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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Abstract

Foot-and-mouth disease (FMD) infects multiple food-animal species and disseminate among ungulate species. Here, we present a multiscale compartmental stochastic model that considers population dynamics, births, deaths, and species-specific transmission dynamics. The model considers two between-farm modes of FMD transmission integrating disease dynamics at the between-farm and within-farm levels. Our model outputs include the number of secondarily infected animals and farms, spatial dissemination, the role of animal movement and between-farm distances as transmission pathways, and the effectiveness of countermeasures. Here, we demonstrated that after 20 days of FMD dissemination, the median number of infected farms was 8. Spatial proximity was the predominant route associated bovine infection while in swine were linked with animal movements. Furthermore, the median distance between seeded and secondary infections was 5.77 with the highest spatial dissemination reaching 695.40 kilometers. The simulated control strategy results showed that depopulating 12 farms and vaccinating 15,000

farms per day after 20 days of silent FMD dissemination would contain 93.4% of epidemics with a median of 9 infected farms within 54 days after implementing control actions. In conclusion, the developed model highlights the need for developing multispecies FMD transmission models, especially in regions where multiple species are raised on the same premises.

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 that affects multiple species, including pigs, sheep, goats, and wildlife[1]. During the 2001 FMD epidemic in the U.K. and the Netherlands, more than 6.7 million animals were slaughtered, including those from healthy (preemptive measures) and infected farms [2]. The infected animals in both outbreaks were not solely from one species; for example, infection was also detected in goats on mixed dairy-goat/veal-calf farms[2,3]. The agricultural sector loss was approximately 3.2 billion euros, and there were additional costs to other sectors, such as tourism, with a total expenditure of approximately 2.7 to 3.2 billion euros[4]. In addition, the distribution of FMD outbreaks in South America has changed over the years, with the most recent outbreaks (in 2017 and 2018) occurring in Colombia[5]; no epidemics have been reported in Latin America since then, despite Venezuela's absence of official international status for FMD[6].

The official data from the World Organisation for Animal Health[7], consisting of more than 57,000 outbreaks in 99 counties from 1996 to 2012, show that 68% of FMD cases were associated with cattle, 22% with swine, and 21% with small ruminants and other species; buffalo were not directly mentioned[8]. Despite strong evidence indicating that all susceptible species can drive large FMD epidemics[9], such as the 2001 UK epidemic (traced back to an infected Essex

swine slaughterhouse[10]), control measures and surveillance programs have mostly targeted dissemination within cattle populations, thus neglecting the role of other species in FMD transmission[11].

Notably, FMD pathogenesis and transmission dynamics vary among species, given differences in viral loads needed to cause infection, viral latency and infection duration[12–15]. For example, swine shed more viral particles than cattle and sheep, with widespread epidemics expected when swine are also infected[14]. Thus, it is pivotal to consider such heterogeneity in transmission dynamics when modeling within- or between-farm FMD dissemination[11]. While between-farm transmission primarily occurs through direct contact among susceptible and infected animals[12,16], field observations and experimental trials have demonstrated the spread of the virus via indirect contact with fomites and long-distance transport of aerosols, a process known as spatial transmission[16].

Mathematical models have been widely used to investigate FMD epidemic propagation. Although significant technical and computational advancements have been achieved, these models are simplified because of computational costs and/or lack of details about herd structure (e.g., number of individuals, number born alive) and animal movements. The most common simplification is restricting the epidemiological models to a single species[4,17,18]. Despite the different applications and efforts in modeling FMD, outstanding questions remain regarding measurements of the epidemic trajectory and epidemic control strategies given heterogeneous transmission dynamics among the different susceptible species coexisting on the same farm[11].

In this work, we propose a novel multihost, single-pathogen, multiscale model that incorporates heterogeneous (species-specific) transmission dynamics. We present a quantitative assessment of each species' epidemiological role in FMD dissemination, aiming to quantify

transmission routes and the spatial distance of spread. Our simulations utilized population data, including birth and death information for the entire food-animal species population of Rio Grande do Sul, Brazil. Additionally, we examine the effectiveness of control and elimination actions according to the national FMD control plan[19], which includes i) vaccination; ii) depopulation; iii) various restrictions regarding between-farm movement; and iv) surveillance activities within control zones.

2. Material and Methods

2.1 Data sources

We collected information from 415,364 farms officially registered in Rio Grande do Sul, Brazil[20]. The data contained information on the population (of cattle and buffalo, pigs, and sheep and goats), number of farms, and daily between-farm movement and movements to slaughterhouses from January 1st, 2018 to December 31st, 2020. Population and movement data from cattle and buffalo farms were combined into one category: “bovines”. Similarly, we grouped sheep and goats into “small ruminants". Inspection of the population data revealed 5,709 (1.37%) farms with missing geolocation data; these farms were excluded from subsequent analysis. Further information about the species population distributions is available in Supplementary Figure S1. In Brazil, producers are required to report farming activities to the state animal health office once a year; this report includes information about food-animal production activities. We utilized producer-reported data combined with the 2020 data to classify farms as “active” if at least one food animal was present. Farms that were declared inactive by the producer or that had zero animals were considered inactive and were not included in this study. Therefore, our final active population included 409,655 farms.

2.2 Birth and death data

Similar to the requirements regarding the total number of individuals, producers must report the number of animals born alive and the number of animal deaths, including natural deaths. We accessed such data through the state database[20]. Producers can report birth and death data at any time throughout the year; however, reporting is mandatory at least once a year in a window from January 1st to May 30th. We collected 256,504 individual records associated with birth and death. The monthly births and deaths (by specie) is presented in Supplementary Figure S2. Farm population data were computed based on animal movement, birth, and death records; of the 409,655 farms, 1.14% were found to have negative populations. Farms with a negative population caused by animal movement or death were allocated a population value equal to their most recent positive population.

2.3 Movement data

From January 1st, 2018 to December 31st, 2020, 1,634,940 unique between-farm and slaughterhouse movements were registered in the state database. We inspected the movement data and found 181 movements missing farm identification, 93,871 movements with the exact identification of the origin and destination, 51,490 movements to or from other states, and 112,834 movements from or to farms with missing geolocation information. After removing these movement data, the final database comprised 1,564,487 movements and 73,823,866 animals transported (Supplementary Figure S3 shows the movement data variations over time).

2.4 Model formulation

We implemented a multihost, single-pathogen, coupled multiscale model to simulate FMD epidemic trajectories[21] with and without implementing control actions. This model led to the development of a novel R package, “MHASpread: A animal spread stochastic multilevel model” (version 0.1.0). MHASpread allows the explicit specification of species-specific transmission probabilities and latent and infectious periods of a disease that infects multiple species. The within-farm level includes the entry and exit of animals due to between-farm movements, movements to slaughterhouses, births, and deaths for each species (Figure 1). Between-farm movements and spatial proximity drive the between-farm dynamics.

2.5 Within-farm dynamics

The within-farm dynamics consist of mutually exclusive health states (i.e., an individual can only be in one state per discrete time step) for animals of each taxa (bovines, swine, and small ruminants). These health states (hereafter, “compartments") include susceptible (S), exposed (E), infectious, (I), and recovered (R), defined as follows:

(i) Susceptible: animals that are not infected but susceptible to infection.

(ii) Exposed: animals that have been exposed to disease but not yet infected.

(iii) Infectious: infected animals that can successfully transmit the infection.

(iv) Recovered: animals that have recovered and are no longer susceptible.

Here, we also consider the birth and death data described in the section above. The total population is calculated as $N = S + E + I + R$. The number of individuals within each compartment transitions from $S\beta \rightarrow E$, $1/\lambda_1 \rightarrow I$, $1/\lambda_2 \rightarrow R$ according to the following equations:

$$\frac{dS_i(t)}{dt} = u_i(t) - v_i(t) - \frac{\beta S_i(t) I_i(t)}{N_i} \tag{1}$$

$$\frac{dE_i(t)}{dt} = \frac{\beta S_i(t) I_i(t)}{N_i} - v_i(t) E_i(t) - \frac{1}{\lambda_1} E_i(t) \tag{2}$$

$$\frac{dI_i(t)}{dt} = \frac{1}{\lambda_1} E_i(t) - \frac{1}{\lambda_2} I_i(t) - v_i(t) I_i(t) \tag{3}$$

$$\frac{dR_i(t)}{dt} = \frac{1}{\lambda_2} I_i(t) - v_i(t) \tag{4}$$

In these equations, births are represented by the number of animals born alive ($u_{i,t}$) that enter the S compartment on farm i at time t according to the day-to-day records; similarly, $v_{i,t}$represents the exit of the animals from any compartment due to death at time t (Figure 1). The transition from E to I is driven by $1/\lambda_1$ and the transition from I to R is driven by $1/\lambda_2$; these values are both drawn from the distribution generated from each specific taxa according to the literature (Table 1). As infection progresses, animals transition into a recovered (R) state based on $1/\lambda_2$ (derived from the infectious period); both λ_1 and λ_2 are specific to the host taxa (Table 2).

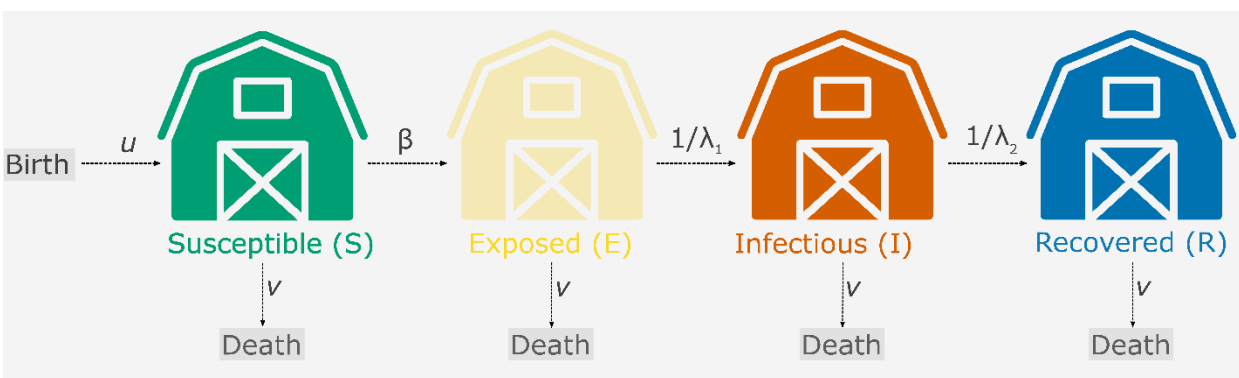

Figure 1. Within-farm dynamics. The framework represents the transition between compartments, $S\beta \rightarrow E$, $1/\lambda_1 \rightarrow I$, $1/\lambda_2 \rightarrow R$. Susceptible animals ($u$) are introduced in the S compartment, whereas deaths (v) were removed from any compartment.

For within-farm dynamics, we assumed that populations were homogeneously distributed and that species were homogeneously mixed. The frequency-dependent transmission depends on both the infected and the susceptible host taxa, as reflected by the species-specific FMD transmission coefficient β (Table 1, Supplementary Figure S4, and Figure 2A). Similarly, the transition from E to I and from I to R occurs according to each taxon's parameters (listed in Table 1).

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

Infected taxon	Susceptible taxon	Transmission coefficient (β), shape and distribution	Reference
Bovines	Bovines	PERT (0.018, 0.024, 0.056)	Calculated from the 2000-2001 FMD outbreaks in the state of Rio Grande do Sul[22]
Bovines	Swine	PERT (0.018, 0.024, 0.056)	Assumed
Bovines	Small ruminants	Triangular (0.020, 0.026, 0.031)	[23,24]
Swine	Bovines	PERT (0.014, 0.044, 0.033)	[25]
Swine	Swine	PERT (0.014, 0.044, 0.033)	[25,26]
Swine	Small ruminants	PERT (0.014, 0.044, 0.033)	[25]
Small ruminants	Bovines	PERT (0.012, 0.031 0.065)	[27]
Small ruminants	Swine	PERT (0.006, 0.024, 0.09)	[28]

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 parameter	Taxon	Distribution	Reference
Latent period, λ_1	Bovines	Weibull (a = 1.78, b = 3.97)	29
	Swine	Log-logistic (shape = 7.60; scale = 1.06)	14
	Small ruminants	PERT (m = 3.96, a = 0, b = 13.98)	29
Infectious period, λ_2	Bovines	Gamma (a = 3.97, b = 1.11)	29
	Swine	Weibull (shape = 7.16; scale = 11.04)	14
	Small ruminants	Pearson type 5 (a = 6.19, b = 17.19)	29

Note: The time unit is days.

2.6 Between-farm dynamics

For the farm-level dynamics, we considered two transmission pathways: i) between-farm movements and ii) spatial transmission. We utilized the number of unique movements (batches) and animals from each taxa to model between-farm transmission and considered the current within-farm transmission dynamics (Figure 2). For each movement batch, we determined the

corresponding infection status of the available population at the farm of origin to determine the proportions of animals in each compartment transferred to the destination farm (Figure 2B). Animal movements to slaughterhouses were similarly considered; we drew the number of animals to be removed from the current state of the system (Figure 2B).

2.7 Spatial transmission dynamics

Spatial transmission encompasses a variety of transmission processes, such as airborne transmission, animal contact over fence lines and equipment sharing between farms. We also used each farm's geolocation to group farms according to a grid hexagon of 0.76 km, representing an area of 503,516 m^2 (Supplementary Figure S5A). Farms within the same hexagon had the same spatial transmission probability (Figure 2C). Local spread was fitted using a spatial transmission kernel, in which the likelihood of transmission decreased as a function of the between-farm distance. The probability PE at time t describes the probability that a farm becomes exposed and is calculated as follows:

$$PE_j(t) = 1 - \prod_i \left(1 - \frac{I_i(t)}{N_i}\varphi e^{-\alpha d_{ij}}\right) \tag{5}$$

where j represents the uninfected population and ad_{ij} represents the distance between farm j and infected farm i, with a maximum of 40 km. Given the extensive literature on distance-based FMD dissemination and a previous comprehensive mathematical simulation study[30], distances above 40 km were not considered. Here, $1 - \frac{I_i}{N_i}\varphi e^{-\alpha d_{ij}}$ represents the probability of

transmission between farms i and j (scaled by infection prevalence on farm i, $\frac{I_i}{N_i}$) given the distance between the farms in kilometers (Supplementary Figure S5B). The parameters φ and α control the shape of the transmission kernel; $\varphi = 0.12$ is the probability of transmission when $d_{ij} = 0$, and $\alpha = 0.6$ controls the steepness with which the probability declines with distance[31].

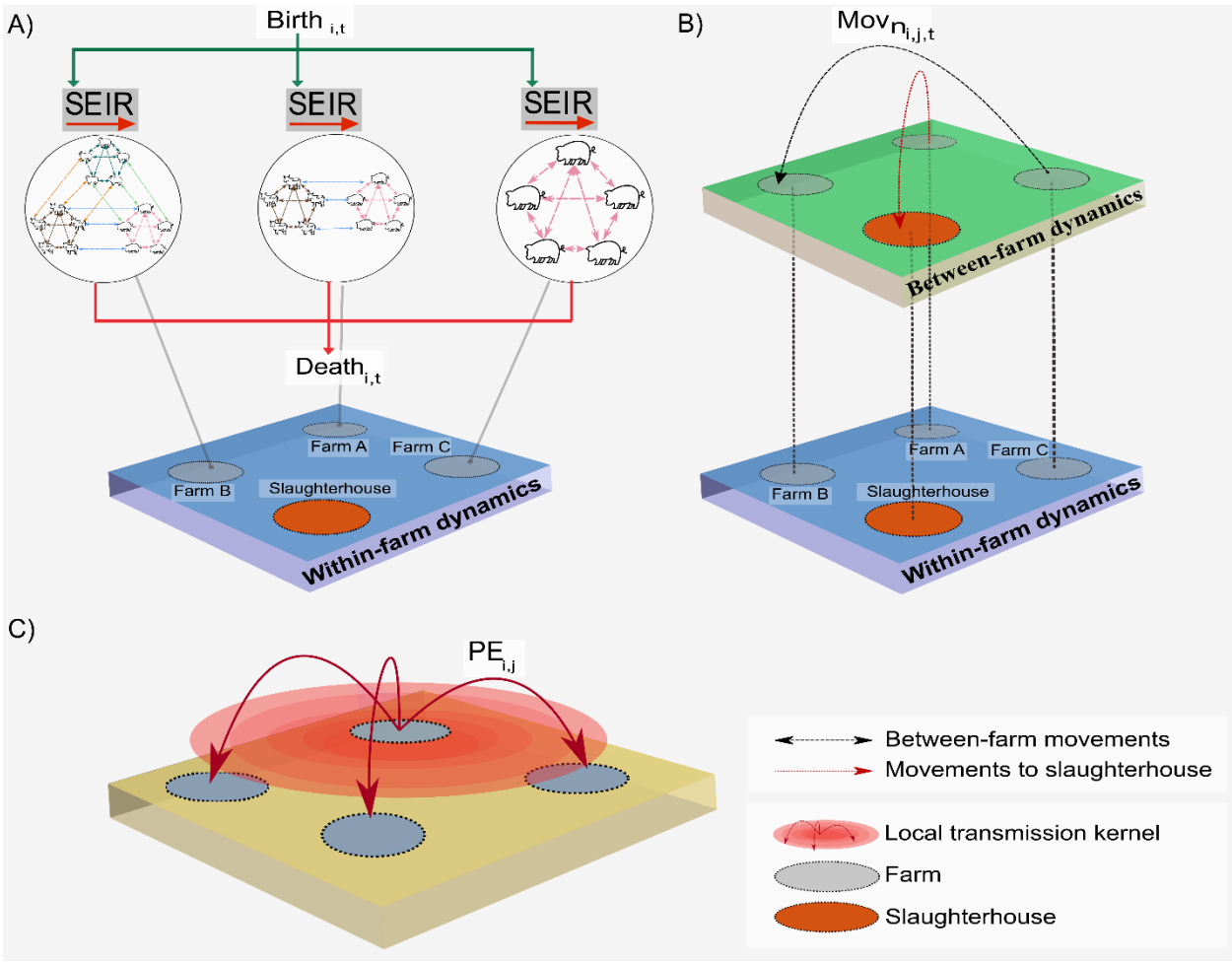

Figure 2. Schematic of state transitions during within-farm and between-farm dynamics. A) Within-farm dynamics: green arrows indicate the introduction of animals (births) into the susceptible (S) compartment at farm i at time t. Each circle indicates a farm with single or multiple taxa with specific host-to-host transition parameters (β, λ_1, λ_2); dashed lines represent interactions within and between host taxa. The red arrows represent the removal of animals

(deaths) regardless of infection status. B) Between-farm dynamics: the layer represents the number of animals moved (batches; n) from the farm of origin (i) to a destination farm (j) at time t (indicated by the black dashed arrows). Animals moved to the slaughterhouse were removed from the simulation regardless of their infection status and are indicated by red dashed arrows. C) Spatial transmission distances.

2.8 Initial model conditions

We used 2018 population data to represent the initial susceptible population. However, the sheer number of farms (409,655) within Rio Grande do Sul constituted a computational bottleneck; we therefore drew a representative sample to model the Rio Grande do Sul population. Briefly, a multistage and stratified sample was collected according to the number of farms containing each taxa per municipality[32]. The sample size was obtained by considering a prevalence of 50% with a level of significance of 95% and a margin of error of 1%, resulting in a total of 15,721 farms used to seed FMD infection for ten repeats. Each repeat was given a random start date between January 1st, 2018 and December 31st, 2020, commencing with one infected animal. In farms with more than one species, the infection seed priority order was as follows (in descending priority): bovines, swine, and small ruminants. Of note, we assumed that all animals were susceptible to FMD because the annual vaccination campaign has been suspended in Rio Grande do Sul since May 2021[22].

2.9 Local sensitivity analysis

We used a combination of Latin hypercube sampling (LHS), developed by McKay[33], and the partial rank correlation coefficient (PRCC) technique to perform a local sensitivity analysis. LHS

is a stratified Monte Carlo sampling method without replacement that provides unbiased estimates of modeling output measures subject to combinations of varying parameters. The PRCC approach can be used to classify how output measures are influenced by changes in a specific parameter value while linearly accounting for the effects of other parameters[34]. As input model parameters, we selected the parameters and distributions listed in Tables 1 and 2 with population sizes of each host taxa (bovines, swine, and small ruminants) ranging from ten to 1,000. In total, 18 parameters were used to classify the monotone relation infection status with our input variables to classify model sensitivity. The inputs include one farm where the initial conditions varied across 10,000 simulations over the LHS space. A positive PRCC indicates a positive relationship with the number of infected animals, whereas a negative PRCC indicates an inverse relationship with the number of infected animals; however, the magnitude of PRCC does not necessarily indicate the importance of a parameter[35].

3.1 Evaluation of control and eradication scenarios

We simulated FMD epidemic trajectories for up to 20 days after the initial outbreaks were seeded. The decision to implement control actions at a maximum of 20 days was based on historic FMD outbreak data in the region and consultation with local animal health officials. Consequently, our simulated control actions were implemented after ten and 20 days of silent FMD dissemination. Thus, the initial numbers of infected farms at ten and 20 days under a predefined baseline control scenario based on the national FMD response plan[36] were compared with the numbers of infected farms after implementing the three alternative control scenarios described below.

Baseline control scenario: This scenario constituted the national FMD control and eradication plan[36], which includes the following measures: i) depopulation of infected farms, ii) vaccination of uninfected farms, iii) cessation of animal movement for 30 days, and iv) establishment of three distinct control zones around infected farms at the following distances: 3 km (infected zone), 7 km (buffer zone), and 15 km (surveillance zone) (Supplementary Figure S6). In the infected zones, infected farms are depopulated as FMD is detected, and vaccination is implemented first in uninfected farms within these infected zones. If vaccine doses are still available after vaccinating the farms in the infected zones, then farms in buffer zones will be vaccinated. Surveillance activities are defined as clinical examinations. In our simulation, all farms within control zones were visited every three days. Contact tracing was used to identify farms with direct links to infected farms within the past 30 days; these farms underwent surveillance. If positive cases were detected in these farms, animals were moved into the infected compartment. We also incorporated the state budget as follows: i) the maximum number of farms depopulated per day was set to four, and ii) the maximum number of animals vaccinated per day was set to 5,000; both assumptions are based on the state's maximum personnel and equipment capacity (personal communication, Animal Health Official Working Group). We also included a delay in the implementation of vaccination equal to seven days after the first case was detected; vaccination was assumed to be effective immediately, and thus vaccinated animals were moved into the recovered compartment. In addition, we assumed that i) surveillance was 100% sensitive to FMD and ii) farms exhibited 100% compliance with the 30-day animal movement cessation.

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

Scenario 1: Vaccination & depopulation. This scenario differed from the baseline control scenario by increasing the depopulation and vaccination of farms, with depopulation of infected farms set to eight (vs. four) farms per day and vaccination set to 10,000 (vs. 5,000) animals per day.

Scenario 2: Depopulation only. This scenario differed from the baseline control scenario by increasing the depopulation of infected farms to eight (vs. four) per day.

Scenario 3: Enhanced vaccination & depopulation. This scenario differed from the baseline control scenario by extensively increasing the depopulation and vaccination of farms, with depopulation of infected farms set to 12 (vs. four) per day and vaccination set to 15,000 (vs. 5,000) animals per day.

3.2 Model outputs

Our simulations tracked the number of animals and farms in each health compartment at each daily time step. We also utilized the epidemic trajectories to calculate the geodesic distances between the seeded infections and secondary cases. In addition, we determined the probability of distance-dependent transmission by calculating the cumulative empirical spatial distribution. By tracing the average number of secondarily infected animals resulting from each transmission route, we estimated the contribution of between-farm movement and spatial transmission to infection in each taxa; here, we present the average contribution of each route along with credible intervals estimated by using an equal-tailed interval method[37]. We also determined the numbers of animals and farms within control zones at 10 and 20 days post-FMD dissemination.

We used 10 and 20 days of silent FMD spread as the initial model conditions. We first removed simulations with more than 400 infected farms because such large epidemics exceeded

the maximum capacity of the State of Rio Grande do Sul (State Animal Health Official, personal communication, 2022). We then implemented control actions in the remaining simulations (99.51%). Simulations with control actions were then classified according to the success of FMD elimination. Specifically, simulations were categorized as having unsuccessful FMD elimination if the number of infected farms exceeded 450 or the control action duration exceeded 100 days; otherwise, the simulations were considered successful. Finally, we tracked the number of days that control actions were applied.

The software used to develop MHASpread, graphics, and maps was R v. 4.1.1[38] in RStudio with the following packages: sampler [39], tidyverse[40] (Wickham et al., 2019), sf [41], brazilmaps[42], doParallel[43], and lubridate[44].

3. Results

3.1 Farm- and animal-level FMD temporal dynamics

Of 15,721 seeded infections, 10,473 simulations started in bovine farms, 5,179 in swine farms, and 69 in small-ruminant farms; 4,702 farms (29%) had multiple taxa on the same premises. Examining the epidemic trajectories at 20 days after infection seeding, we estimated a median of 15 (IQR: 5-41) infected animals, of which 12 (IQR: 4-32) were bovines, 5 (IQR: 2-12) were swine, and 1 (IQR: 1-2) was a small ruminant (Supplementary Table S1 and Figure S7). The compartment distribution at 10 and 20 days after each animal-level infection was seeded is shown in Supplementary Table S1.

The FMD distribution at the farm level after 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) were swine farms, and 1 (IQR: 1-1) was a small-ruminant farm (Figure 3). We observed

large-scale epidemics with up to 2,197 infected farms; however, these rare events were outside the 95% credibility interval (CI) (Figure 3). The farm-level infection distribution at 10 and 20 days after infection seeding is available in Supplementary Table S2.

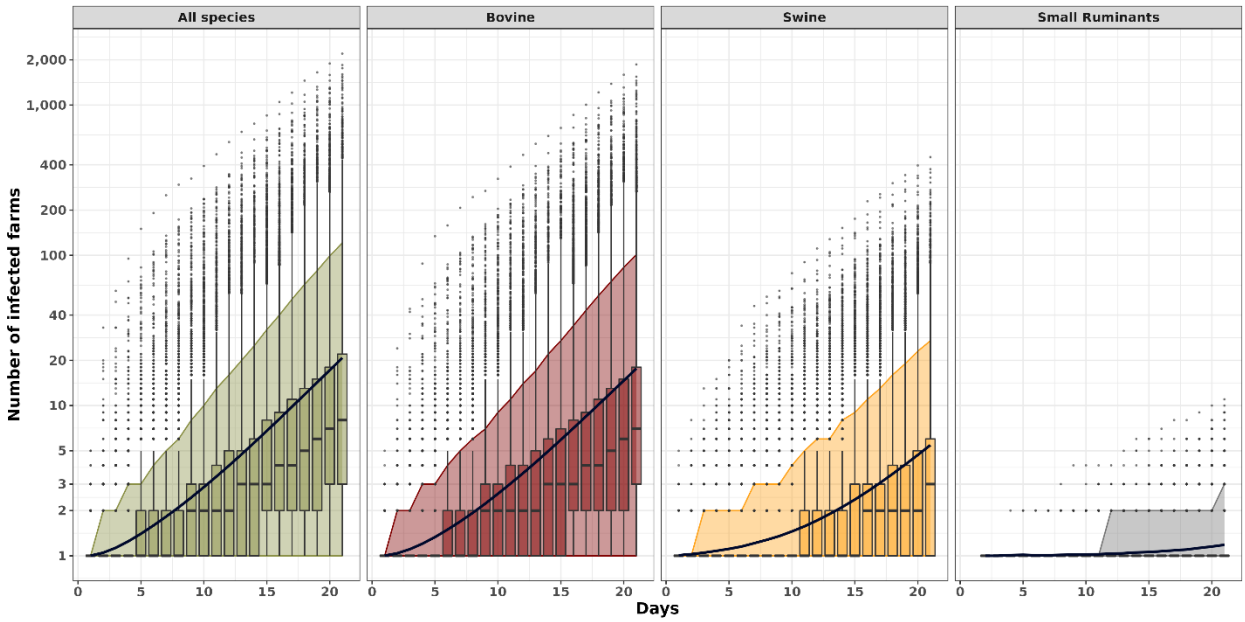

Figure 3. Distribution of the daily number of infected farms. The boxplots with outliers show the number of infected farms. The colored background area represents the 95% credible interval for the daily number of infected farms. The y-axis is on a $\log_{10}$ scale.

3.2 Contribution of each transmission route

We evaluated the contributions of the between-farm and spatial-transmission routes. Overall, during the first 17 days of FMD dissemination, the main transmission route was animal movements, which led to a daily average of 4.9 (CI: 1-23) newly infected animals; however, at 20 days after FMD dissemination, spatial transmission was by far the dominant route, with a daily average of 11 (CI: 1-95.6) newly infected animals. We then examined transmission contributions by taxa. At 10 days, bovine infection shifted from spreading via animal movement to spreading via spatial transmission. At 20 days, new bovine infections occurred predominantly

by spatial transmission, with an estimated average of 10.7 (CI: 1-57) new infections per day, while animal movement resulted in an average of 4.5 (CI: 1-32) new infections. For swine, animal movement was the most critical route throughout the simulation period; at 20 days, animal movement generated an average of 11.4 (CI: 1-123) newly infected pigs, while spatial transmission produced an average of 3.1 (CI: 1-90) newly infected pigs. Finally, for small ruminants, both routes appear to have a similar contribution (Figure 4). The summary statistics of the contribution of each route at 10 and 20 days are available in Supplementary Table S3.

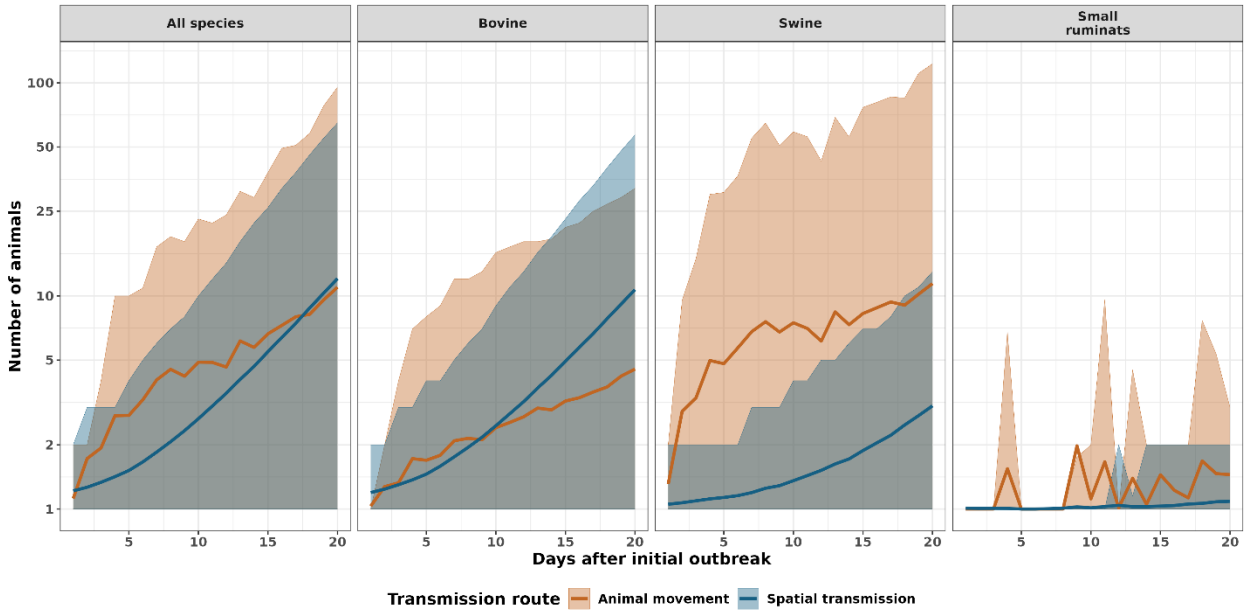

Figure 4. FMD transmission due to between-farm movement or spatial transmission. The x-axis represents the number of days after the FMD infection was seeded. The y-axis (represented on a $\log_{10}$ scale) shows the number of newly infected animals, the solid line represents the average number of infected individuals, and the colored background represents the 95% credible interval.

3.3 Spatial transmission dynamics

Of the 15,721 seeded infections, 386,043 simulations generated secondary infections. The median distance between seeded 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; the maximum dispersal distance was 695.40 km (Figure 5A). As noted in Figure 5B, the probability of infection decreased by 11% at 20 km compared with one km.

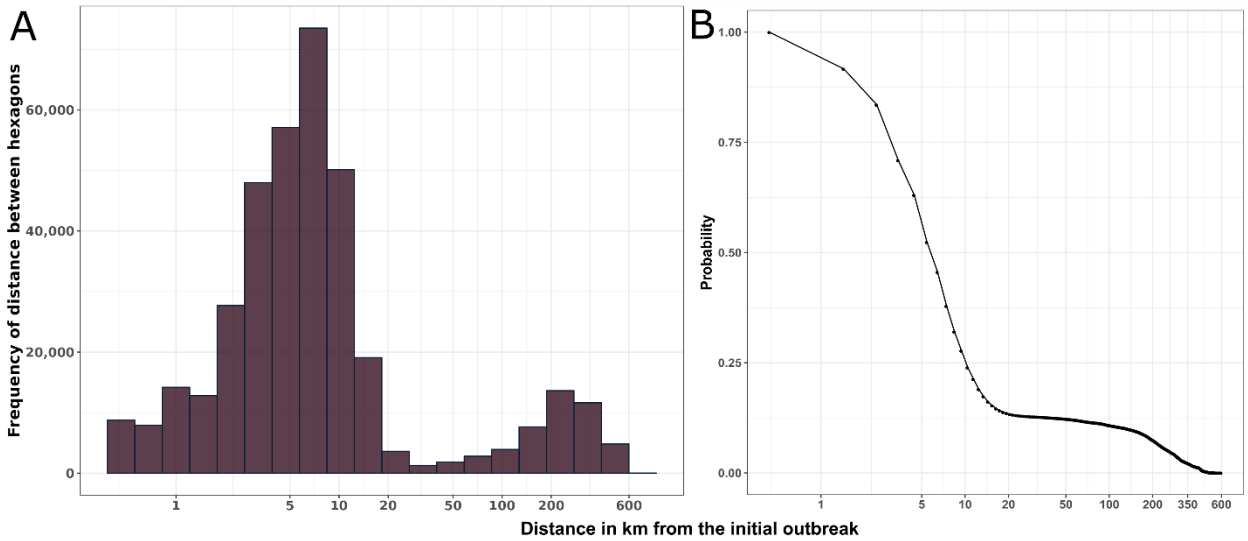

Figure 5. Distribution of the cumulative epidemic distances. A) Frequency histogram of secondary infections at varying distances from the seeded infection. B) Empirical cumulative distribution function (1-ECDF) probability of infection according to distances from the initial outbreak. Both x-axes are a $\log_{10}$ scale.

3.4 Sensitivity analysis

We evaluated the sensitivity of 18 model parameters with weights ranging from -0.17 to 0.24; this sensitivity indicated a limited influence of model parameters on the number of simulated secondary infections. Specifically, λ_1 of each host taxa had a negative influence on the number of secondary infections; in contrast, β for small ruminants to swine, small ruminants to bovines, and small ruminants to small ruminants as well as λ_2 for small ruminants positively influenced

the number of secondary infections. The complete sensitivity analysis results are depicted in Supplementary Figure S10.

3.5 Effectiveness of control strategies

On day 20 of silent FMD dissemination, infected zones contained a median of 8,660 (IQR: 308 - 53, max: 783) animals and 1,785 (IQR: 583 - 4,804) farms; in buffer zones, the median was 77,679 (IQR: 2,408 - 384,439) animals, and 2,303 (IQR: 4,357 - 30,900) farms; and within surveillance zones, the median was 369,541 (IQR: 9,599 - 1,460,202) animals and 50,148 (IQR: 19,295 - 105,943) farms (Figure 6 and Supplementary Figure S8, for the animal-level distributions). Results at 10 days at the animal level are shown in Supplementary Table S4 and Supplementary Figure S9; at the farm level, they are shown in Supplementary Figure S11 and Table S5.

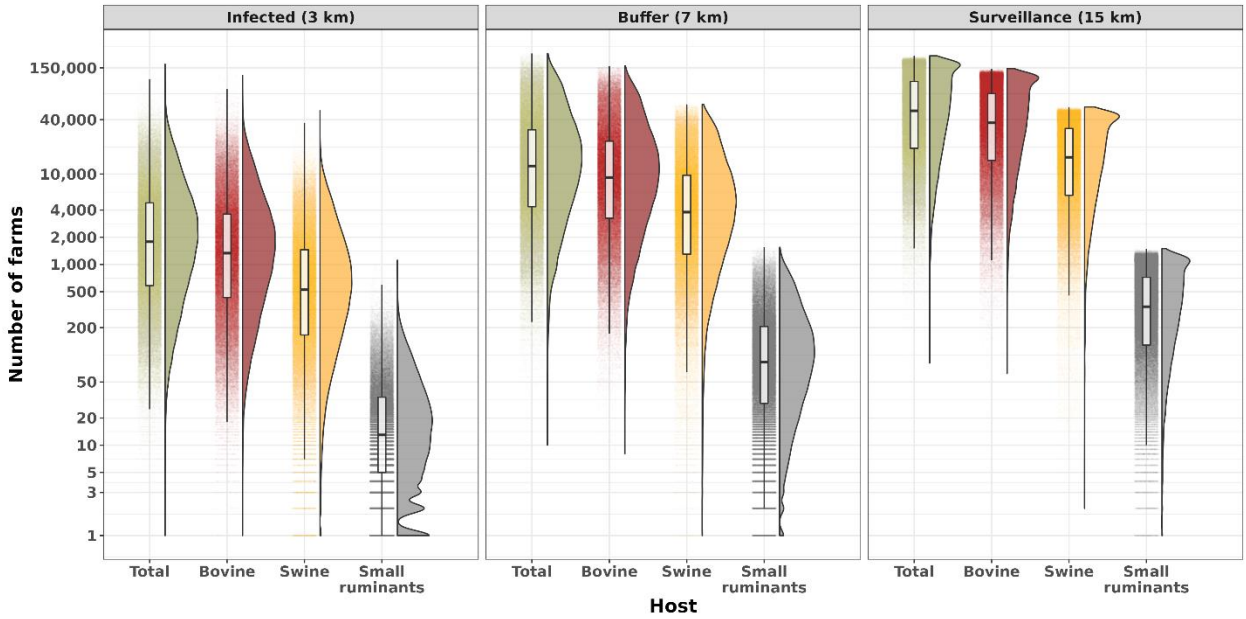

Figure 6. Distribution of farms within control zones at 20 days after the initial infection. The y-axis shows the number of animals within infected zones, buffer zones, and surveillance zones on a $\log_{10}$ scale. The box plots (left) include outliers and the density distribution (right).

As expected, the number of days necessary to eliminate most epidemics was dependent on the number of secondary infections at 20 days and the duration of control action implementation (Figure 7). The baseline control scenario handled 93.4% of the epidemics with a median of 9 (IQR: 3 - 23, max: 221) infected farms; scenario one, which has twice the depopulation and vaccination rates of the baseline scenario, eliminated 97.8% of the simulated epidemics with a median of 10 (IQR: 4 - 26, max: 223) infected farms. Scenario two (depopulation only) eliminated 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 involved depopulation and vaccination rates three times those of the baseline control scenario, could control 98.3% of epidemics with a median of 10 (IQR: 4 - 26, max: 248) initially infected farms (Figure 7 and Supplementary Table S6). Regarding 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 simulated epidemics with a median of 116 (IQR: 82-161, max: ≥400) infected farms, while scenarios one and three were unable to eliminate epidemics with medians of 183 (IQR: 152 - 244, max: ≥400) and 203 (IQR: 170 - 264, max: ≥400) initially infected farms, respectively (Figure 7).

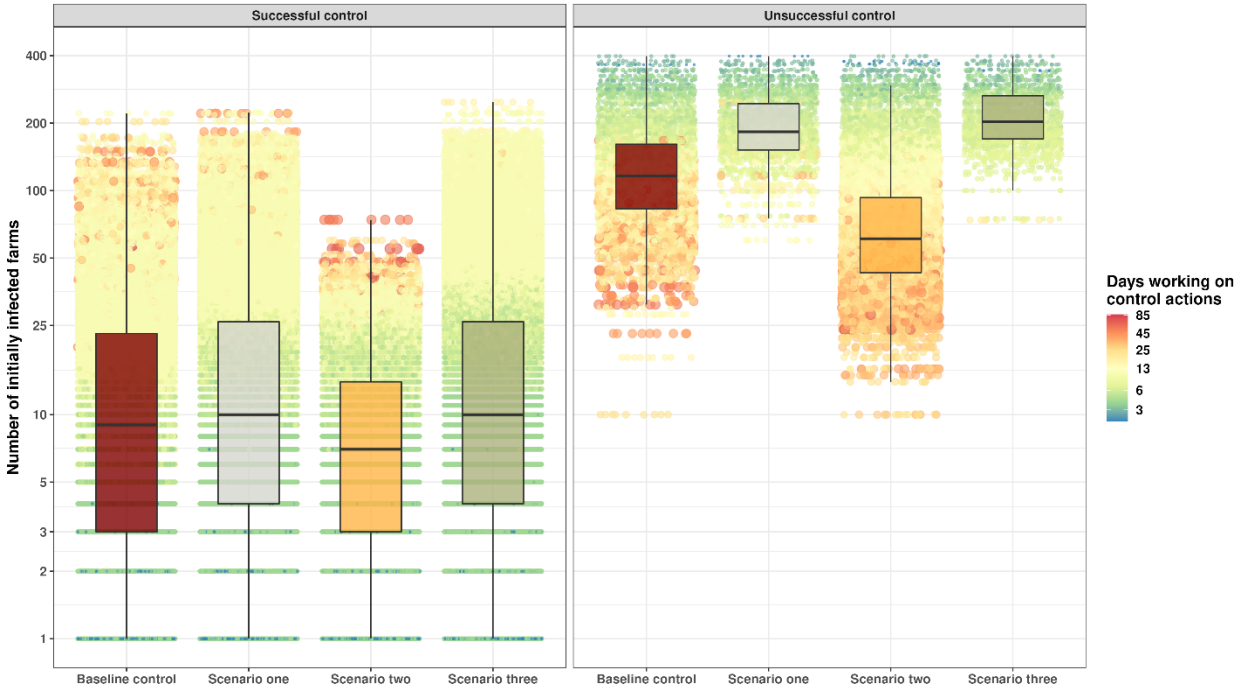

Figure 7. Distribution of successfully and unsuccessfully halted FMD epidemics under four control and eradication scenarios of 20 days of silent spread. The box plot (y-axis: $\log_{10}$ scale) shows the distribution of secondarily infected farms before the implementation of control actions. The background scatter plot represents each stochastic simulation, in which the color represents the number of days since control and eradication actions were implemented. The x-axis represents the control action scenarios implemented to halt the epidemic.

Of the successfully halted epidemics shown in the left panel of Figure 7, the baseline control scenario and scenario two eliminated all epidemics within 99 days after implementing control actions (Figure 8). In contrast, scenarios one and three took only 84 days and 54 days, respectively, to eliminate the simulated epidemics (Figure 8).

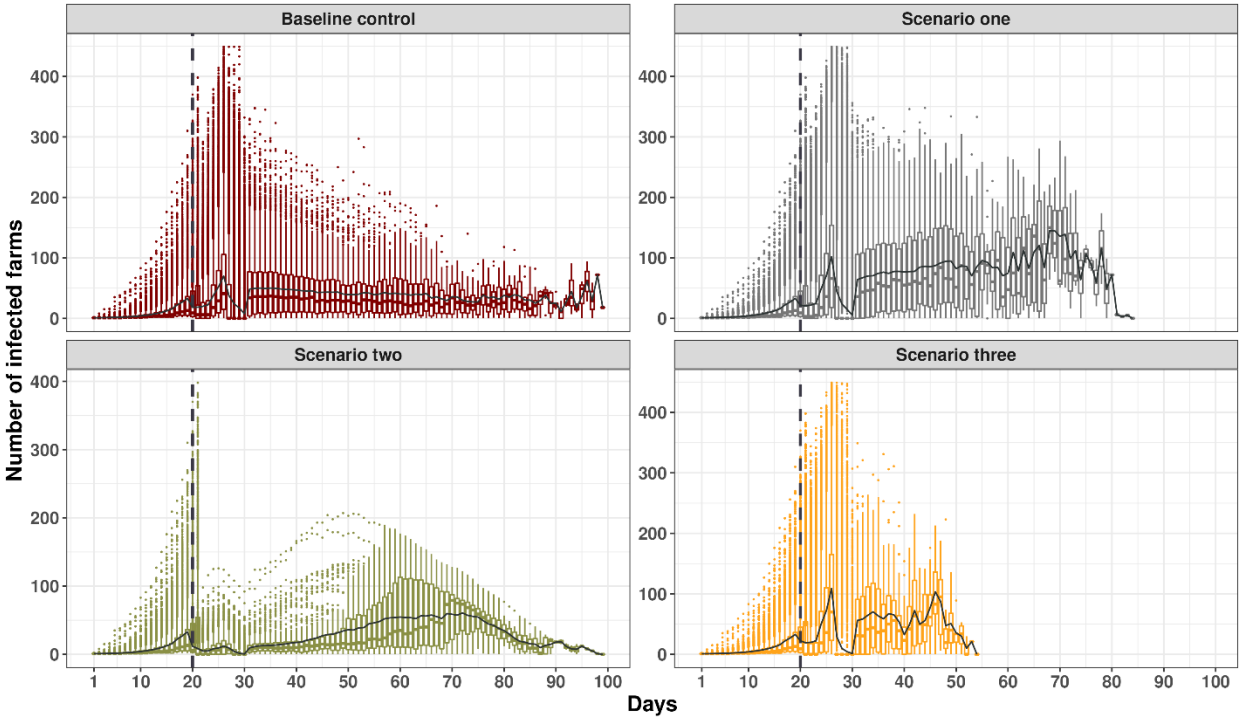

Figure 8. Average number of days to successfully eliminate FMD epidemics. The vertical dashed line marks the 20th day of silent FMD spread and the implementation of control actions. The solid black line represents the average daily number of infected farms. In addition, we simulated control actions starting 10 days after seeding. The initial infection is described in greater detail in the Supplementary Material ("Effectiveness of control actions started 10 days after initial simulated infection").

4. Discussion

We developed a multiscale and multispecies stochastic model that explicitly incorporated species-specific transmission coefficients. However, even after including interactions among different taxa, bovines remained the most infected taxa in the simulated epidemics, followed by swine and small ruminants. Animal movement was the most effective transmission route at the beginning of the epidemic, after which bovine infection developed predominantly by spatial

transmission, while swine infection developed mainly through between-farm movement for the first 20 days. Our results also demonstrated that most (74.7%) secondary cases resulted from spread to farms within 10 km of the initially seeded infection. We also demonstrated that the baseline control scenario and alternative scenarios were able to eradicate most epidemics within 100 days from the start of the simulated outbreaks.

By incorporating population characteristics and between-farm animal movements in the State of Rio Grande do Sul, we demonstrated that FMD is likely to disseminate between different taxa, e.g., bovines to swine and vice versa, regardless of which taxa was infected first (Supplementary Figure S14). The preferred route of infection was not consistent across taxa, a phenomenon that has been demonstrated previously[45]. Specifically, until day 17, between-farm movement was the predominant dissemination route of swine and small ruminants, whereas for bovines, spatial transmission became the preferred transmission route at day 10. This dominance of spatial transmission later in the epidemic may be explained, at least to some degree, by climactic conditions (i.e., cool temperatures and high humidity) in some regions that favor the spread of FMD[4,30,46], areas with a high density of farms and spatial clustering. More importantly, given the high connectivity of bovine farms in some municipalities[47], the initial peak in bovine infection could be explained by animal movement, while the shift toward spatial transmission could have been facilitated when secondary cases spread into densely populated areas with up to 12.23 farms per km^2 [47]. These densely populated areas coincide with areas in our simulations in which control actions were not sufficient to eliminate large-scale epidemics (Supplementary Figure S15). Even though we considered two main transmission routes, data regarding other important indirect transmission routes, such as fomites and transportation vehicles, were not considered[1,48]. Importantly, when we evaluated swine infection, animal movements were by far

the most relevant transmission pathway, consistent with other findings [49,50]. Regarding small-ruminant dynamics, we did not determine any dominant transmission route. Even though small ruminants did not significantly contribute to FMD dissemination, their contribution was not negligible. Thus, we suggest prioritizing control interventions by improving animal traceability early in an FMD epidemic, especially within the first 10 days; if FMD is detected after 10 days of dissemination, enhancing surveillance activities within control zones should be prioritized.

Assuming that animal health official veterinarians can vaccine 1,000 animals per day (personal communication, animal health officials), simulations in which FMD was identified at 20 days after the initial infection would require 160 veterinarians to oversee an average of 4,222 farms within infected zones and administer approximately 53,434 vaccine doses (if all taxa are vaccinated) or 21,640 vaccine doses (without vaccinating swine). If vaccination is also deployed in buffer zones, 320,223 vaccine doses and 961 veterinarians (all taxa) or 137,046 vaccine doses and 411 veterinarians (without vaccinating swine) would be needed. Similar modeling work in Denmark has predicted an average of 22 epidemics that last 34 days would need 123 veterinarians[31]. Importantly, the estimated number of veterinarians and vaccine doses in our study was similar to those recorded by the UK and Argentina during their past large-scale outbreaks that included up to 398 secondarily infected farms[51,52]. If such a large-scale epidemic was to occur in Rio Grande do Sul, there would not be sufficient animal health officials to implement the various disease control activities nor sufficient vaccine doses. Hence, future work should focus on estimating not only the necessary number of animal health officials but also administrative, direct, and indirect costs, including those resulting from large-scale epidemics. In addition, the revised transmission model should include longer delays in disease detection (e.g.,

30 days or 40 days), the necessary biosecurity downtime between farm visits, and other relevant logistical roadblocks linked to controlling and eliminating large-scale FMD epidemics [51].

Several modeling studies have demonstrated the effectiveness of combining vaccination and depopulation to achieve FMD eradication[53–55], with some exceptions in high-density livestock areas, such as in the Netherlands, where vaccination combined with ring culling was insufficient[31]. In our study, scenarios that combined vaccination and depopulation were consistently more effective than depopulation alone (Figures 7 and 8). One potential explanation is related to the predominance of spatial transmission, since most simulated FMD cases occurred within a median of seven km from infected farms, which falls within the infected zones. Even though the use of depopulation alone exhibited the lowest rate of successful FMD elimination, this strategy was still able to eliminate small-scale epidemics (with maximum of 74 infected farms). One advantage of eliminating FMD without vaccination is the speed at which the state could reclaim an FMD-free status[56]. Regarding our alternative control scenarios, scenario three was the most aggressive and most effective; this scenario assumed that the state would be able to depopulate 12 farms and vaccinate 15,000 farms per day. Unfortunately, this strategy was still unable to eliminate large-scale epidemics (with more than 400 infected farms detected after 20 days of silent FMD dissemination). Ultimately, to eliminate all simulated epidemics, we estimated that 120 farms would need to be depopulated and 25,000 animals would need to be vaccinated within seven days; these recommendations are extremely unrealistic given the current staffing and available resources in the State of Rio Grande do Sul, Brazil. Thus, we reached the same conclusion as the modeling work in Austria: the number of animal health officials needs to be doubled to eliminate large-scale epidemics[31,53,57]. Even though large-scale FMD epidemics are expected to challenge veterinary services worldwide, our simulations in Rio Grande do Sul

showed that secondary infections at three to 23 infected farms would be eliminated within 100 days, even using the baseline control scenario. While we simulated 100 days of control action implementation, most epidemics could be eliminated within 50 days if there were enough veterinarians to depopulate 12 farms and vaccinate 15,000 animals per day (i.e., scenario three). It is also important to consider the profile of infected farms, such as location and the size of the farm's contact network[47], along with the results of these simulations, to reach more informed decisions. Finally, as described earlier, we assumed full compliance with all associated surveillance actions and movement restrictions; thus, the results should be interpreted in this light.

5. Limitations and Further Remarks

We have identified a number of limitations, mostly related to assumptions made in the control scenarios. We utilized the FMD outbreak in 2000-2001 as well as published data to select transmission parameters that could impact the final simulations. Our sensitivity analysis of the population characteristics, latent and infection periods, and β of each taxa did not indicate that these parameters significantly affected the number of infected animals. Thus, our model has an acceptable level of robustness. Additionally, other important between-farm transmission routes, such as transportation vehicles and farm-staff movements, which have been previously associated with FMD dissemination[58,59], were not included in our model. If such indirect contact networks are considered, the results would likely change, and model realism would be improved[53].

We assumed 100% compliance with the restriction of between-farm movement from infected farms and farms directly linked to infected farms as well as the restriction of movement

into and from control zones; we also assumed that the disposal of depopulated animals eliminated any possibility of further dissemination. Nevertheless, real-world compliance with the control actions is not perfect, and future work could consider partial compliance with movement restriction and delays in the time and effectiveness of depopulation to increase model realism. Additionally, given the volume of vaccines necessary to vaccinate animals in infected and buffer zones, further work should consider restricting vaccination to each taxa, thus allowing benchmarking and better estimation of vaccine stockpiles[54,55,60]. Another limitation of the present study is that we assumed vaccination provided instantaneous efficacy, which is an obvious model simplification; in a future version of this model, vaccination waning should be considered.

Notably, FMD virulence, infectivity, and transmission can also vary among strains[1,13]. Even though the most recent outbreaks in the State of Rio Grande do Sul were caused by serotypes O and A [22], we cannot rule out the possibility that other strains were introduced and exhibited different dissemination patterns. Future work could include transmission scenarios with strains circulating in neighboring countries.

To our knowledge, this is the first FMD transmission model developed for Latin American countries. While previous FMD transmission models have included multiple species in their transmission dynamics [30,31,55,60], to our knowledge, none have explicitly considered the heterogeneity of transmission rates among species. Another unique feature of our model is the estimation of successful and unsuccessful epidemic management strategies while also assessing the maximum number of outbreaks and the number of days needed to complete FMD elimination. Thus, we provided rules of thumb for the four main control and eradication strategies by estimating the number of secondary infections that the simulated scenarios could eliminate. These results thus offer scientific support to decision-makers.

In addition, rather than selecting a limited number of farms to seed infection, our modeling approach was designed to generate a fair representation of the entire at-risk population. While our approach was more computationally expensive, our results provide policy-makers with an overview of all possible introduction scenarios, which 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 data and between-farm movement data from Rio Grande do Sul, the interpretation of our findings should not be extrapolated to other Brazilian states. However, since the MHASpread model infrastructure is highly flexible, if the necessary population data and animal-movement data is made available, MHASpread can be easily extended to other Brazilian states and, possibly, other Latin American countries.

6. Conclusion

After 20 days of silent FMD dissemination, we estimated that the number of secondarily infected farms ranged from three to 22. Early detection was pivotal to the success of FMD elimination, and we demonstrated that the deployment of depopulation alone was effective in simulations with up to 22 infected farms. However, large-scale epidemics required the depopulation of 100 farms and vaccination of 25,000 animals per day to eliminate 100% of simulated outbreaks. We showed that during the first 17 days of an FMD epidemic, animal movement was the predominant transmission route among the taxa; however, there were significant differences in the dissemination of bovine and swine infections. Regardless of which taxon FMD was first introduced in, the median spread distance fell within the control zones (from one to 10 km). We also showed that the baseline control scenario, which was based on the Brazilian response plan,

was sufficient to eliminate 93.83% of epidemics within 100 days of deploying the countermeasures. Our model projections, along with the necessary software, are available to local animal health officials. Thus, our model can be used as a policy tool not only for future responses to FMD epidemics through computer-based preparedness drills and capacity building but also during an emergency response to an FMD epidemic, 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 study design. FPNL coordinated the data collection. NCC performed data processing and cleaning, designed the model and simulated scenarios with the assistance of GM. NCC and GM planned 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

The authors declare that they have no conflicts of interest.

Ethical statement

The authors confirm that this study conformed to the ethical policies of the journal, as provided on the journal's author guidelines page. Since this work did not involve animal sampling or the collection of questionnaire data by researchers, no ethics permits were needed.

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Data availability statement

The datasets analyzed in the current study are not publicly available due to data protection but may be available from the corresponding author on reasonable request.

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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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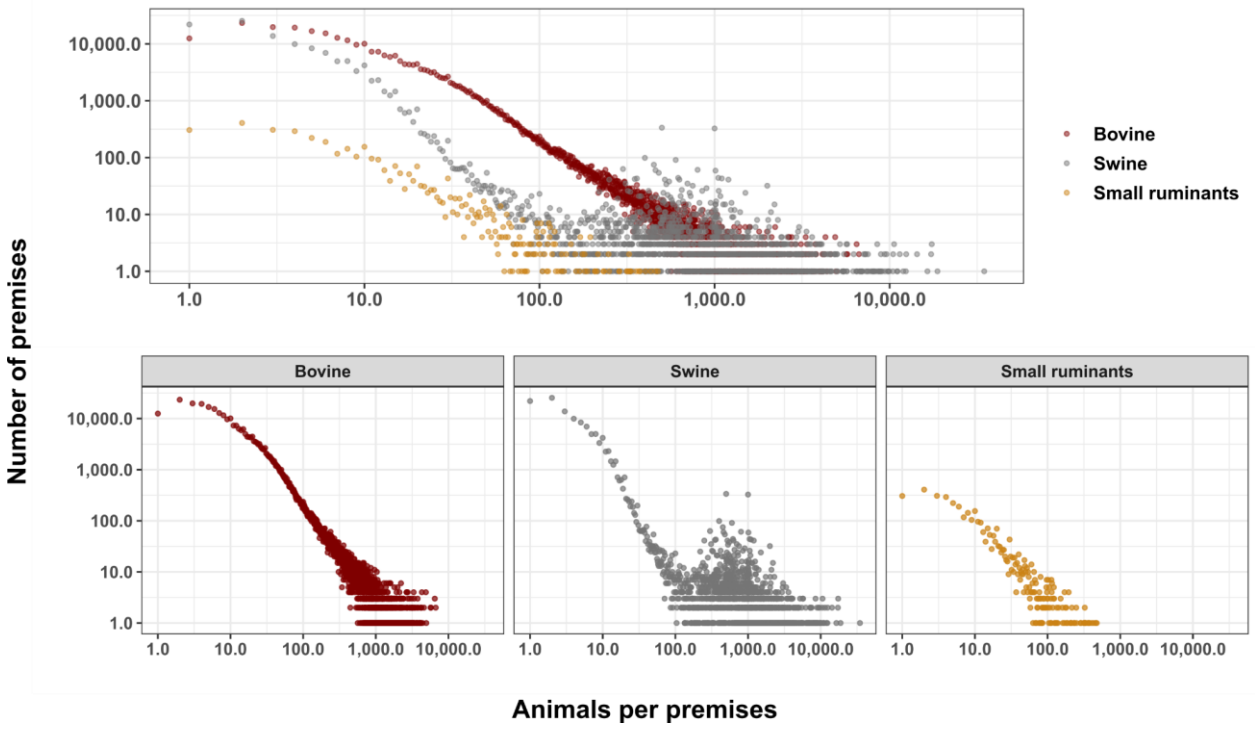
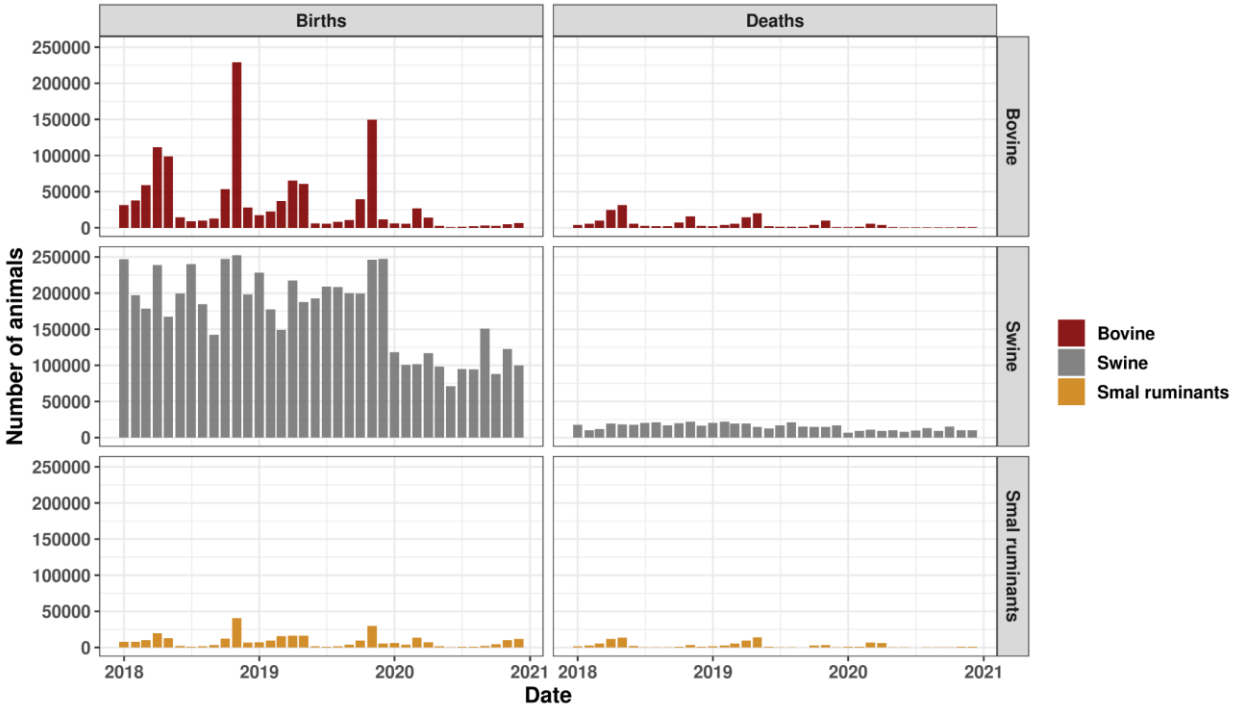
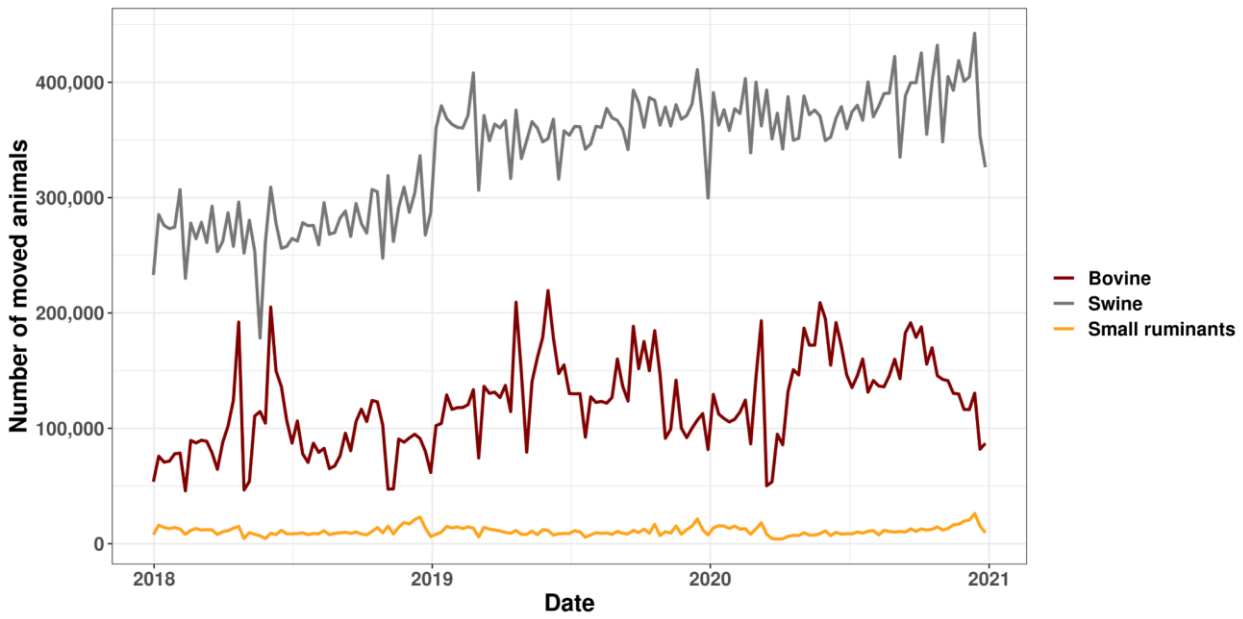


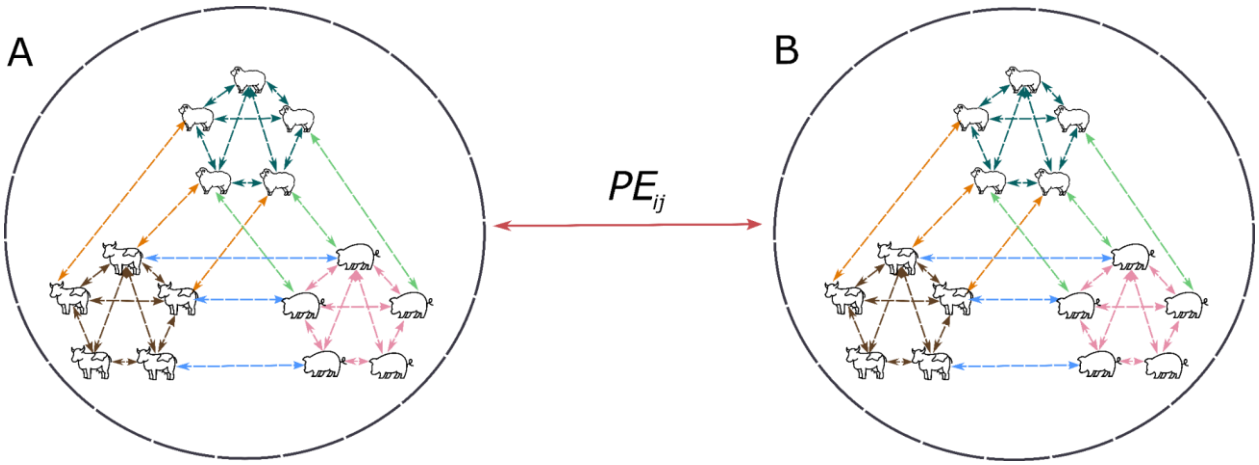
Supplementary Figure S1. The 2018 distribution of farm-level population for each species in the state of Rio Grande do Sul, Brazil. The y-axis is the number of farms and the x-axis is the number of animals, both on a log10 scale.



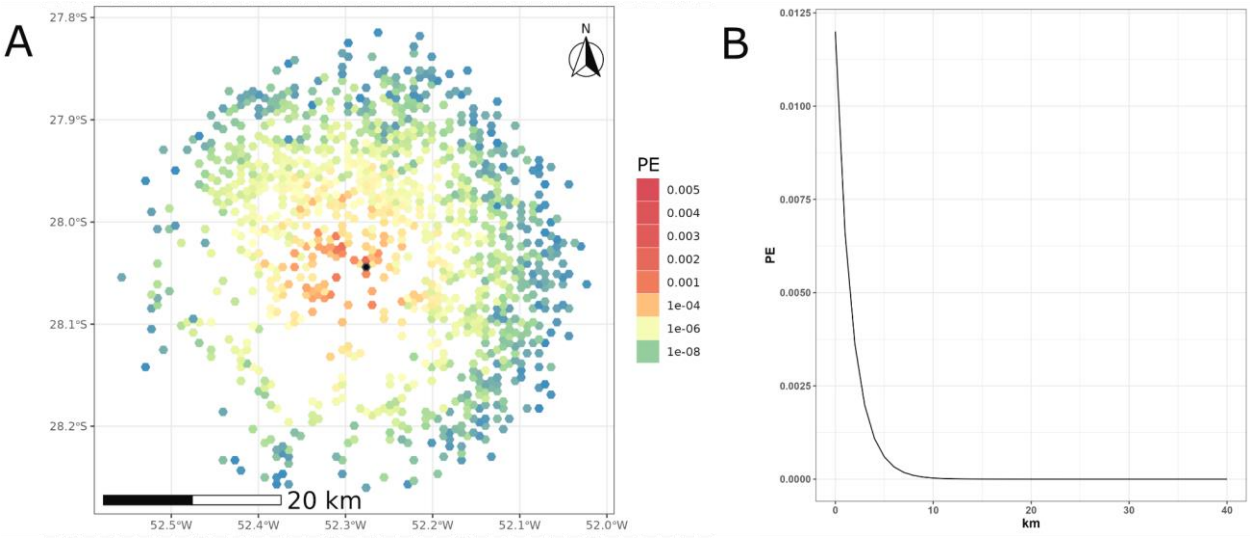
Supplementary Figure S2. The monthly distribution of animal births and deaths by species, from January 1st, 2018 to December 31st, 2020.



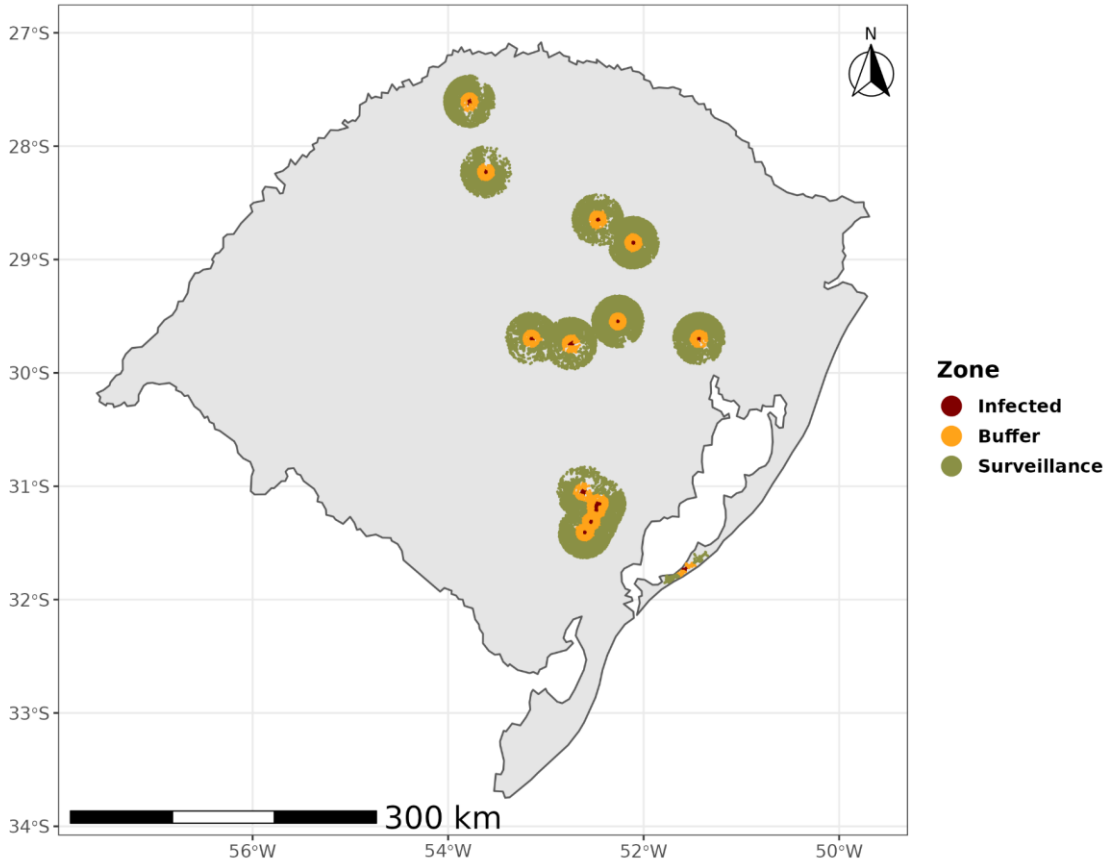
Supplementary Figure S3. The weekly between-farm animal movements, from January 1st, 2018 to December 31st, 2020.



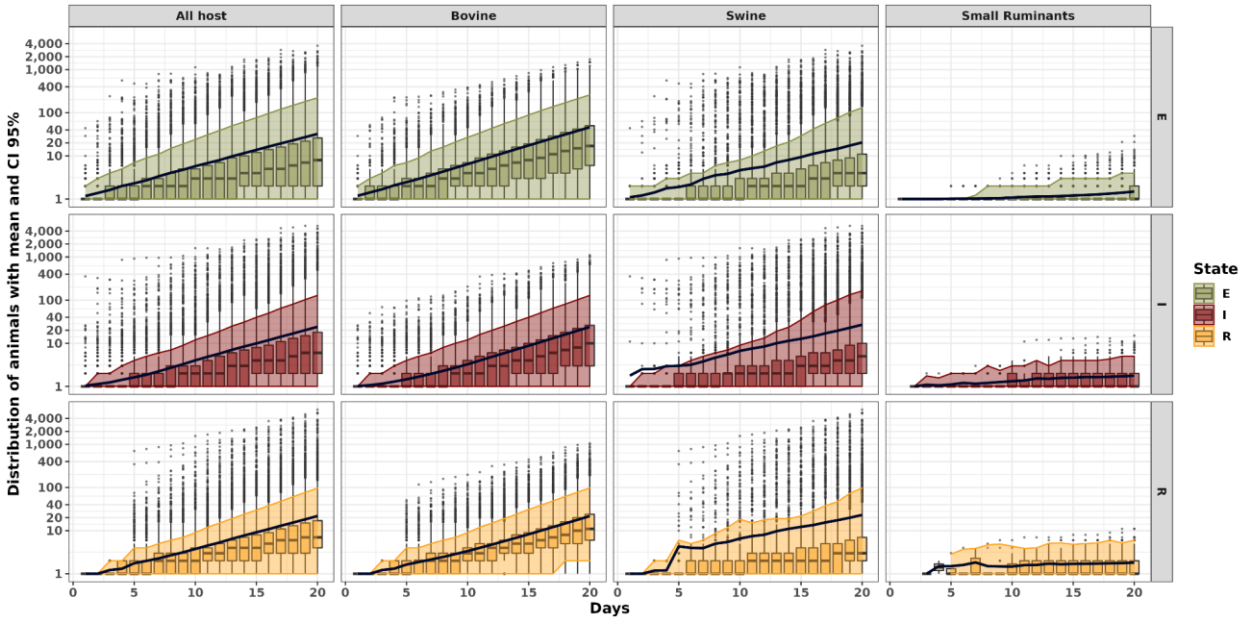
Supplementary Figure S4. Representation of the different population interactions at the within-farm level. For this example, we considered farms with all three species. In A and B, the dashed line represents the interaction within and between species, and the color denotes a β for each host-to-host interaction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



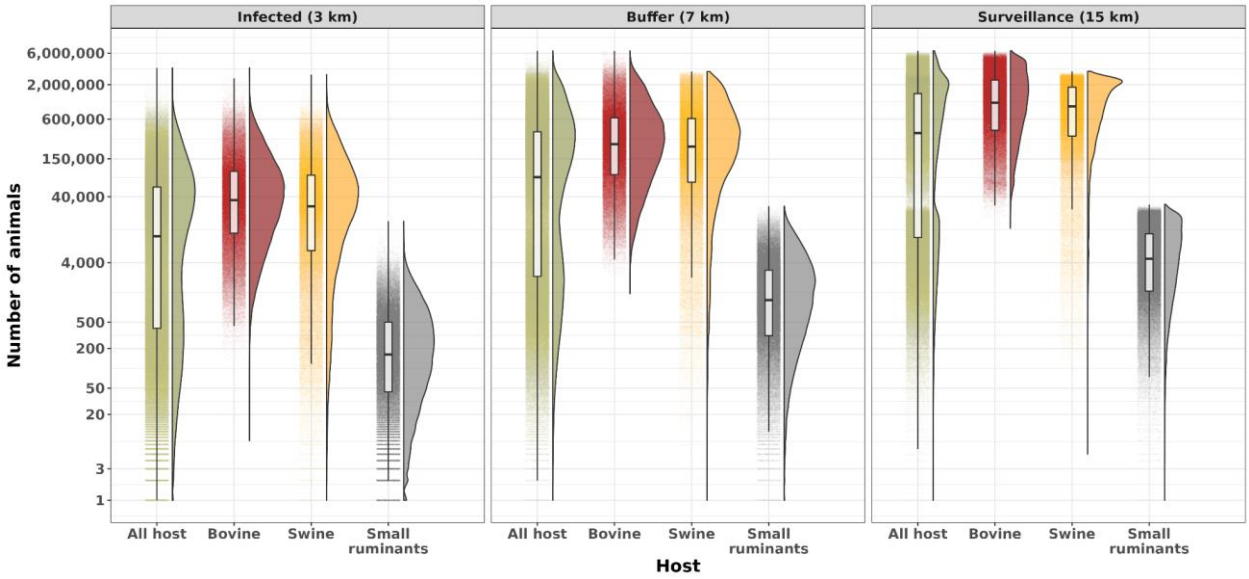
Supplementary Figure S5. A) Representation of grid-hexagons of size 0.76 km (503,516 m^2). Each hexagon can host one or more farm locations. The color of the hexagon represents the probability of PE exposure assuming ten infected animals in the center (black hexagon). B) PE distance in km.



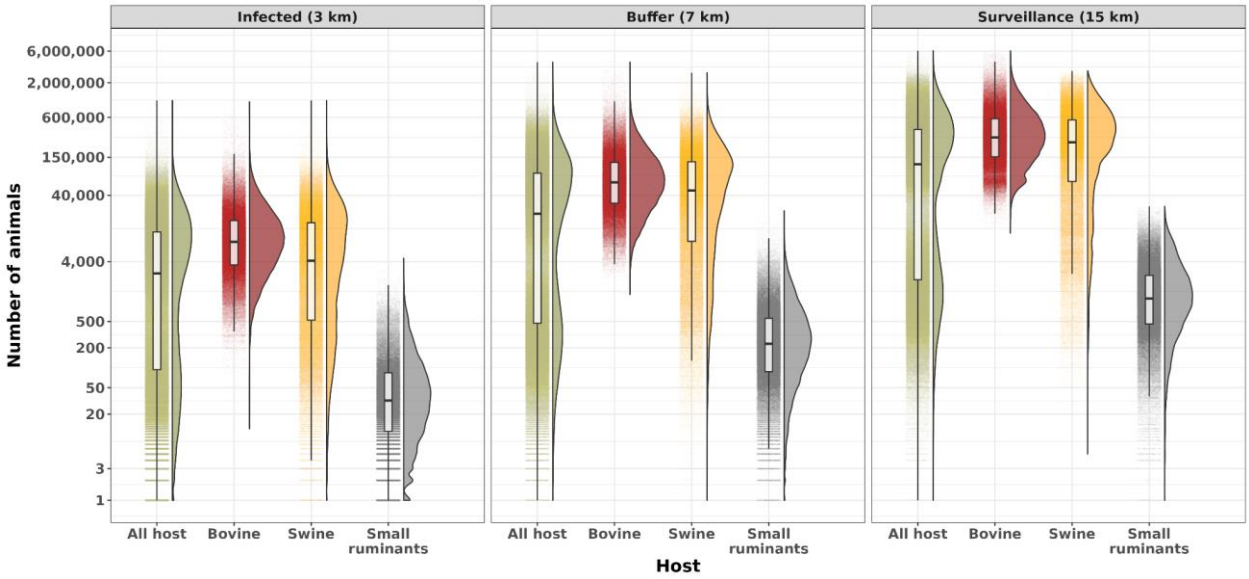
Supplementary Figure S6. **Control zones mapping.** The infected control zones of 3 km are represented as red dots, the 7 km buffer zone is represented as yellow dots, and the 15 km surveillance zone is represented as green dots. Of note, control zones with overlapping are merged.



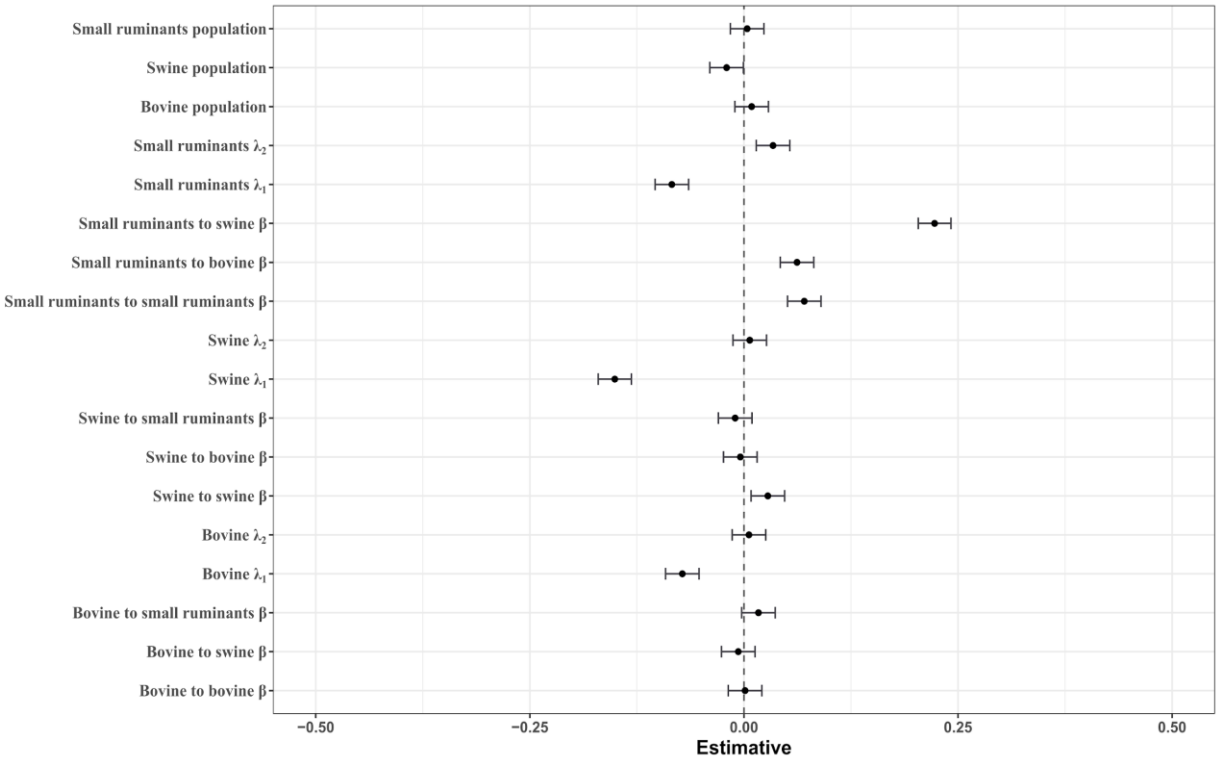
Supplementary Figure S7. Distribution of animals per compartment, exposed (E), infected (I), and recovered (R) by species. Because the number of susceptible animals is very large (19,267,676), the S compartment is not shown. The solid line represents the mean and the dots are outliers. The colored background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



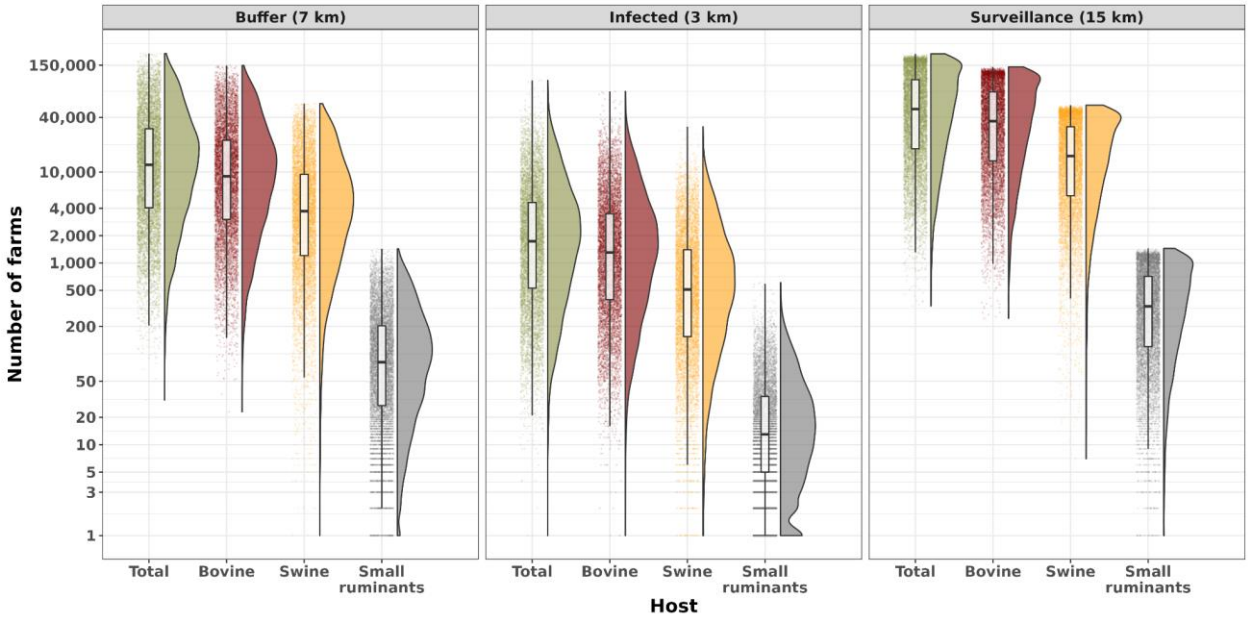
Supplementary Figure S8. The distribution of animals within control zones at 20 days from the initial infection. The y-axis shows the number of animals within infected zones, buffer zones, and surveillance on a log10 scale. The left side boxplots include outliers and the right size density distribution.



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.



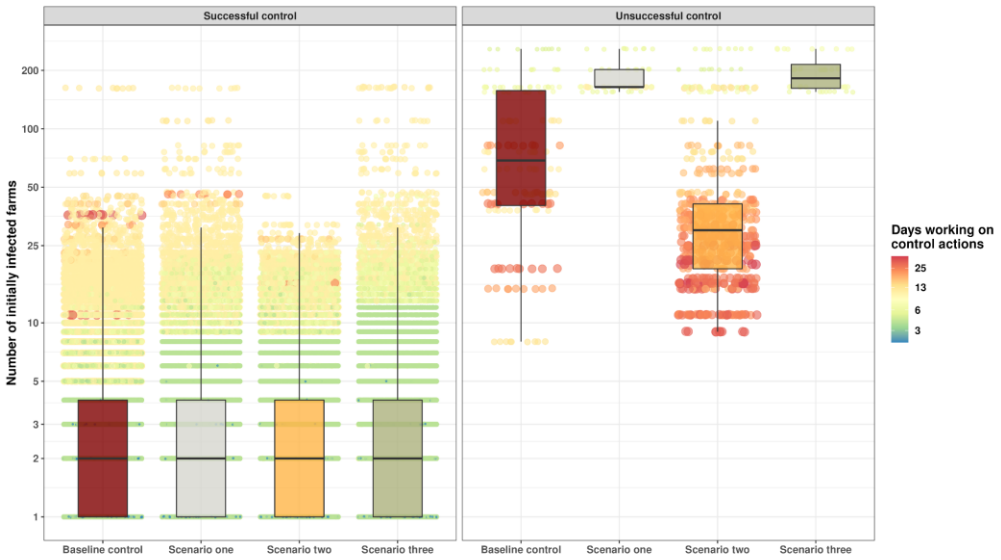
Supplementary Figure S10. Sensitivity of the number of infectious animals to changes over the parameters using LHS-PRCC.



Supplementary Figure S11. 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.

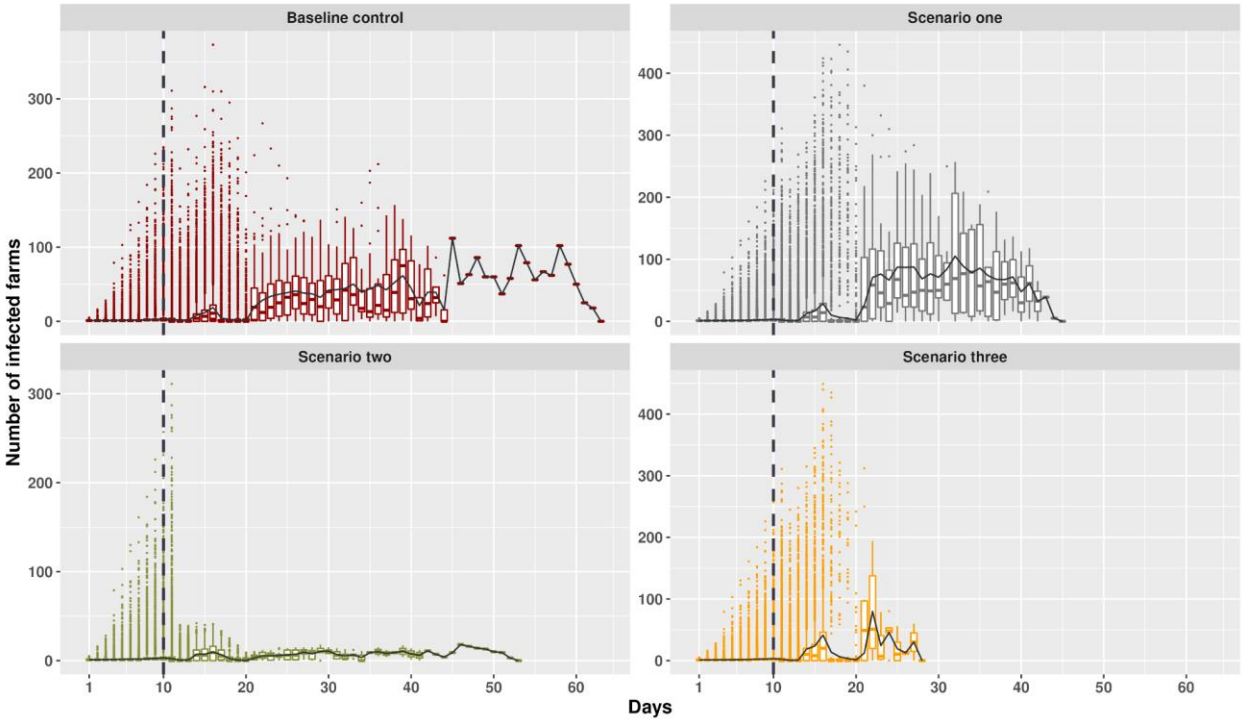
Effectiveness of control actions started 10 days after initial simulated infection

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 S12). 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 S12).



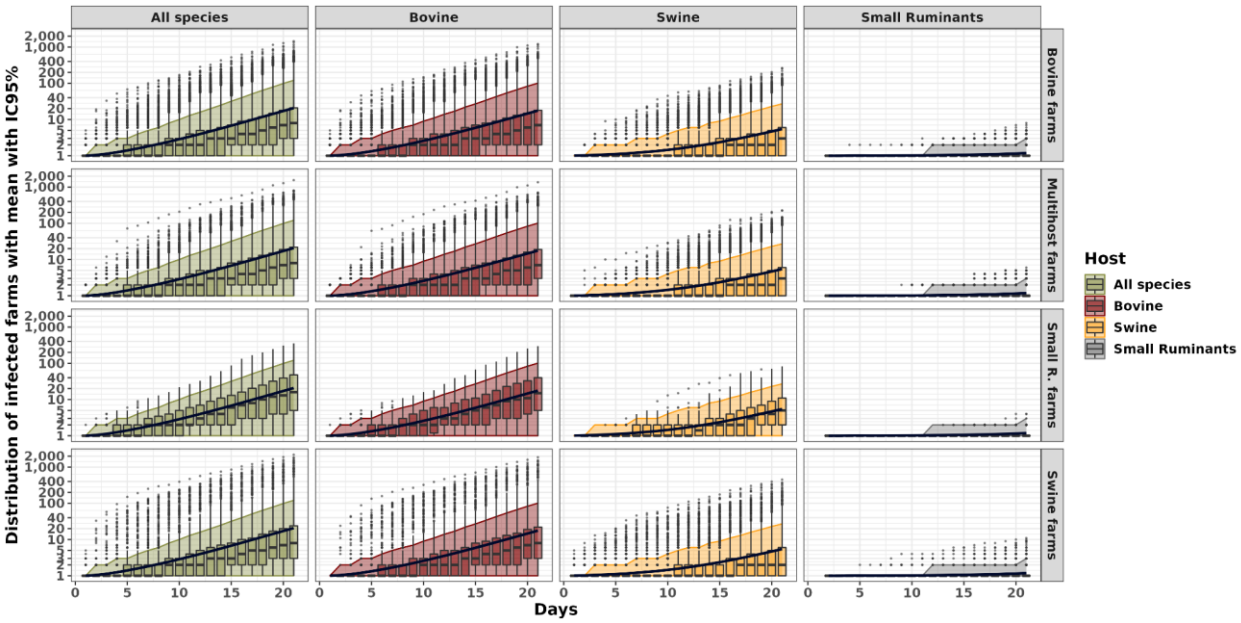
Supplementary Figure S12. The distribution of FMD epidemics successfully and unsuccessfully halted under four control and eradication scenarios after 10 days from the initial seeded infection. The boxplot shows the distribution of secondarily infected farms at 10 days, the background scattered plot shows 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 63 days to fade out epidemics. In comparison with the baseline scenario, scenario two took 53, scenario one 45, and scenario three 28 days (Supplementary Material Figure S13).

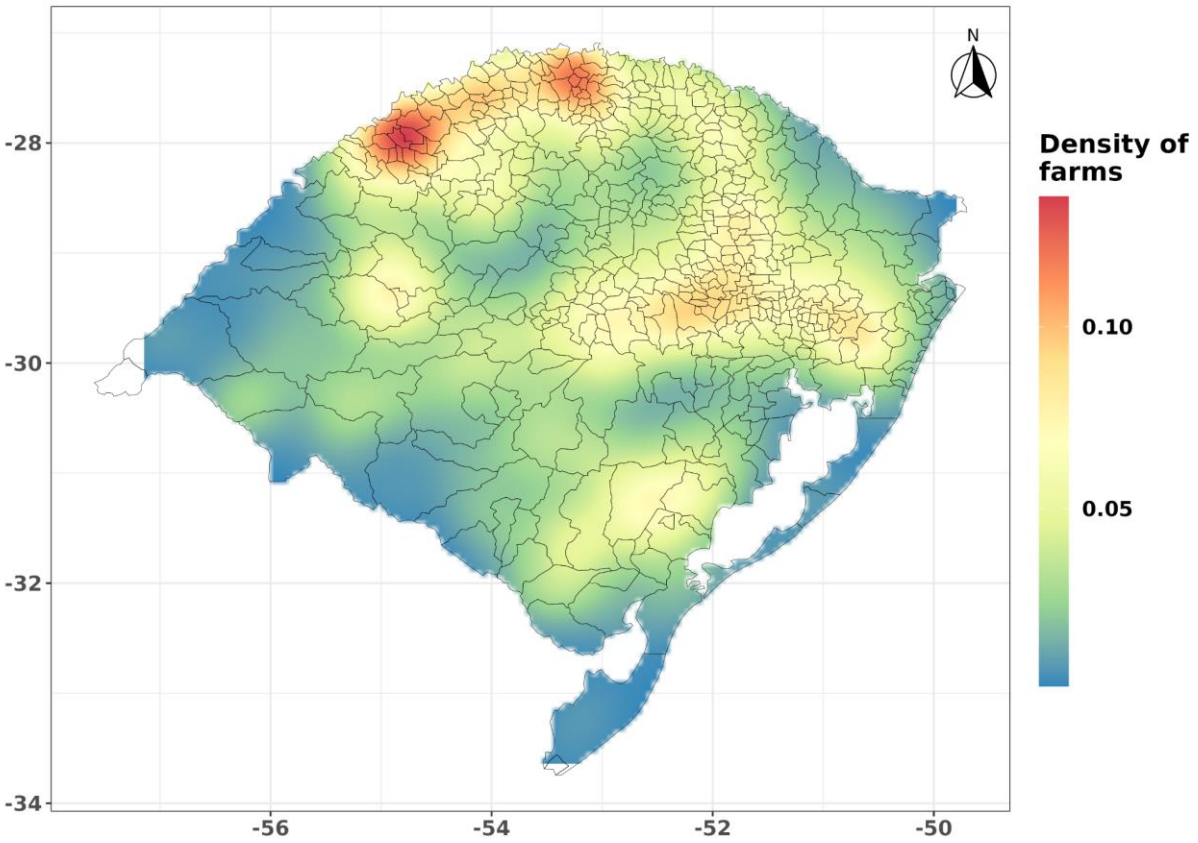


Supplementary Figure S13. The average number of days to stamp out FMD epidemics (of simulation that successfully eliminated outbreaks). The vertical dashed line marks the 10 days of

silent spread and the start of control actions. The solid black line represents the average of infected farms per day. The box plot shows the distribution of secondarily infected farms.



Supplementary Figure S14. 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 S15. 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	104,598 (93.39%)
Baseline control scenario: Vaccination of 5,000 animals/day + depopulation of 4 farms/day	Unsuccessfully control	7,407 (6.61%)
Scenario one: Vaccination of 10,000 animals/day) + depopulation of 8 farms/day	Successfully control	109,593 (97.85%)
Scenario one: Vaccination of 10,000 animals/day) + depopulation of 8 farms/day	Unsuccessfully control	2,412 (2.15%)
Scenario two: Depopulation of 8 farms/day	Successfully control	87,759 (78.35%)

Scenario two: Depopulation of 8 farms/day	Unsuccessfully control	24,246 (21.65%)
Scenario three: Vaccination of 15,000 animals/day + depopulation of 12 farms/day)	Successfully control	110,115 (98.31%)
Scenario three: Vaccination of 15,000 animals/day + depopulation of 12 farms/day))	Unsuccessfully control	1,890 (1.69%)

Supplementary Equation 1.

The following simple formula was used for calculating the adequate sample size in prevalence study

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where n is the sample size, z is the statistic corresponding to level of 95% confidence, P is expected prevalence is this case 0.5 or 50%.