021).

Mathematical models have been widely used to investigate epidemic propagation, although major technical and computation advancements have been achieved, in most cases because of computational cost and/or lack of details about herd structure (e.g. number of heads, number of born alive), animal movements, models are oversimplified. The most common simplification is to restrict the epidemiological models to a single species (Chanchaidechachai et al., 2021; Sseguya et al., 2022). Despite the different applications and efforts in modeling FMD, questions on measuring the epidemic trajectory and epidemic control strategies while considering heterogeneous transmission dynamics among the different susceptible species coexisting on the same farms remain outstanding (Seymour et al., 2022).

In this work, we proposed a novel multi-host single-pathogen multiscale model with heterogeneous transmission dynamics with species-specific transmission coefficients. We present a quantitative assessment of the epidemiological role that each species plays in FMD dissemination aimed to quantify transmission routes and the spatial distance spread. Our simulations utilize population data including the birth and death of the entire food-animal species population of the state of Rio Grande do Sul, Brazil. Finally, we examined the effectiveness of control and elimination actions according to the national FMD control plan (MAPA, 2020), which includes i) vaccination of uninfected animals; ii) depopulation of infected animals; iii) various between-farm movement restrictions; and iv) surveillance activities within control zones. The resulting model delineates epidemic trajectories from each species along with the contribution of transmission routes, assesses the quantities of farms with control zones, and

estimates the effectiveness of epidemic control scenarios while predicting the success rates and duration of various countermeasure actions to FMD elimination.

1. Material and Methods

2.1 Data sources

We collected information from 415,364 farms officially registered in the state of Rio Grande do Sul (SEAPI-RS, 2018). The data contained the population of cattle, buffalo, swine, sheep, and farms, along with the daily between-farm animal movement and movements into slaughterhouses, from January 1st, 2018 until December 31st, 2020. Population and movement data of cattle and buffalo farms were combined into one species category named hereafter “bovine”. In the same vein, we grouped sheep and goats into the “small ruminants" category. By analyzing the population data, we found 5,709 (1.37%) farms with missing geolocation, which were excluded from the analysis. More information about the population distribution by species is presented in Supplementary Material Figure S1. In Brazil, producers are required to report farming activities to the state animal health office once a year, the reporting includes information about food animal production activities every twelve months. We utilized producer-reported data combined with the 2020 headcounts to classify farms as “active” if at least one food animal was present. Farms that were either declared inactive by the producer or had zero animals were considered inactive and not considered in this study. Therefore, our final active population included 409,655 farms.

2.2 Birth and death data

In the same way that producers are required to report the total number of heads, there are requirements to report the number of animals born alive and dead, including natural death. We had access to this state database (SEAPI-RS, 2018). Briefly, producers can report birth and death at any time throughout the year, however, reporting is mandatory at least once a year from January 1st until May 30th. We collected 256,504 individual records associated with birth and/or death. The monthly description of births and deaths by species is depicted in Supplementary Material Figure S2. We found that 1.14% of the total 409,655 farms had negative headcounts after the farm's population was computed, based on animal movements, births, and death records. In order to keep these farms in our simulations, any negative population values caused by the movement or animal death were prevented by reestablishing the population values to their most recent positive record.

2.3 Movement data

Overall, from January 1st, 2018 until December 31st, 2020, the state database registered 1,634,940 unique between-farm and slaughterhouse movements. By analyzing the movement data, we found 181 movements with missing farm identification, 93,871 movements with the same farm identification at origin and destination, 51,490 movements to or from other states, and 112,834 movement records from or to farms with missing geolocation. After removing the movement data described above, the final database comprised 1,564,487 movements and 73,823,866 animals transported (Supplementary Material Figure S3 shows the movement data variations across the years).

2.4 Model formulation

We implemented a multi-host single-pathogen coupled multiscale model to simulate FMD epidemic trajectories (Garira, 2018) and the effectiveness of countermeasure actions. This modeling work leads to the development of a novel R package, MHASpread: A multi-host animal spread stochastic multilevel model (version 0.1.0). MHASpread allows for explicit specification of species-specific transmission probability, among other important transmission dynamics of disease infecting multiple species. At the within-farm dynamics level, we consider the entry and exit of animals given between-farm animal movements, movements into slaughterhouses, births, and, deaths, for each species (Figure 1). The between-farm level dynamics are driven by the between-farm movements and spatial proximity.

2.5 Within-farm dynamics

The within-farm dynamics consist of mutually exclusive health states in which animals of each species, bovine, swine, and small ruminants, can only be in one compartment per discrete time step, susceptible (S), exposed (E), infected, (I), and recovered (R), where:

(i) Susceptible: denotes animals who are not infected but susceptible.

(ii) Exposed: denotes animals who are exposed but not yet infected.

(iii) Infected: denotes animals who are infected and can successfully transmit infection.

(iv) Recovered: denotes animals who have recovered and are not susceptible.

Here we also take into account birth and death data described in the section above. The total population is represented as $N = S + E + I + R$, where the number of individuals within each compartment transit from $S\beta \rightarrow E, 1/\lambda_1 \rightarrow I, 1/\lambda_2 \rightarrow R$ as follows:

$$\frac{dS}{dt} = u_{i,t,} - v_{i,t,} - \frac{\beta S_i I_i}{N_i} \tag{1}$$

$$\frac{dE}{dt} = \frac{\beta S_i I_i}{N_i} - v_{i,t,}O - \left(E_i \ \frac{1}{\lambda_1}\right) \tag{2}$$

$$\frac{dI}{dt} = \left(E_i \frac{1}{\lambda_1}\right) - \left(I_i \frac{1}{\lambda_2}\right) - v_{i,t,}\mathrm{I} \tag{3}$$

$$\frac{dR}{dt} = I_i \frac{1}{\lambda_2} - v_{i,t,} \tag{4}$$

Briefly, birth is represented by the number of animals born alive $u_{i,t}$entering into the S compartment, farm i at a time t according to the day-to-day records; in the same vein $v_{i,t}$represents the exit of the animals from any compartment due to death a time t (Figure 1). The transition from E to I is driven by $1/\lambda_1$ and I to R by the $1/\lambda_2$ both drawn from distribution generated from each specific species according to the literature (Table 1). As the infection progresses animals transit into a recovered (R) state based on $1/\lambda_2$ drawn from the infectious period, again for both λ_1 and λ_2 are specific to host species (Table 2).

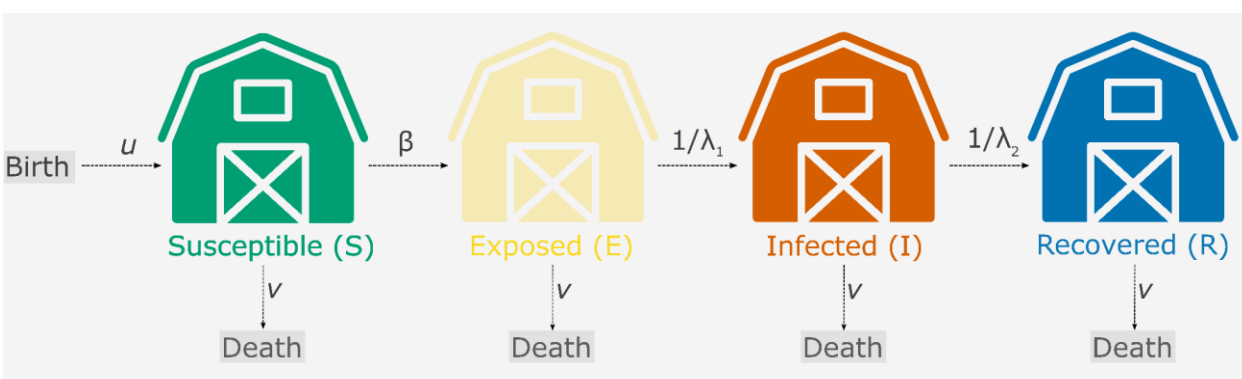

Figure 1. Within-farm dynamics. The framework represents the transit from between compartments, $S\beta \rightarrow E, 1/\lambda_1 \rightarrow I, 1/\lambda_2 \rightarrow R$, while the introduction of susceptible animals u is introduced in S, and deaths ν are removed from all compartments.

In the within-farm model dynamics, we assume that populations were homogeneously distributed and species were homogeneous-mixing, but each species has a species-specific FMD transmission coefficient β (Table 1, Supplementary Material Figure S4, and Figure 2A).

Table 1. The distribution of each host-to-host transmission coefficient (β) along with the parameter distribution per animal^{-1} day^{-1}.

Species	Species	Transmission coefficient (β)	References
Bovine	Bovine	Pert (0.018, 00.24, 0.056)	Calculate from the FMD outbreaks 2000-2001 in the state of Rio Grande do Sul (da Costa et al., 2022).
Bovine	Swine	Pert (0.018, 0.024, 0.056)	Assumed.
Bovine	Small ruminants	Triangular (0.020, 0.026, 0.031)	(Cabezas et al., 2021; Chis Ster et al., 2012)
Swine	Bovine	Pert (0.014, 0.044, 0.033)	(van Roermund et al., 2010)
Swine	Swine	Pert (0.014, 0.044, 0.033)	(Kinsley et al., 2018; van Roermund et al., 2010)
Swine	Small ruminants	Pert (0.014, 0.044, 0.033)	(van Roermund et al., 2010)

Small ruminants	Bovine	Pert (0.012, 0.031 0.065)	(Bravo de Rueda et al., 2014)
Small ruminants	Swine	Pert (0.006, 0.024, 0.09)	(Goris et al., 2009)
Small ruminants	Small ruminants	Pert (0.018, 00.24, 0.056)	Assumed

Table 2. The within-farm distribution of latent and infectious FMD parameters for each species.

FMD parameters	Species	Distribution parameters	Reference
Latent period λ_1	Bovine	Weibull (a = 1.78, b = 3.97)	(Mardones et al., 2010)
	Swine	Log logistic (shape = 7.60; scale = 1.06)	(Moreno-Torres et al., 2022)
	Small ruminants	Pert (m = 3.96, a = 0, b = 13.98)	(Mardones et al., 2010)
Infectious period λ_2	Bovine	Gamma (a = 3.97, b = 1.11)	(Mardones et al., 2010)
	Swine	Weibull (shape = 7.16; scale = 11.04)	(Moreno-Torres et al., 2022)
	Small ruminants	Pearson 5 (a = 6.19, b = 17.19)	(Mardones et al., 2010)

Note: The time unit is day.

2.6 Between-farm dynamics

For the farm-level dynamics, we consider two transmission pathways i) between-farm animal movements and ii) spatial transmission. We utilized the number of unique movements (batches)

and animals for each species to model the between-farm transmission while considering the current within-farm transmission dynamics status (Figure 2). Briefly, for each movement batch, we access the corresponding infection status from the available population at the farm of origin to draw the necessary animals to be transferred to the destination farm (Figure 2B). The animal movements to slaughterhouses were also taken into account in the same way as the between-farm moment, thus, we draw the number of animals to be removed from the current state of the system (Figure 2B).

2.7 Spatial transmission dynamics

The spatial transmission was modeled in the same way for all farm types (Figure 2C). Here, we modeled the probability of exposure (PE) for each farm i at the time t, as follows:

$$PE = 1 - exp(-\beta_{sp} * I_{it} / N_{jt}) \quad (5)$$

Where β_{sp} represents the spatial transmission probability that is modulated by the Euclidean distance between farms. Here, $\beta_{sp}$is defined by the expression:

$$\beta_{sp} = a * exp(-b * k) \quad (6)$$

Where a = 0.012 and b= 0.6 and k represents the Euclidean distance in kilometers between two farms (Boklund et al., 2013). Moreover, I_{it} represents the number of infectious animals at the farm i at time t, and, N_{jt} represents the current animal population at the farm j at a time t. We have restricted our spatial transmission distances to a maximum of 40 km around infected farm(s) because of the extensive literature about distance-based FMD dissemination and a previous comprehensive mathematical simulation study (Björnham et al., 2020). Briefly, spatial

transmission combines different transmission processes such as airborne, shared fence lines, and sharing equipment, into one dynamic process. Furthermore, we used each farm's geolocation and grouped them within a grid-hexagon of size 0.76 km, representing an area of 503,516 m^2 (Supplementary Material Figure S5A). Here, farms within the same hexagon have the same spatial transmission probability. Farms with one infected animal regardless of the species and the population in a farm i were allowed to infect other farms nearby with a probability of 0.012, 0.006, and 0.001 when the nearby farms are within a range of 1-2 km and 2-3 km, and 10-30 km, respectively (Boklund et al., 2013) (Supplementary Material Figure S5B).

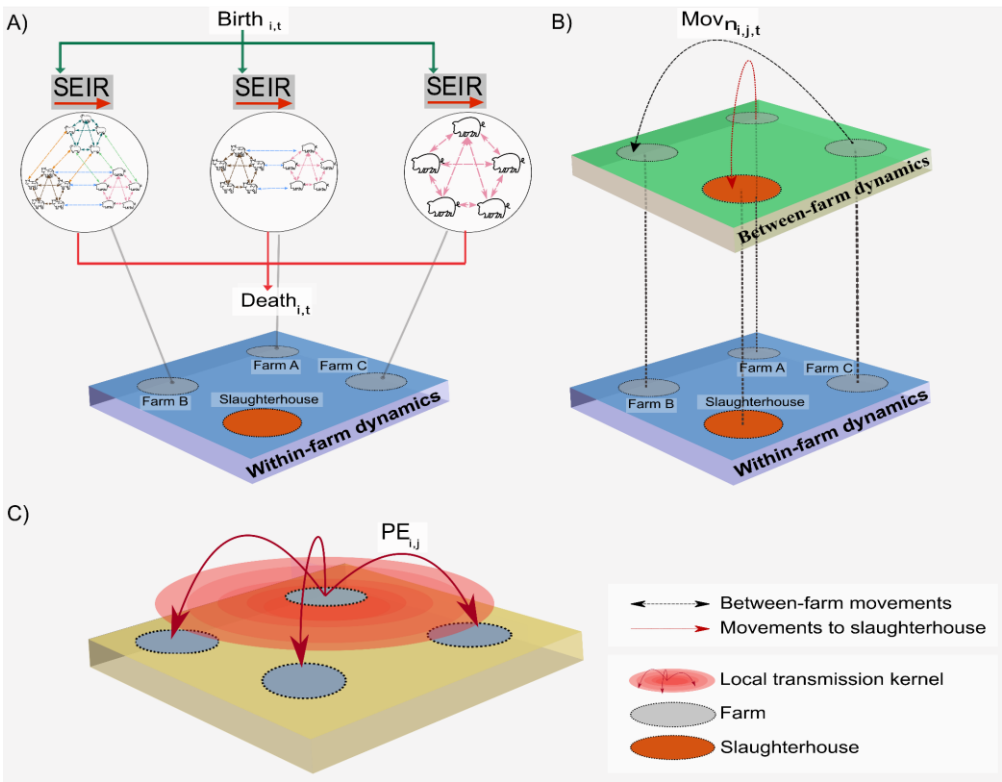

Figure 2. Schematic of state transitions of the within-farm and between-farm dynamics. A) Within-farm dynamics: green arrow lines indicate introduction events (births) into the susceptible (S) compartment at the farm i, at a specific time t. Each circle shows a farm with its single or multiple species representing factorial host-to-host transition parameters (β, λ_1, λ_2)

where the dashed color line represents the interaction within and between hosts. The red arrow lines represent the animal death removed regardless of their infection status. B) The between farms dynamics layer represents the number of animals moved (batches) n, from the farm of origin i, to a farm of destination j, in a specific time t, (indicated by the black dash arrows). The animals that are moved to the slaughterhouse are removed from the simulation regardless of their infection status indicated by red dash arrows. C) The spatial transmission distances.

2.8 Initial model conditions

We utilize 2018 population headcounts as the initial population condition. Because of the large number of farms, 409,655 considered computationally prohibitively high, we alternatively drew a sample of 15,721 farms to be used as initially infected locations. We used a multistage stratified sample design, in which strata were defined based on each municipality's animal population so that farms were sampled proportionally by species densities (Ziegel and Lohr, 2000). The sample size was calculated to maximize sample size, thus we used an expected prevalence of 50% with a level of significance of 95% and a margin of error of 1%.

We ran ten repetitions for each of the 15,721 sampled farms, each repeat started at any date sampled between January 1st, 2018, and December 31st, 2020, in total we analyzed 157,210 simulations. For each repeat, the infection started with one infected animal. In farms with more than one species, seed infection priority order was bovine, swine, and small ruminants. All farms were assumed to be fully susceptible to FMD infection since vaccination has been suspended in the Rio Grande do Sul since May 2021 (da Costa et al., 2022).

2.9 Evaluation of control and eradication scenarios

We simulate FMD epidemic trajectories for up to 20 days. Based on the historic FMD outbreaks in Brazil and in consultation with animal health officials, control actions were started at ten and 20 days of silent FMD dissemination. We compared three alternative control scenarios with a pre-demined baseline control scenario based on the national FMD response plan (MAPA, 2022, 2020), described below.

Baseline control scenario: This scenario incorporated the national FMD control and eradication plan (MAPA, 2022), which included the following measures i) depopulation of infected farms, ii) vaccination of uninfected farms, iii) animal movements standstill for 30 days, iv) three distinct control zones around infected farms of 3 km (infected zone), 7 km (buffer zone), and 15 km (surveillance zone) (Supplementary Material Figure S6). In the infected zones, infected farms are depopulation as they are detected, while vaccination is implemented stating in farms within infected zones, alternatively, if vaccine doses are still available then farms in buffer zones are vaccinated. Surveillance activities are defined as clinical examinations. In our simulation, all farms within control zones are visited every three days. Contact tracing of farms with direct links from infected farms for the past 30 days undergo surveillance, and if positive moved into the infected compartment. Here, we also take into consideration the state budget as follows i) four is a maximum number of farms that can be depopulated per day, ii) a maximum number of animals vaccinated per day to 5,000, both assumptions based on the state's maximum personal and equipment capacity (personal communication, animal health official working group). We also included a delay in the start of vaccination of seven days after the first case is detected, vaccination was assumed to be effective instantaneously, and thus vaccinated animals were moved into the recovered compartment (R). In addition, we assumed that i) surveillance

was 100% sensitive in FMD detection and, ii) we also assume 100% compliance for animal movement standstill for 30 days.

In addition to the baseline control scenario, three alternative scenarios were considered:

Scenario 1: Vaccination & depopulation. Depopulation of eight infected farms per day and vaccination of 10,000 animals per day.

Scenario 2: Depopulation only. Depopulation of eight infected farms per day.

Scenario 3: Enhanced vaccination & depopulation. Depopulation of 12 infected farms per day and vaccination of 15,000 animals per day.

3.0 Model outputs

Our simulations track the number of animals and farms in each health state throughout the daily time steps. We also utilized the epidemic trajectories to calculate the geodesic distances between the seeded infections and secondary cases. In addition, we elucidate the probability of distance-dependent transmission by calculating the cumulative empirical spatial distribution. By tracing the average of secondarily infected animals resulting from each transmission route, we estimated the contribution of between-farm movement and spatial transmission in infecting each species, here we present the average contribution for each route along with credible intervals were estimated by using an equal-tailed interval method (Lecoutre, 2011). We also determined the volume of animals and farms within control zones at ten and 20 days post-FMD dissemination.

In collaboration with the Brazilian animal health officials, we defined the maximum capacity to control and eradicate large-scale FMD epidemics, more than 400 infected farms, or more than 90 days of deployed control actions. Therefore, simulations above these cut-offs were discarded before the control and eradication scenarios were set to start. In addition, simulations

with more than 450 infected farms or more than 100 days with more than one infected farm after control actions started were also eliminated from our results. Finally, the outcomes of the control scenarios were classified as successful when no infected farms were present after 100 days of control actions and unsuccessful otherwise. Accordingly, the simulations that were successful in eliminating epidemics were used to benchmark the effectiveness of control scenarios regarding the number of days necessary to fade out epidemics.

The software used in the development of MHASpread, graphics, and maps was R statistical software v. 4.1.1 (R Core Team, 2021) with RStudio editor using the packages: sampler (Baldassaro, 2019), tidyverse (Wickham et al., 2019), sf (Pebesma, 2018), brazilmaps (Prado Siqueira, 2021), doParallel (Corporation and Weston, 2022a), doSNOW (Corporation and Weston, 2022b), RSQLite (Muller et al., 2021), EpiContactTrace (Noremark and Widgren, 2014), and lubridate (Grolemund and Wickham, 2011).

2. Results

3.1 Farms and animal-level FMD temporal dynamics

Of 15,721 seeded infections, 10,473 simulations started in cattle farms, 5,179 swine farms, and 69 small ruminant farms, while 4,702 (29%) had multiple species. Examining the epidemic trajectories at 20 days post seeded infection, we estimated a median of 15 (IQR: 5-41) infected animals, of which 12 (IQR: 4-32) were bovine, 5 (IQR: 2-12) were swine, and 1 (IQR: 1-2) small ruminants (Supplementary Material Table S1 and Supplementary Material Figure S7). Animal level infection distribution of each compartment at ten and 20 days is shown in Supplementary Material Table S1.

The FMD epidemics distribution at the farm level at 20 days was highly variable, the median number of infected farms was 8 (IQR: 3-22), of which 7 (IQR: 3-18) were bovine farms, 3 (IQR: 1-6) swine farms, and 1 (IQR: 1-1) small ruminants farm (Figure 3). While we observed large-scale epidemics with up to 2,197 infected farms, these rare events were outside the 95% credibility interval (Figure 3). Farm-level infection distribution at ten and 20 days post seeded infection is available in Supplementary Material Table S2.

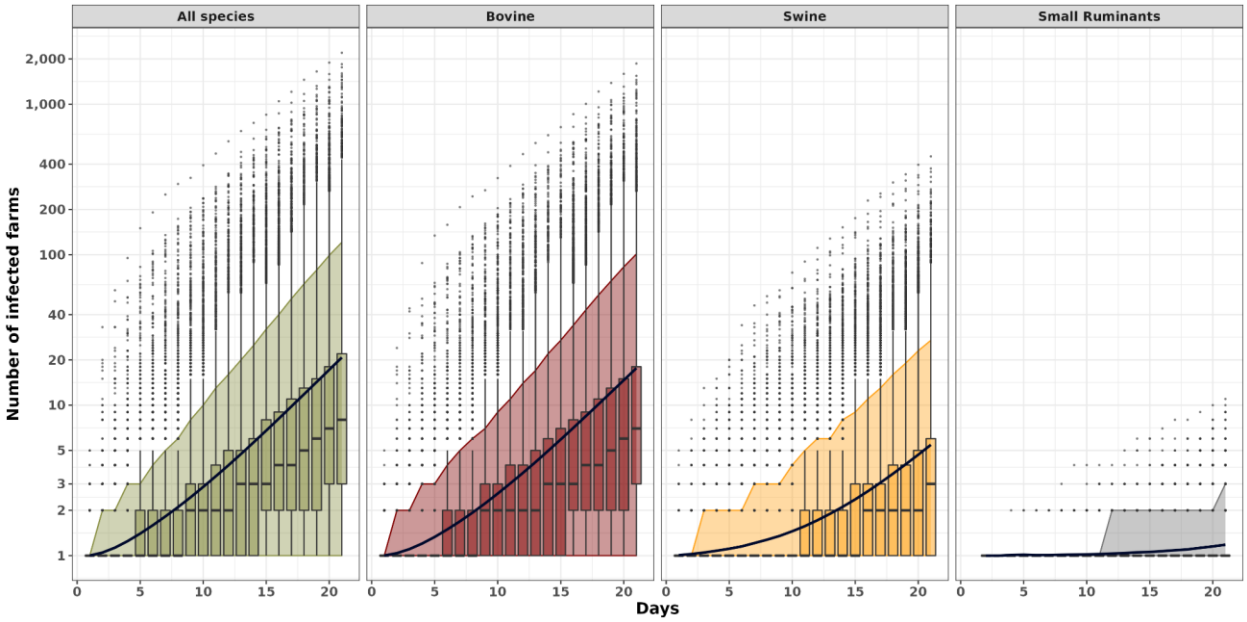

Figure 3. Distribution of the daily number of infected farms. Boxplots with outliers of the number of infected farms. The colored background area represents the 95% credible interval for the daily number of infected farms. The y-axis is on a log10 scale.

3.2 Contribution of transmission routes

Evaluating the contribution of the between-farm and spatial transmission routes, we demonstrated that overall for the first 17 days of FMD dissemination, the main transmission route was animal movements with an average of 4.9 (CI: 1-23) newly infected animals, while at 20 days the spatial transmission was by far the dominant route, with a daily average of 11 (CI: 1-

95.6) newly infected animals. When we examined transmission contributions by species, at ten days bovine infection shifts from spreading via animal movement to spatial transmission route. Whilst, bovine new infections at 20 days were dominated by the spatial transmission route, we estimated that on average 10.7 (CI: 1-57) new infections, while animal movement represented on average 4.5 (CI: 1-32) new infections. In swine, the animal movement route was undoubtedly the most important route throughout the simulation period, at 20 days it generated on average 11.4 (CI: 1-123) newly infected pigs while the spatial transmission produced on average 3.1 (CI: 1-90) of newly infected pigs. Finally, for small ruminants, both routes appear to contribute at a similar rate (Figure 4). The summary statistics of each route at ten and 20 days are available in Supplementary Material Table S3.

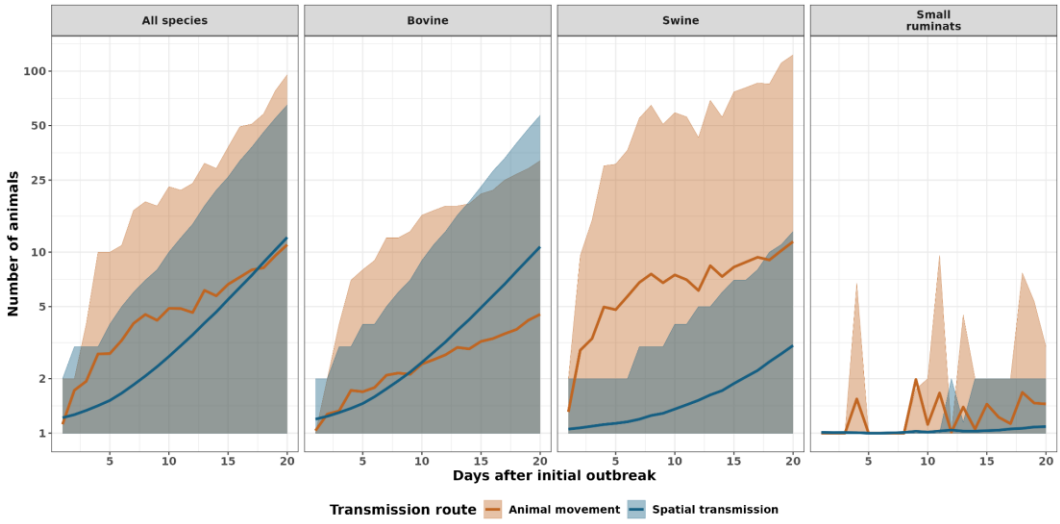

Figure 4. FMD transmission via between-farm movement and spatial transmission. The x-axis represents the number of days after seeded FMD infection. The y-axis (represented in a log10 scale) shows the number of newly infected animals, the solid line represents the average and the colored background represents 95% of credible interval distribution.

3.3 Spatial transmission dynamics

Of the 15,721 seeded infections, we measured the distance between 386,043 simulations that generated secondary infection. The median distance between seeded infection and secondary infections was 5.77 km (IQR: 1-10.29 km). Our simulations also captured long-distance spread at 100 km and 500 km, while the maximum dispersal was at 695.40 km (Figure 5A). As noted in Figure 5B the probability of infection decreased by 11% when we compared one km with 20 km.

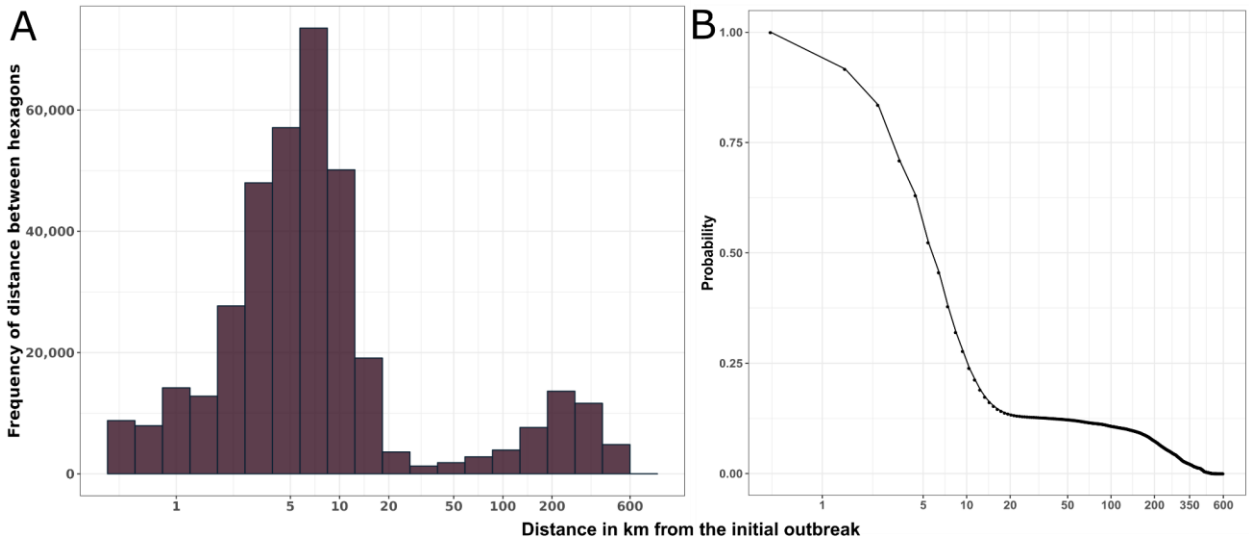

Figure 5. Distribution of the cumulative epidemic distances. A) Frequency histogram of distances from seeded infection and secondary infections. B) Empirical cumulative distribution function (1-ECDF) probability of distances from the initial outbreak. Both x-axes are a log10 scale.

3.4 Effectiveness of control strategies

We calculated the number of animals and farms within control zones. On day 20 of silent FMD dissemination, the total number of animals and farms within infected zones had a median of 8,660 (IQR: 308-53,783) animals and 1,785 (IQR: 583-4,804) farms, in buffer zones, the median was of 77,679 (IQR: 2,408-384,439) animals and 12,303 (IQR: 4,357-30,900) farms, and within surveillance zones a median of 369,541 (IQR: 9,599-1,460,202) animals and 50,148 (IQR:

19,295-105,943) farms (Figure 6 and Supplementary Material Figure S8 for the animal-level distributions). Animal-level results at ten days are presented in Supplementary Material Table S4 and Supplementary Material Figure S9, at farm-level in Supplementary Material Figure S10 and Table S5.

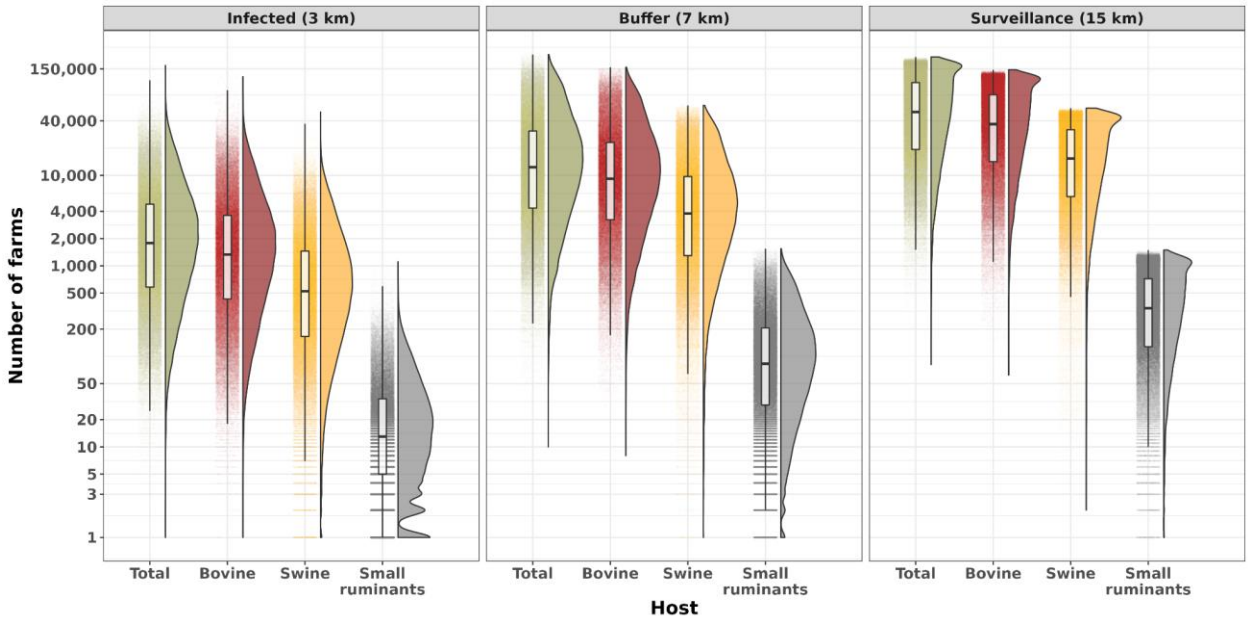

Figure 6. The distribution of farms within control zones at 20 days from the initial infection. The y-axis shows the number of animals within infected zones, buffer zones, and surveillance on a log10 scale. The left side boxplots include outliers and the right size density distribution.

We demonstrated that the number of days necessary for successfully fading out FMD depended on the number of secondary infections at 20 days and the duration of control actions (Figure 7). The baseline control scenario fade out 93.4% of the epidemics with a median of 9 (IQR: 3-23, max: 221) infected farms, while scenario one which has twice the depopulation and vaccination of the baseline scenario eliminated 97,8% of simulated epidemics with a median of 10 (IQR: 4-

26, max: 223). Scenario two eliminated (depopulation only) 78.4% of simulated epidemics stopping mostly small-scale epidemics with a median of 7 (IQR: 3-14, max: 74) infected farms. Scenario three which has three times the depopulation and vaccination of the baseline control scenario was enough to fade out 98.3% of epidemics with a median of 10 (IQR: 4-26, max: 248) initially infected farms (Figure 7 and Supplementary Material Table S6). Interrogating epidemics in which control actions were unsuccessful, scenario two (depopulation only) was the least effective scenario, it was unable to contain epidemics with a median of 61 (IQR: 43-93, max: >=400) initially infected farms. The baseline control scenario was unsuccessful in eliminating simulations with a median of 116 (IQR: 82-161, max:>=400) infected farms, while scenarios one and three did not stop epidemics with a median of 183 (IQR: 152-244, max: >=400) and median of 203 (IQR: 170-264, max: >=400), respectively (Figure 7).

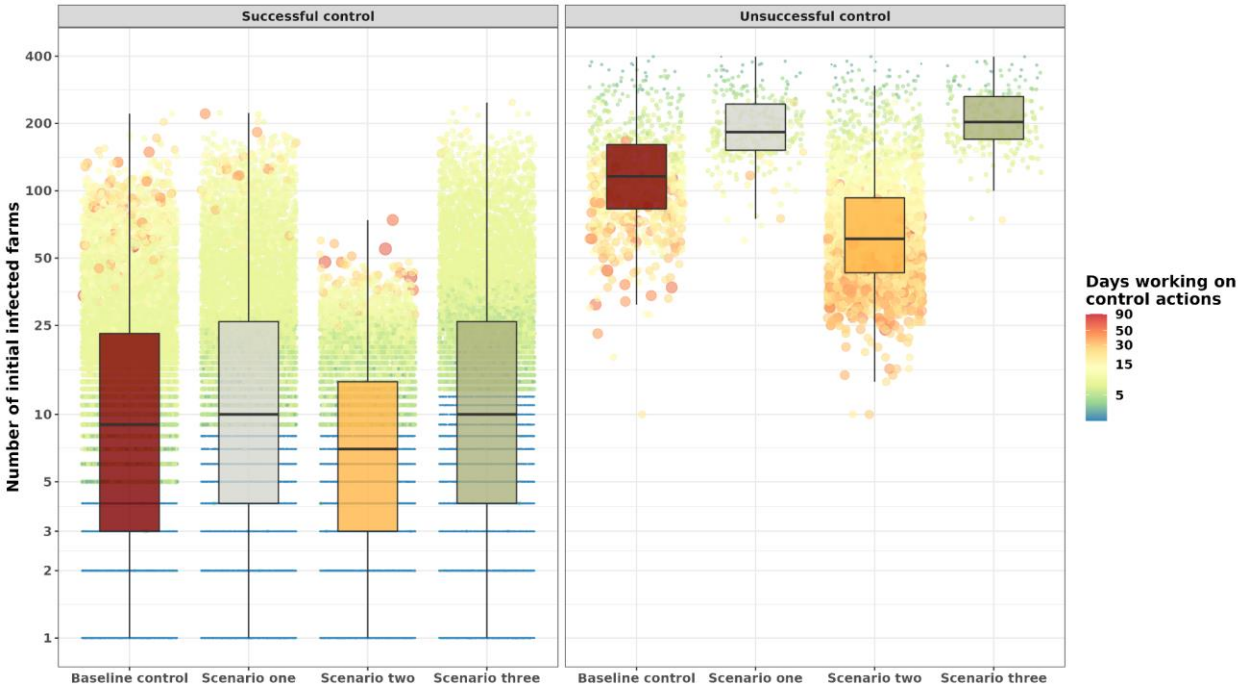

Figure 7. The distribution of FMD epidemics successfully and unsuccessfully halted under four control and eradication scenarios after 20 days from the initial seeded infection. The

boxplot shows the distribution of secondarily infected farms at 20 days, the background scattered plot shows individual stochastic simulations in which color represents the number of days control and eradication measures were applied. The y-axis is represented in the log10 scale.

For the baseline control scenario from the initial deployment of control actions at 20 days, the maximum average number of infected farms was 94, for scenario one 126.11 farms, in scenario two 60.33 farms, and 157 farms for scenario three. From the successfully halted epidemics, the baseline control scenario took 100 days to fade out epidemics. The differences in days to fade out epidemics between the baseline control scenario and the alternative scenarios which all took less time, scenario two 11 fewer days, scenario one 37 fewer days, and scenario three 51 fewer days (Figure 8).

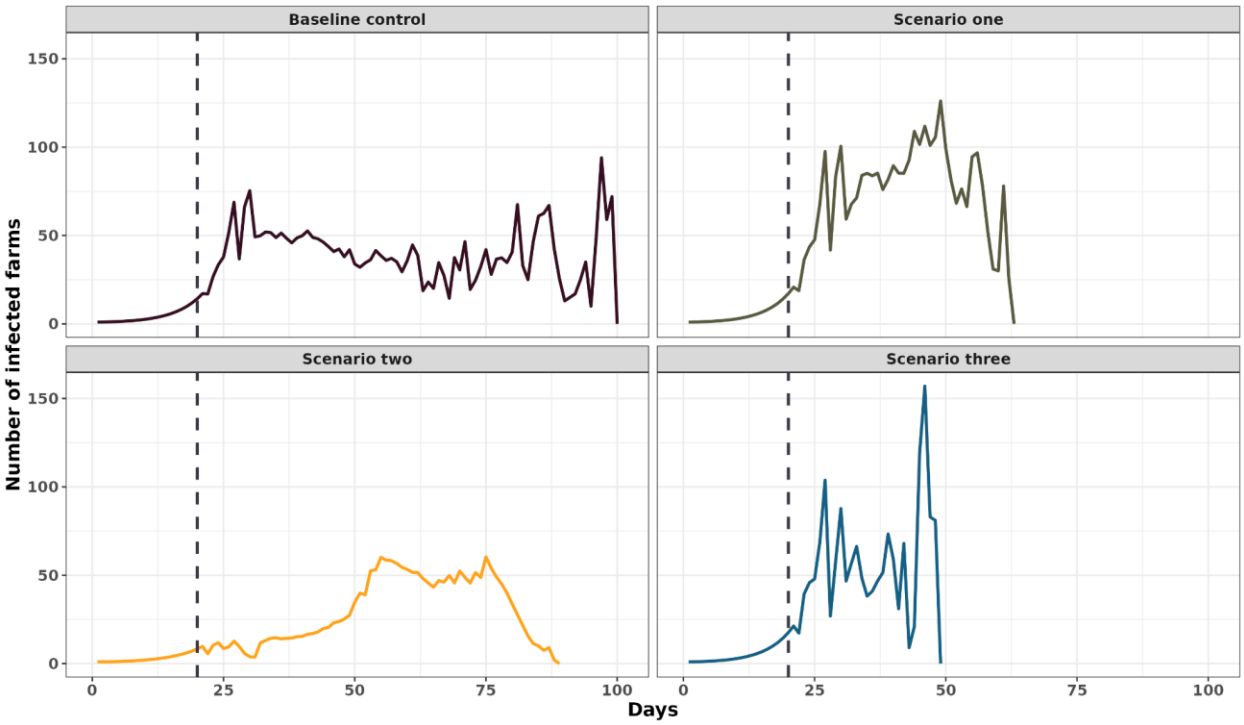

Figure 8. The average number of days to stamp out successfully eliminated FMD epidemics. The vertical dashed line marks the 20 days of silent FMD spread and the start of control actions. The solid black line represents the average daily infected farms.

In addition, we simulated control action starting interventions 10 days after seeding the initial infection is described in greater detail in the Supplementary Material Section "*Effectiveness of control actions started 10 days after initial simulated infection*".

4. Discussion

We developed an SEIR multi-species stochastic model that explicitly incorporates species-specific transmission coefficients. However, even by including different species interactions, bovine remained the most infected species. The animal movement was the most effective transmission route for the first ten days for all species infections, after that bovine infection was dominated by the spatial transmission, while for swine between-farm movement was the most important route thought the first 20 days. Our results also demonstrated that most (74.7%) secondary cases were disseminated to farms within ten km from the initial seeded infection. We also demonstrated that while the baseline control scenario and alternative scenarios were sufficient to fade out the majority of epidemics within 100 days. The necessary scenario to completely eliminate all large-scale epidemics requires the depopulation of 120 farms per day plus vaccination of 25,000 animals per day deployed within seven days of the first detection.

Based on the 2018/2020 population and between-farm animal movement patterns in the state of Rio Grande do Sul, we demonstrated that FMD is likely to disseminate between different production systems e.g. bovine to swine and vice-versa, regardless of which species are infected first (Supplementary Material Figure S13). Our results showed that the preferred route of

infection was not the same across species, a phenomenon that has been demonstrated previously (McReynolds et al., 2014; Probert et al., 2018; Sanson et al., 2014; Ward et al., 2009). We demonstrated that until day 17 if we take all species together the between-farm movement dominated dissemination, while for bovines at day ten the spatial transmission became the preferred transmission route. The demonstrated dominance of spatial transmission later in the epidemic could be explained at least to some degree by the windborne spread across short to mid distances in some areas of the state of Rio Grande do Sul, characterized by the cool temperature and high humidity known to favor virus survival rates (Björnham et al., 2020; Chanchaidechachai et al., 2021; Green et al., 2006). More importantly, based on the high connectivity of bovine farms in some municipalities described earlier (Cardenas et al., 2022), could explain the initial peak in bovine infection by the movement of animals, while the flip toward spatial transmission could have been facilitated when secondary cases spread into areas densely populated with up to 12.23 km^2 farms (Cardenas et al., 2022). These densely populated areas coincide with our model simulation in which control actions were not sufficient to stamp out large-scale epidemics (Supplementary Material Figure S14). Even though our modeling work considered main transmission routes, data regarding other important indirect transmission routes were not considered i.e. fomites, and transportation vehicles (Galvis et al., 2022; Rossi et al., 2017), future iterations could include these additional routes. Importantly, when we evaluated swine infection, as expected because of the high specialization of pork production operations with farms producing animals of a specific production phase e.g. breeding, feeder-pigs (Cardenas et al., 2021; Machado et al., 2021b), the pig movements were by far the most relevant transmission pathway in our study and elsewhere (Andraud et al., 2022; Machado et al., 2021a; Shimizu et al., 2020). For small ruminants' dynamics, our results did not clearly uncover any

dominant transmission route, we remark that even though small ruminants did not contribute significantly to the transmission it was not null. Overall, our result implies the need for the enhancement of FMD control strategies should also include swine and small ruminants. Prioritizing control interventions related to traceability early in an FMD epidemic, especially in the first ten days is likely to increase the chances of finding more secondary infections, while if FMD is detected after ten days of silent dissemination, enhancing surveillance activities within control zones should be prioritized.

Based on the estimated number of animals and farms within control zones at 20 days of FMD dissemination, and assuming that three qualified veterinarians can vaccine approximately 1,000 animals per day (personal communication, animal health officials), we estimated the daily need to be at 160 veterinarians to oversee an average 4,222 farms within infected zones, and approximately 53,434 vaccine doses if all species are vaccinated or 21,640 without vaccination of swine. If vaccination is also deployed to buffer zones 320,223 doses of vaccine and 961 veterinarians would be required or 137,046 doses and 411 veterinarians without vaccinating swine. Similar modeling work in Denmark has predicted an average of 22 epidemics that last for 34 days and would need 123 veterinarians (Boklund et al., 2017). It is important to note that the estimations provided in the current study were based on the median epidemic sizes of the ones recorded in the UK and Argentine (Anderson, 2002; Perez et al., 2004), which included large-scale epidemics with up to 398 secondary infections, thus much larger than the scenarios in Denmark. We remark that if such large-scale FMD epidemics occur in the state of Rio Grande do Sul, the current resources necessary, trained animal health officials, adequate vaccine stockpiles, and supplies for depopulation would be beyond the local capacities and FMD would become endemic. Hence, future work should focus on estimating not only the number of animal health

officials but also administrative, direct, and indirect costs, including large-scale epidemics scenarios. In addition, this new transmission modeling study should include delays longer delay in disease detection, the necessary downtime between farm visits, and other relevant logistic roadblocks bonded to controlling and eliminating large-scale epidemics (Anderson, 2002).

Several modeling works have demonstrated the effectiveness of the combination of vaccination with depopulation in FMD elimination (Capon et al., 2021; Dürr et al., 2014; Sanson et al., 2017), with some exceptions in highly dense livestock areas such as in The Netherlands in which vaccination combined with ring culling was not sufficient (Boklund et al., 2013). Among the simulated scenarios, implementing vaccination in conjunction with depopulation was always more effective when compared with depopulation alone (Figures 7 and 8). One potential explanation could be related to the spatial transmission being the dominant transmission route after the 20 days, in which most transmission events occurred with a median up to six km from infected farms which encompass infected zones' size. Even though we demonstrated that the use of the depopulation scenario alone exhibited a lower rate of successful FMD elimination it was capable of eliminating small-scale epidemics (maximum of 74 infected farms), while less successful if the region decides against vaccinating (da Costa et al., 2022), one would expect the region to regain FMD-free status sooner if compared with using vaccination (Geale et al., 2015). From our alternative control scenarios, scenario three was the most aggressive, considering that the state would be able to depopulate 12 farms and 15,000 farms vaccinated per day, unfortunately, it was still not sufficient to eliminate large-scale epidemics (more than 400 infected farms at 20 days of silent FMD dissemination). Ultimately, we estimated the need to depopulate 100 farms and vaccinate 25,000 animals within seven days to eliminate all simulated epidemics, which seems extremely unrealistic given the current state of Rio Grande do Sul

staffing and available resources. Thus, we conclude in a similar way as the modeling work done in Austria, in which the number of animal health officials for surveillance and control activities would need to be doubled to allow proper large-scale epidemic management (Boklund et al., 2017; Marschik et al., 2021; Sanson et al., 2021). Finally, our model provides guidance to the Brazilian policymakers, our results are the first to provide rules of thumb based on the number of infected farms, to choose to deployment or not vaccination. We demonstrated that in situations in which the number of secondary cases varies between thee and 23, the baseline control scenario is likely to be sufficient when applied for 100 days. However, we highlight that a significant number of simulations with less than 50 infected farms at 20 days of dissemination, were not successful control by the baseline control scenario. Thus, it is important to consider the profile of infected farms, such as location and the size of the farm's contact network (Cardenas et al., 2022) along with simulated results to make field-level decisions. Finally, we remark that as described earlier we assume full compliance with all associated surveillance actions and movement restrictions, thus results should be interpreted with this in mind.

5. Limitations and further remarks

We identify a number of limitations mostly related to assumptions made in the simulated FMD control scenarios. We assume perfect compliance with between-farm movement restrictions for infected and farms directly linked with infected farms, and movement restrictions within control zones, while also assuming that disposal of depopulated animals eliminated any possibility of further dissemination. Nevertheless, there are uncertainties about the implementation of control measures, future work could include delays in response times. Additionally, given the volume of vaccines necessary to vaccinate all animals within infected and buffer zones, further work should

consider restricting vaccination to each species, thus allowing for benchmarking, and better estimation of vaccine stockpiles (Capon et al., 2021; Dürr et al., 2014; Roche et al., 2015). Another limitation was the assumption of instantaneous vaccination efficacy, future work should consider a variation on vaccination waning (Ringa and Bauch, 2014).

It is worth noting that FMD virulence, infectivity, and transmission, vary among strains (Arzt et al., 2019; Paton et al., 2018). Even though the most recent outbreaks in the state of Rio Grande do Sul were caused by serotypes O and A (da Costa et al., 2022), we cannot rule out the chances of other strains being introduced and exhibiting different dissemination patterns. Future work could include transmission scenarios with strains in circulation across the globe (Mahapatra and Parida, 2018).

To our knowledge, this is the first FMD transmission model developed for Latin American countries. While previously FMD transmission models have included multiple species in their transmission dynamics (Björnham et al., 2020; Boklund et al., 2013; Dürr et al., 2014; Roche et al., 2015), to the author's knowledge none considered the heterogeneous transmission rates of each species explicitly. Another unique feature of our model is that estimation of successful and unsuccessful epidemics fade out, while also assessing the maximum number of outbreaks and the number of days needed to complete FMD elimination. Thus, we provided rules of thump for the four main control and eradication strategies, by estimating the number of secondary infections that the simulated scenarios are capable of stamping out, our results offer scientific support to decision-makers.

In addition, rather than selecting a limited number of farms to seed infection, our modeling approach considers an honest representation of the entire population at risk. While our approach is more expensive, our results provide policymakers an overview of all possible

introduction scenarios, this is important because it is nearly impossible to predict where FMD may resurface. Finally, our model can also provide a distribution of expected FMD epidemics for any current or future control actions listed in the Brazilian control and elimination plan. Nevertheless, because our results are based on population and between-farm movement data from the Rio Grande do Sul, the interpretation of our findings should not be extrapolated to other Brazilian states. But, since the MHASpread model infrastructure is highly flexible, upon the availability of the necessary population data and animal movement data, MHASpread can be easily extended to any other Brazilian state, and also be considered in other Latin American countries.

6. Conclusion

We demonstrated that 20 days of silent FMD dissemination resulted in a median of eight, ranging between three to 22 secondary infected farms. Early detection was pivotal to the success of FMD elimination, we demonstrated that the deployment of depopulation alone was effective if applied to simulation with up to 22 infected farms. However, large-scale epidemics simulated in this study required the depopulation of 100 farms and vaccination of 25,000 animals per day to fade out 100% of the simulated outbreaks. We showed that for the first 17 days of epidemics, the movement of animals dominated the overall dissemination, and significant differences in bovine and swine infections were shown. Regardless of which species FMD was introduced the median distance spread was within the range of control zones from one to ten km. We also shown that the baseline control scenario, based on the Brazilian response plan, was not sufficient to stamp out all epidemics within 100 days of the deployment of countermeasure actions. Ultimately, our model projections are available to the local animal health official along with the software developed. Thus our model can be used as a policy tool not only for future FMD response

through computer-based preparedness drills and capacity building but ultimately during an emergency response by providing rules of thumb generated from simulated control scenarios.

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Authors' contributions

NCC and GM conceived the study. NCC and GM participated in the design of the study. FPNL coordinated the data collection. NCC conducted data processing and cleaning designed the model and simulated scenarios with the assistance of GM. NCC and GM designed the computational analysis. NCC conducted the formal coding. GM and NCC wrote and edited the manuscript. All authors discussed the results and critically reviewed the manuscript. GM secured the funding.

Conflict of interest

All authors confirm that there are no conflicts of interest to declare.

Ethical statement

The authors confirm the ethical policies of the journal, as noted on the journal's author guidelines page. Since this work did not involve animal sampling or questionnaire data collection by the researchers, there was no need for ethics permits.

Data Availability Statement

The data that support the findings of this study are not publicly available and are protected by confidential agreements, therefore, are not available.

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Supplementary Material

Modeling foot-and-mouth disease dissemination in Brazil and evaluating the effectiveness of control measures

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Running title: Foot-and-mouth disease dissemination across species.

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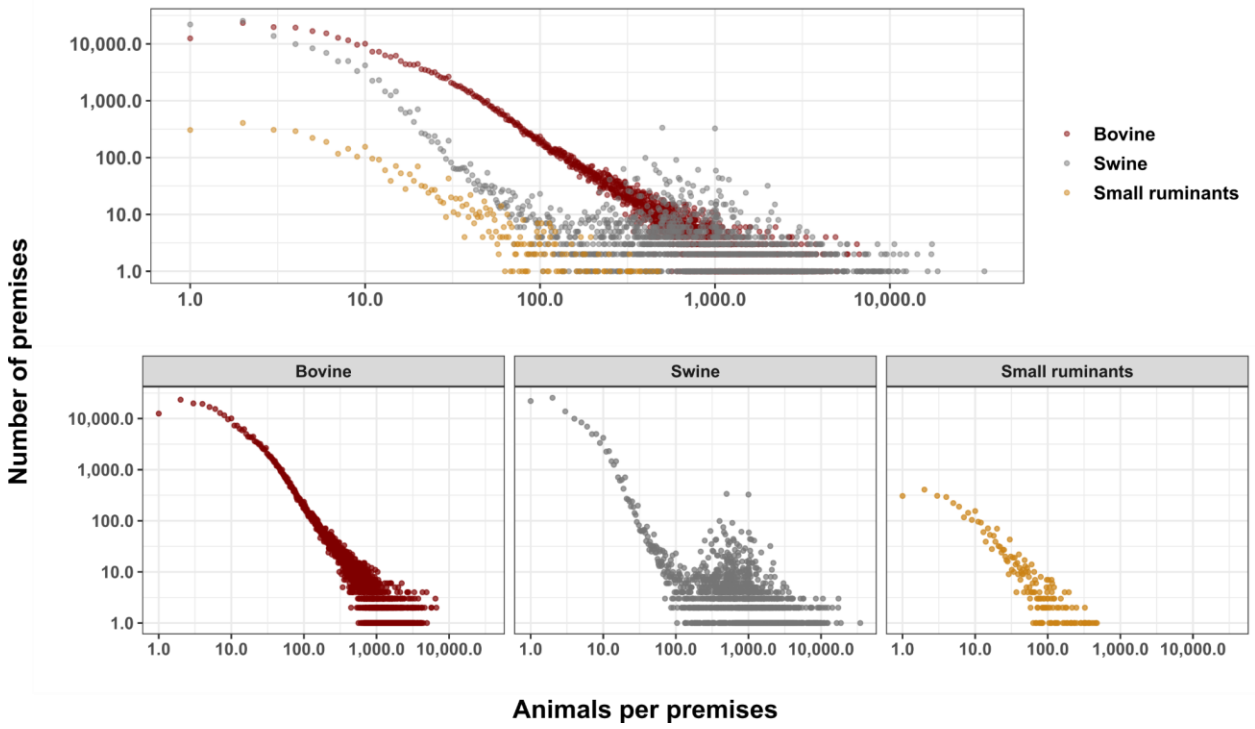
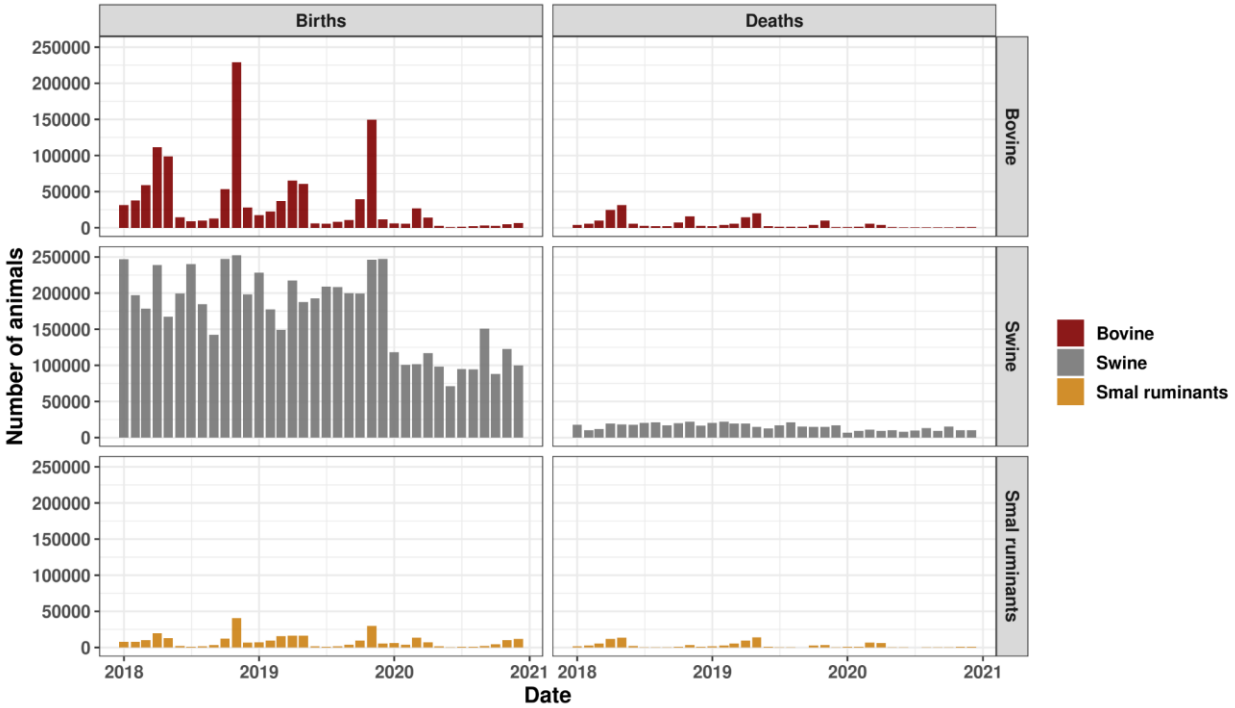
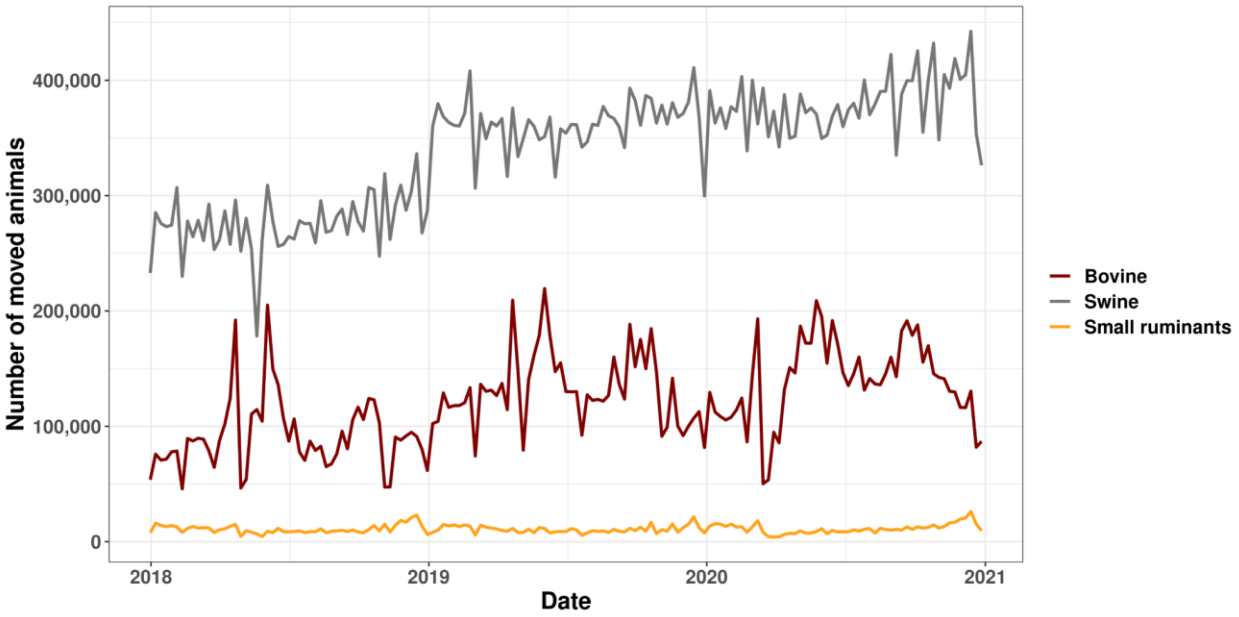


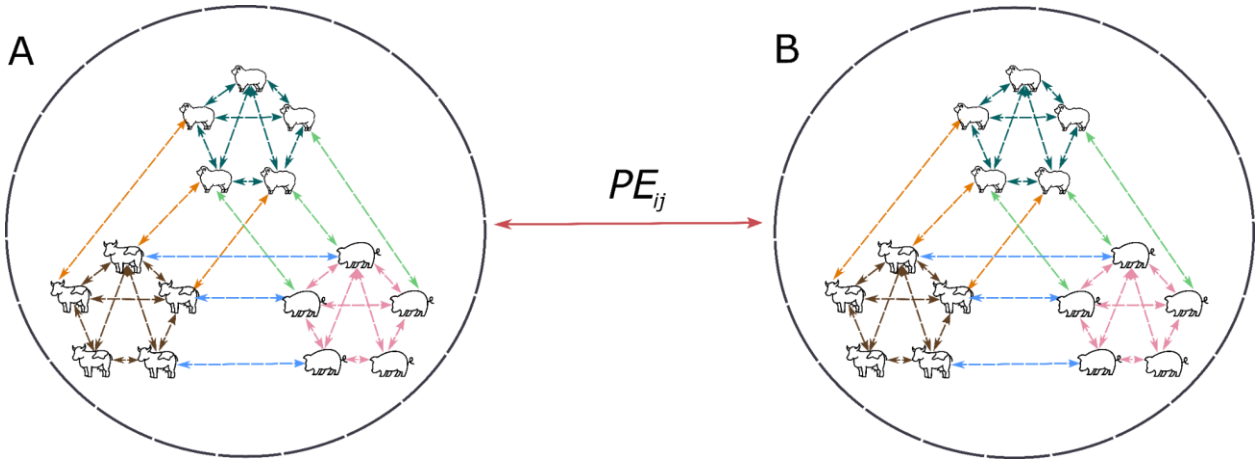
Supplementary Figure S1. The 2018 distribution of farm-level population for each species in the state of Rio Grande do Sul, Brazil. The y-axis is the number of farms and the x-axis is the number of animals, both on a log10 scale.



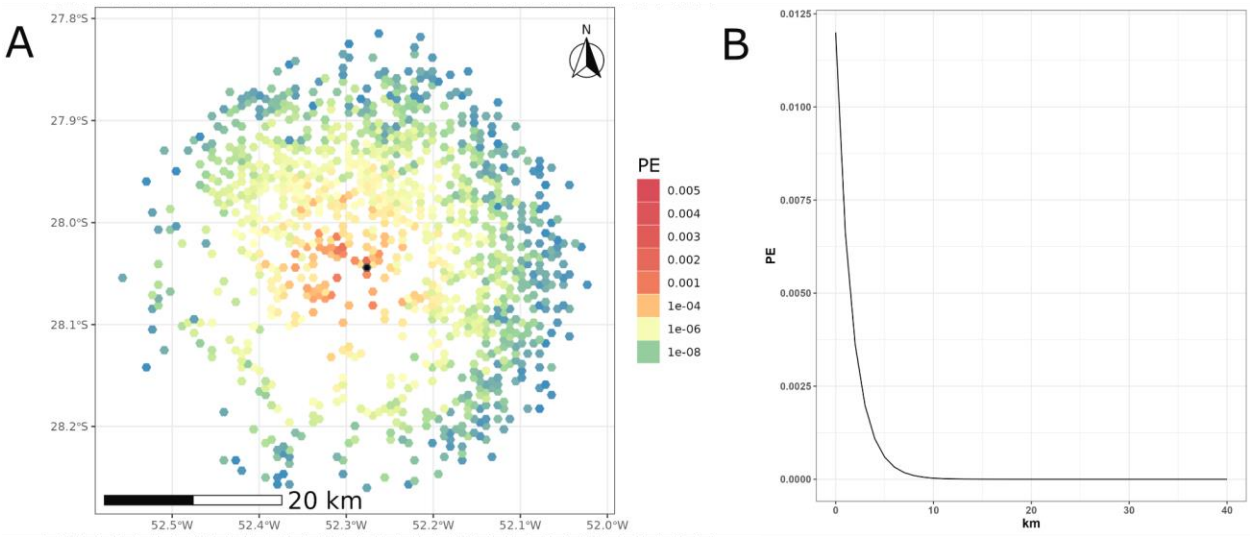
Supplementary Figure S2. The monthly distribution of animal births and deaths by species, from January 1st, 2018 to December 31st, 2020.



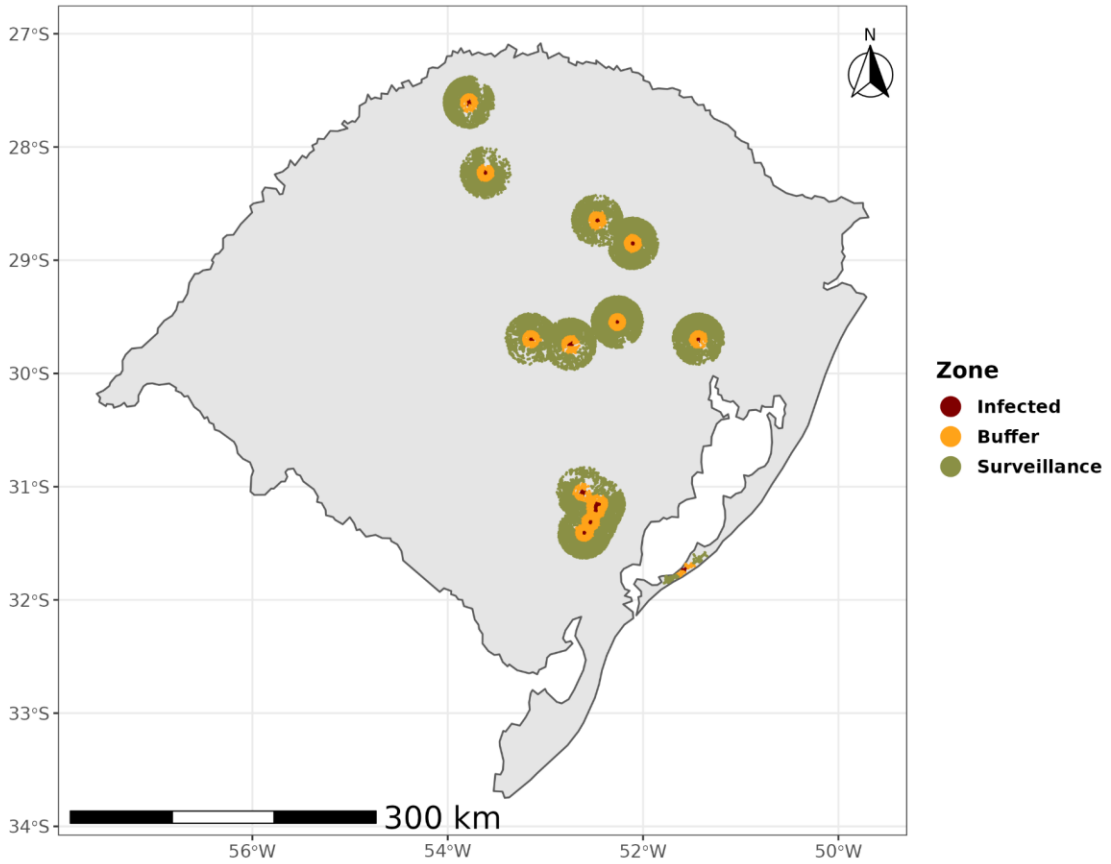
Supplementary Figure S3. The weekly between-farm animal movements, from January 1st, 2018 to December 31st, 2020.



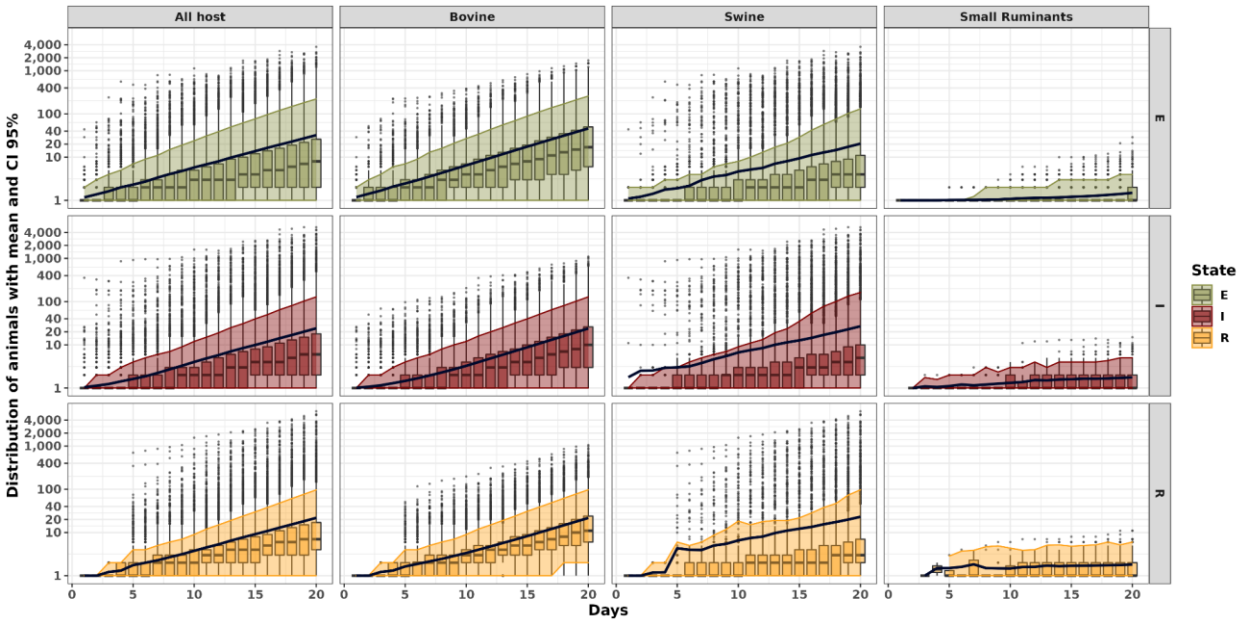
Supplementary Figure S4. Representation of the different population interactions at the within-farm level. For this example, we considered farms with all three species. The dashed line represents the interaction within and between species, and the color denotes a β for each host-to-host interaction (Table 2). The solid line represents the interaction among the farms with different infection probabilities modulated by the spatial proximity (spatial transmission). PE denotes the transmission probability given a distance between farm i to farm j.



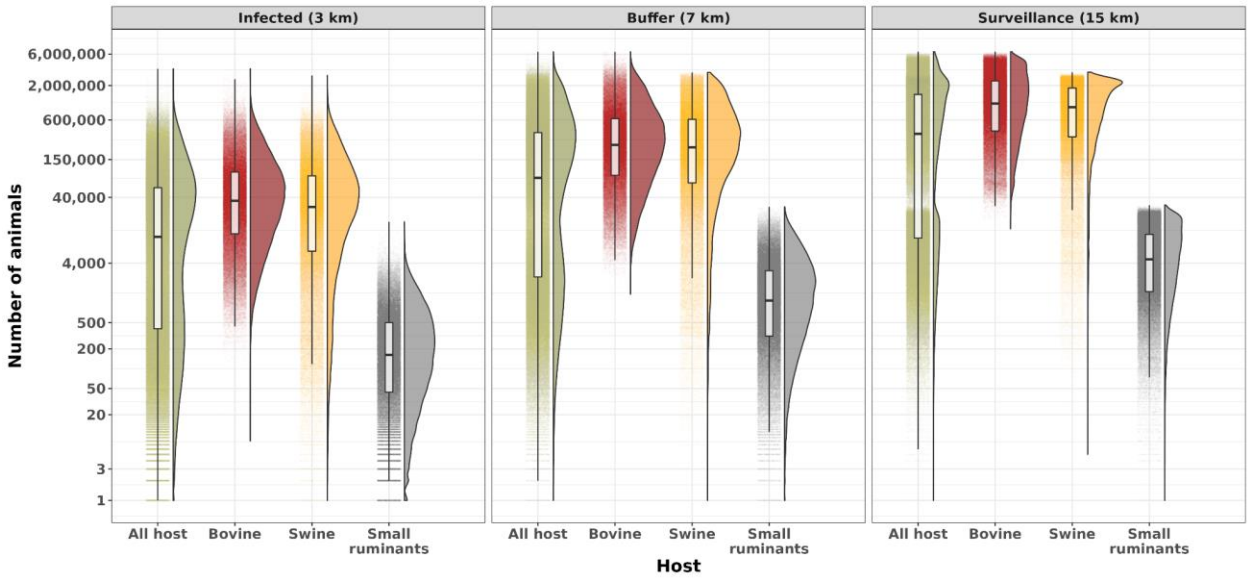
Supplementary Figure S5. A) Representation of grid-hexagons of size 0.76 km (503,516 m^2). Each hexagon can host one or more farm locations. The color of the hexagon represents the probability of PE exposure assuming ten infected animals in the center (black hexagon). B) PE distance in km.



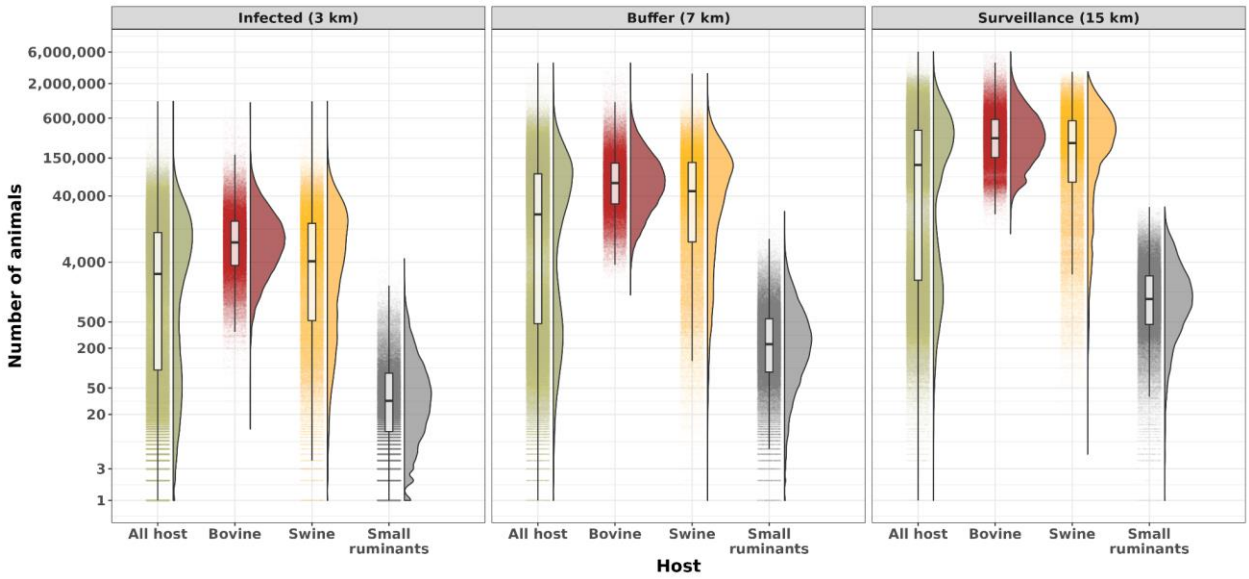
Supplementary Figure S6. **Control zones mapping.** The infected control zones of 3 km are represented as red dots, the 7 km buffer zone is represented as yellow dots, and the 15 km surveillance zone is represented as green dots. Of note, control zones with overlapping are merged.



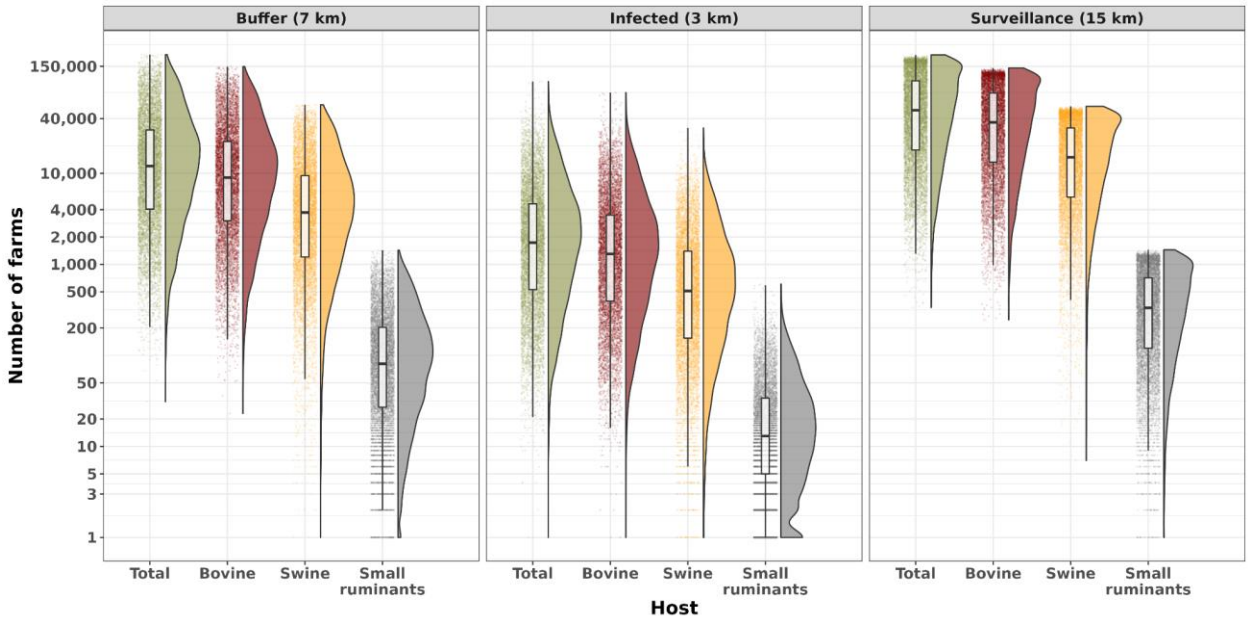
Suplementary Figure S7. Distribution of animals per compartment, exposed (E), infected (I), and recovered (R) by species. Because the number of susceptible animals is very large (19,267,676), the S compartment is not shown. The solid line represents the mean and the dots are outliers. The colored background area represents the 95% credible interval. The y-axis is on a log10 scale.



Supplementary Figure S8. The distribution of animals within control zones at 20 days from the initial infection. The y-axis shows the number of animals within infected zones, buffer zones, and surveillance on a log10 scale. The left side boxplots include outliers and the right size density distribution.



Supplementary Figure S9. The distribution of animals within control zones at 10 days from the initial infection. The y-axis shows the number of animals within infected zones, buffer zones, and surveillance on a log10 scale. The left side boxplots include outliers and the right size density distribution.

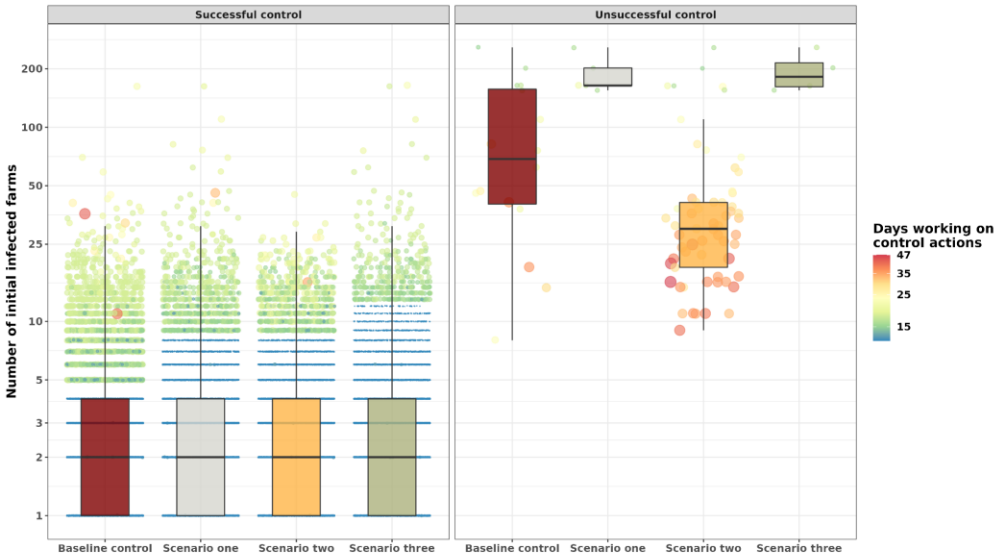


Supplementary Figure S10. The distribution of farms within control zones at 10 days from the initial infection. The y-axis shows the number of animals within infected zones, buffer zones, and surveillance on a log10 scale. The left side boxplots include outliers and the right size density distribution.

Effectiveness of control actions started 10 days after initial simulated infection

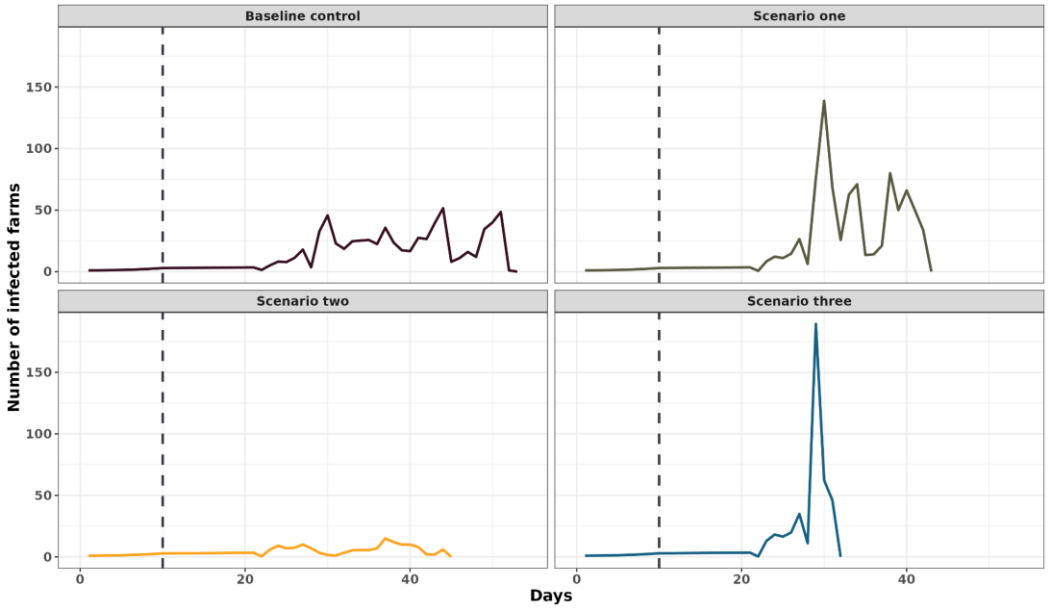
At 10 days of FMD dissemination, the baseline control scenario fade out 99.90% of epidemics with a median of 2 (IQR: 1-4, max: 162) infected farms, while scenario one eliminated 99.96% of simulated epidemics with a median of 2 (IQR: 1-4, max: 162). Scenario two (depopulation only) eliminated 99.5% of simulated epidemics with a median of 2 (IQR: 1-5, max: 45) infected farms. Scenario three which has three times the depopulation and vaccination of the baseline control scenario was enough to fade out 99.97% of epidemics with a median of 2 (IQR: 1-4, max: 164) initially infected farms (Supplementary Material Figure S11). Similar to the control actions simulations at 20 days scenario two (depopulation only) failed more often and was not able to control epidemics with a median of 30 (IQR: 19-41, max: 248) initially infected farms.

In addition, for simulation that was not able to eliminate simulated epidemics, the baseline control scenario failed in eliminating simulations with a median of 69 (IQR: 40-157, max: 258) infected farms, while scenarios one and three, epidemics with a median of 164 (IQR: 164-202, max: 258) and median of 183 (IQR: 162-216, max: 258), respectively (Supplementary Material Figure S11).

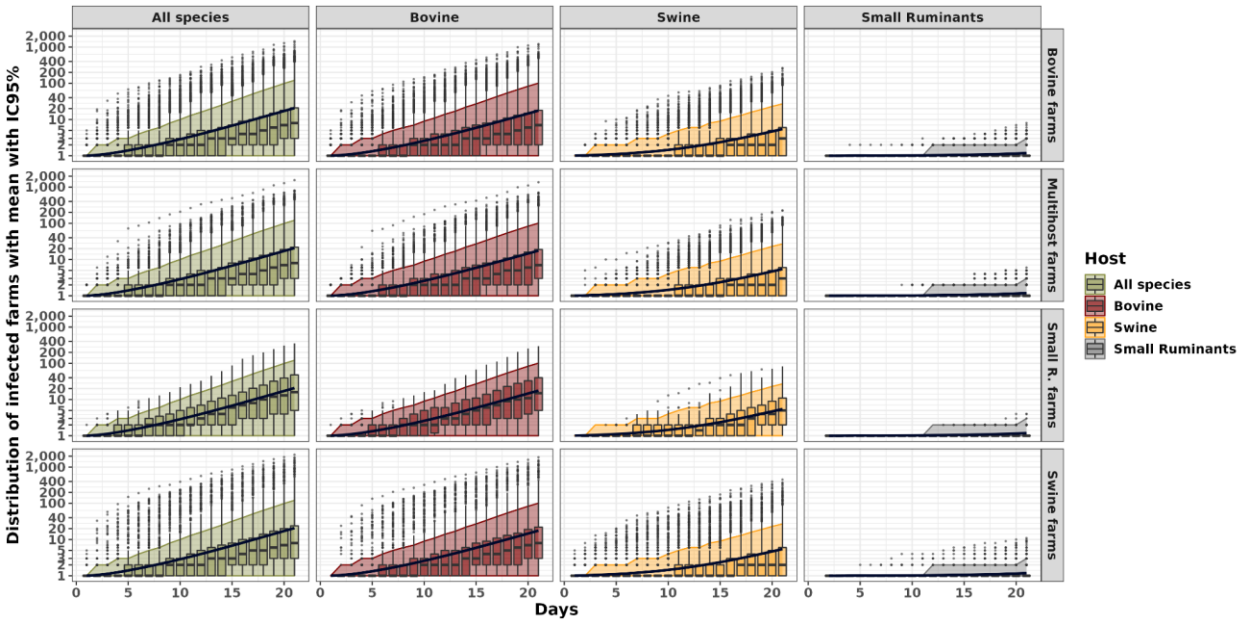


Supplementary Figure S11. The distribution of FMD epidemics successfully and unsuccessfully halted under four control and eradication scenarios after 10 days from the initial seeded infection. The boxplot shows the distribution of secondarily infected farms at 10 days, the background scattered plot shows individual stochastic simulations in which color represents the number of days control and eradication measures were applied.

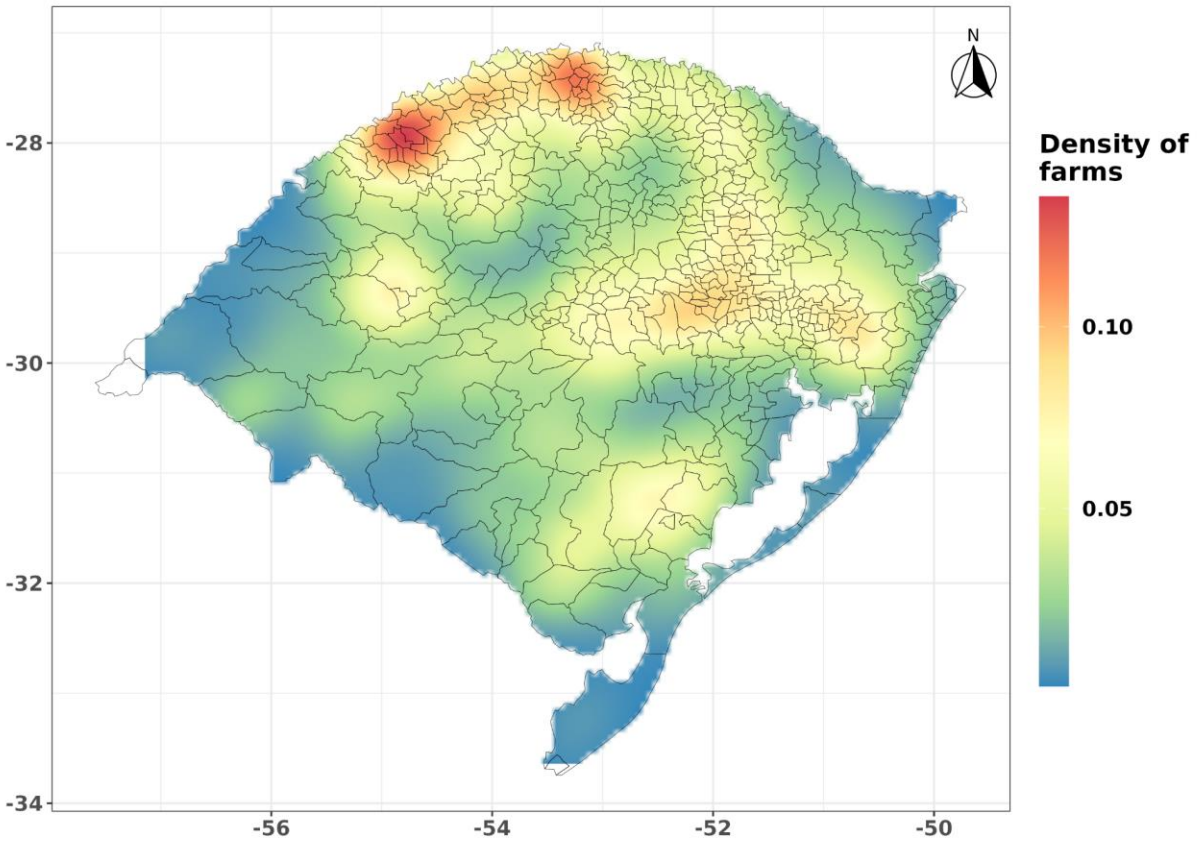
For the baseline control scenario from the initial deployment of control actions, the maximum average number of infected farms was 51.5, for scenario one 139 farms, 15 farms in scenario two, and 189 in scenario three. Of the successfully halted epidemic, the baseline control scenario took 57 days to fade out epidemics. In comparison with the baseline scenario, scenario two needed 8 fewer days, scenario one 10 fewer days, and scenario three 21 fewer days to completely eliminated all simulated epidemics (Supplementary Material Figure S12).



Supplementary Figure S12. The average number of days to stamp out FMD epidemics when were was successfully eliminated. The vertical dashed line marks the 10 days of silent spread and the start of control actions. The solid black line represents the average of infected farms per day.



Supplementary Figure S13. Distribution of animals per compartment, exposed (E), infected (I), and recovered (R) by species and by initial farm type where the simulation started. The right y-axis represents the type of farm where the simulation model started. Because the number of susceptible animals is very large (19,267,676), the S compartment is not shown. The solid line represents the mean and the dots are outliers. The colored background area represents the 95% credible interval. The y-axis is on a log10 scale.



Supplementary Figure S14. Farms density of the Rio Grande do Sul state when considering farms that were not successfully controlled overall control action simulations across all scenarios. The color background represents the farm density value when considering 0.05 units of the latitude and longitude projection. The solid black line represents the municipalities' boundaries of the state of Rio Grande do Sul.

Supplementary Table S1. Estimated animal-level distribution of at 10 and 20 days after initial infection.

Category	State	Quantile 0.25	Mean	Median	Quantile 0.75	Maximum	Days after initial infection
All species	Susceptible	19,459,735	19,495,401	19,490,270	19,525,934	19,717,989	10
All species	Exposed	2	10	5	10	1,783	10
All species	Infected	1	6	3	6	2,735	10
All species	Recovered	2	5	3	5	2,741	10
Bovine	Susceptible	14,330,643	14,330,468	14,330,608	14,330,506	14,306,163	10
Bovine	Exposed	2	8	4	9	983	10
Bovine	Infected	1	4	2	5	518	10
Bovine	Recovered	2	4	3	5	1,129	10
Swine	Susceptible	4,886,604	4,886,448	4,886,600	4,886,591	4,824,419	10
Swine	Exposed	1	5	2	3	1,318	10

Swine	Infected	1	7	2	3	2,586	10
Swine	Recovered	1	7	2	3	2,579	10
Small ruminants	Susceptible	50,408	50,390	50,403	50,391	49,761	10
Small ruminants	Exposed	1	1	1	2	51	10
Small ruminants	Infected	1	1	1	2	25	10
Small ruminants	Recovered	1	1	1	2	10	10
All species	Susceptible	19,675,945	19,719,056	19,708,463	19,751,901	19,958,581	20
All species	Exposed	8	74	25	72	7,215	20
All species	Infected	5	49	15	41	9,765	20
All species	Recovered	8	39	15	34	12,250	20
Bovine	Susceptible	14,330,578	14,329,352	14,330,292	14,329,318	14,218,361	20
Bovine	Exposed	7	56	21	61	4,149	20
Bovine	Infected	4	29	12	32	2,636	20

Bovine	Recovered	7	27	14	30	2,768	20
Swine	Susceptible	4,886,599	4,885,767	4,886,577	4,886,129	4,740,943	20
Swine	Exposed	2	23	5	14	4,098	20
Swine	Infected	2	28	5	12	8,082	20
Swine	Recovered	2	22	4	7	10,234	20
Small ruminants	Susceptible	50,407	50,384	50,401	50,384	49,669	20
Small ruminants	Exposed	1	2	1	2	154	20
Small ruminants	Infected	1	2	1	2	166	20
Small ruminants	Recovered	1	2	1	2	132	20

Supplementary Table S2. Estimated number of infected farms at 10 and 20 days after initial infection.

Category	Quantile 0.25	Mean	Median	Quantile 0.75	Maximum	Days after initial infection
All species	1	3.37	2	4	470	10
Bovine	1	3.02	2	4	389	10
Swine	1	1.57	1	2	90	10
Small ruminants	1	1.02	1	1	4	10
All species	3	20.75	8	22	2,197	20
Bovine	3	17.62	7	18	1,862	20
Swine	1	5.45	3	6	450	20
Small ruminants	1	1.18	1	1	11	20

Supplementary Table S3. Summary statistics for animal movement and spatial transmission. We show the distribution of newly infected animals after 10 and 20 days of FMD dissemination

Route of transmission	Species	Quantile 0.25	Mean	Median	Quantile 0.75	Maximum	Days after initial infection
Animal movement	Bovine	1	2.4	1	16	188	10
Animal movement	Swine	1	7.5	1	58.975	1120	10
Animal movement	Small ruminants	1	1.1	1	2	5	10
Animal movement	All species	1	4.9	1	23	1120	10
Spatial transmission	Bovine	1	2.5	1	9	206	10
Spatial transmission	Swine	1	1.4	1	4	38	10
Spatial transmission	Small ruminants	1	1.0	1	1	2	10
Spatial transmission	All species	1	2.7	2	10	245	10
Animal movement	Bovine	1	4.5	1	32	467	20
Animal movement	Swine	1	11.4	1	123	1617	20
Animal movement	Small ruminants	1	1.4	1	3	105	20
Animal movement	All species	1	11.0	1	95.6	1639	20
Spatial transmission	Bovine	1	10.7	5	57	529	20
Spatial transmission	Swine	1	3.1	2	13	90	20

Spatial transmission	Small ruminants	1	1.1	1	2	4	20
Spatial transmission	All species	1	12.1	5	65	617	20

Supplementary Table S4. Statistics summary of the number of animals in each control zones after 10 and 20 days of FMD dissemination.

Zone	Species	Quantile 0.25	Mean	Median	Quantile 0.75	Maximum	Days after initial infection
Infected	All host	47	8,748.78	1,833	10,078	1,081,512	10
Infected	Bovine	3,560	13,997.84	7,935	16,649	1,031,244	10
Infected	Swine	496	12,184.92	4,028	15,336	1,081,512	10
Infected	Small ruminants	2	63.56	18	62	4,529	10
Buffer	All host	435	66,309.93	20,151	85,476	4,100,452	10
Buffer	Bovine	30,453	103,109.40	62,935	125,653	4,100,452	10
Buffer	Swine	8,047.25	95,344.95	47,321.5	128,585	2,839,570	10
Buffer	Small ruminants	76	475.44	217	541	23,352	10
Surveillance	All host	2,112	278,247.19	117,367	393,387	6,090,216	10
Surveillance	Bovine	152,906	449,516.51	299,849	573,640	6,090,216	10
Surveillance	Swine	6,4614.25	383,209.77	252,319	548,438	3,019,033	10
Surveillance	Small ruminants	452	2,015.28	1,098	2,466	27,256	10

Infected	All host	308	53,434.84	8,660	53,783	3,595,388	20
Infected	Bovine	11,169	84,844.08	35,665	97,155	3,595,388	20
Infected	Swine	6,007	7,5074.99	28,463	84,868	2,853,501	20
Infected	Small ruminants	27	385.46	129	450	17,036	20
Buffer	All Species	2,408	320,223.14	77,679	384,439	6,504,836	20
Buffer	Bovine	87,028	501,054.35	250,295	631,415	6,504,836	20
Buffer	Swine	66,341	457,269.51	230,509	611,856	3,162,750	20
Buffer	Small ruminants	297	2,345.56	1,059	3,046	28,802	20
Surveillance	All host	9,599	885,913.31	369,541	1,460,202	6,546,421	20
Surveillance	Bovine	406,570	1,554,385.98	1,065,027	2,337,789	6,546,421	20
Surveillance	Swine	332,548	1,096,357.88	936,872	1,835,041	3,190,801	20
Surveillance	Small ruminants	1,475	6,996.05	4,581	10,959	30,615	20

Supplementary Table S5. Statistics summary of the number of farms in each control zones after 10 and 20 days of spread disease simulation

Area	Specie	Quantile 0.25	Mean	Median	Quantile 0.75	Maximum	Days after initial infection
Infected	Total	529	4,163	1,736	4,632	102,232	10
Infected	Bovine	395	3,129	1,305	3,481	77,273	10
Infected	Swine	152	1,265	507	1,387	31,567	10
Infected	Small ruminants	3	26	11	30	608	10
Buffer	Total	4,058	23,950	12,032	29,995	202,441	10
Buffer	Bovine	3,022	17,869	8,988	22,397	149,288	10
Buffer	Swine	1,206	7,443	3,711	9,462	56,669	10
Buffer	Small ruminants	26	157	79	199	1,431	10
Surveillance	Total	18,034	65,564	49,450	104,070	200,581	10

Surveillance	Bovine	13,334	47,883	36,420	76,477	144,105	10
Surveillance	Swine	5,499	19,232	15,042	31,569	54,601	10
Surveillance	Small ruminants	120	445	332	710	1,447	10
Infected	Total	583	4,222	1,785	4,804	164,089	20
Infected	Bovine	431	3,176	1,333	3,610	123,200	20
Infected	Swine	165	1,282	521	1,454	50,188	20
Infected	Small ruminants	3	27	11	31	1,114	20
Buffer	Total	4,357	24,247	12,303	30,900	216,163	20
Buffer	Bovine	3,240	18,082	9,177	23,106	156,541	20
Buffer	Swine	1,299	7,517	3,791	9,707	59,156	20
Buffer	Small ruminants	28	159	82	204	1,548	20
Surveillance	Total	19,295	66,457	50,148	105,943	203,462	20

Surveillance	Bovine	14,187	48,514	36,858	77,700	147,013	20
Surveillance	Swine	5,817	19,456	15,346	31,937	55,281	20
Surveillance	Small ruminants	128	453	340	720	1,498	20

Supplementary Table S6. Results for the predicted number of epidemics fade-out for each control and eradication strategy after 20 days of initial simulated infection.

Scenario	FMD fade out	Number of simulations (%)
Baseline control scenario: Vaccination of 5,000 animals/day + depopulation of 4 farms/day	Successfully control	7,194 (93.835%)
Baseline control scenario: Vaccination of 5,000 animals/day + depopulation of 4 farms/day	Unsuccessfully control	473 (6.17%)
Scenario one: Vaccination of 10,000 animals/day) + depopulation of 8 farms/day	Successfully control	7,508 (97.93%)
Scenario one: Vaccination of 10,000 animals/day) + depopulation of 8 farms/day	Unsuccessfully control	159 (2.07%)
Scenario two: Depopulation of 8 farms/day	Successfully control	6,079 (79.29%)
Scenario two: Depopulation of 8 farms/day	Unsuccessfully control	1,588 (20.71%)
Scenario three: Vaccination of 15,000 animals/day + depopulation of 12 farms/day)	Successfully control	7,550 (98.47%)
Scenario three: Vaccination of 15,000 animals/day + depopulation of 12	Unsuccessfully control	117 (1.53%)

farms/day))