Ring Vaccination as a Control Strategy for Foot-and-Mouth Disease

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Abstract

Foot-and-Mouth disease (FMD) is a highly infectious illness of livestock and a serious economic threat. Effort has been placed in modeling various control strategies for eradicating the disease. In this study we will consider a spatial model that incorporates ring vaccination and isolation as a control measure for the dispersal of the epidemic. We found an upper and lower bound of the basic reproductive number for the spatial model in terms of our parameters. Through numerical simulations we were able to show that ring vaccination is effective in controlling the epidemic. We validate our results by using the dataset based on the 2001 FMD epidemic in Uruguay.

1 Introduction

The control of infectious diseases often times is determined by the economical resources as well as the accessible control measures. Even-though control measures can be implemented across the entire population, an emphasis is placed by public health measures to only target the necessary subgroups of the population. Therefore, it is important to develop control measures that will achieve the greatest reduction of disease impact and transmission. Well posed mathematical models of infectious disease spread are necessary tools to test the efficacy of various policies and control measures.

Foot-and-mouth disease (FMD) provides an opportunity to develop detailed epidemiological models because we have accessible spatio-temporal data collected from various outbreaks. These models must capture the spread of disease and provide a framework to explore a variety of alternative control measures. FMD is a very contagious disease caused by an anphthovirus which infects all cloven-hooved animals such as pigs, cattle, and sheep ([1], [11]). The major symptoms are vesicular oral or foot lesions, and are more easily seen in cattle and pigs than in sheep and goats. In this study, we will test the efficacy of adapting ring vaccination as a control measure for the 2001 FMD outbreak in Uruguay.

The last major outbreak of FMD occurred in Uruguay in 2001 along the border with Argentina. The first case was identified on April 24, 2001 in the western state of Soriano. This outbreak spread very rapidly until it was determined by Uruguay that the best course of action would be to vaccinate all cattle.

The disease was clinically confirmed on April 24, immediately Uruguay banned all animal movements in the department of Soriano and started the stamping out of all infected and in-contact animals in affected farms. By April 26, the ban on movement of animals was extended to Colonia with the support of the police and army personnel. The ban was extended to the rest of the country on April 27, and included all slaughter activities, public auctions, and markets. The ban on animal movement was maintained until June 7, in which all major roads were blocked, and all schools, offices, stores and other public gathering places were closed [15]. This date marked the conclusion of the first cycle of emergency vaccination. During the course of the 2001 epidemic, 2057 farms in Uruguay reported infection with FMD [15].

A range of control measures were implemented to try to reduce the transmission of infection. These measures included the implementation of emergency ring vaccination approach, coupled with stamping out of animal populations within the outbreak zone, and of exposed cattle within a 10-km radius of affected herds [15]. However, because the spread of the disease was extensive, Uruguay adopted a mass-vaccination policy on May 5, which would continue into 2003.

Uruguay adopted two vaccination strategies, ring vaccination and mass vaccination. Ring vaccination failed to control the spread of FMD, hence they implemented mass vaccination. A natural question to ask is would the disease been controlled if a wider radius had been considered? Was mass vaccination really necessary? Would Uruguay had been able to control the FMD epidemic by adopting a bigger ring (radius) of vaccination?

It is known that ring vaccination can be a strategy to control and contain a disease. In the spread of FMD, the idea is that the animals who have had close contact to an infected animal are at a higher risk to become infected, and hence they should be protected, i.e. ring vaccination is highly based on the contact structure between single individuals [13]. In this study, we explore the validity of adopting ring vaccination as a strategy to control a disease. The aim of this project is to seek a ring size that balances two goals: prompt vaccination and vaccinating over as large an area as possible. For this purpose, a dataset based on the 2001 Uruguayan FMD epidemic is used.

2 Methodology

In order to capture the dynamic of the spread of FMD more accurately, we construct a compartmental epidemic model that incorporates spatial dynamics, since spatial models describe epidemic spread more accurately than non-spatial models even at early epidemic phases [6]. We assume that "small areas" around one outbreak, ie a patch, are *homogeneously* mixed. However, individuals and the habitats they occupy are *heterogenously*

distributed in space. Under this view, populations are open systems, not independent from nearby populations with which they interact. This ensemble of populations is what is called *metapopulation* [12].

In this work, Uruguay is divided into sub-regions (counties). We are modeling the infection in a single patch, as well as a multi-patch scales, preserving patch-to-patch heterogeneity. Within a given county, we model the infection with a deterministic compartmental epidemiological model, and applied on a patch-by-patch basis. By doing so, we are allowed to investigate the spread of contagion between patches.

2.1 Non-spatial Model

The non-spatial model, models the outbreak of the FMD in any given county in Uruguay. For this purpose, we are working at the epidemiological level of farms. We classify each farm as susceptible (S), latent (L), infectious and undetected (I), vaccinated (V), isolated and detected (J) and protected (P). A susceptible farm (in contact with the virus) enters the latent class (L) (uninfectious and asymptotic) at a transmission rate given by $\beta_1 SI$. The transmission parameter β_1 measures the impact of contacts. These contacts take into account animal relocation such as transporting in contaminated vehicles, or exposed to hay, food or water contaminated with the virus, shared veterinarians or overlapping visitors [6]. Hence, the transmission rate $\beta_1 SI$ assumes that the farms in a county are fully mixed, meaning that contacts of a susceptible farm are chosen at random. It also assumes that all farms have approximately the same number of contacts in the same time and that all contacts transmit the disease with the same probability. It is also assumed that the farms in the latent class will progressed towards the infectious class after a mean time of $1/\kappa$ days. The latent period varies between 2 and 14 days [16]. Once the farm becomes infectious, if symptoms appear then it is moved to the isolated class (J), while the farms who have not had any contact with the virus will get vaccinated. The animals are 1 or 2 days infectious before showing clinical symptoms like fever blisters at mouth, tongue and feet, etc. [16]. If the vaccine is effective, then the farm will progressed to the protected class (P).

The above assumptions and definitions lead the following FMD model for a given county in Uruguay:

$$\begin{cases} \dot{S} = -\beta_1 SI - \nu S \\ \dot{V} = \nu S - \beta_1 VI - \mu V \\ \dot{L} = \beta_1 SI + \beta_1 VI - \kappa L \\ \dot{I} = \kappa L - \alpha I \\ \dot{J} = \alpha I \\ \dot{P} = \mu V \end{cases}$$

2.2 Spatial Model

The model we use to incorporate the spatial dynamics closely follows that developed by Chowell et al [6]. However, in this model we are analyzing the effect of ring vaccination in controlling the spread of FMD. The idea behind ring vaccination is that farms who have close contacts to an infected farm are at a higher risk of becoming infected and hence should be protected. Ring vaccination consist of vaccinating in a ring with a certain radius around diseased counties. To capture this approach, we propose implementing a reactive responsive approach: reactive in that control measures are implemented only after an outbreak has been reported and responsive in that we will target vaccination according to which farms have been diagnosed with FMD and the surrounding neighboring counties. In general, we assume farms and surrounding neighbors are vaccinated in the order they are identified.

In order to add spatial dynamics into the model, we must incorporate transmission between the counties. The transmission parameter β_2 assumes the same modes of transmission as that of β_1 but it takes into account interaction between the counties. This transmission rate is given by $\sum_{j\in\Omega_i}\beta_2(t)I_j$, where Ω_i is the set of neighboring counties of county i. In other words, the nearest neighbors of the county were the first outbreak occurs move to the latent class. The rate of vaccination also incorporates spatial dynamics and is the same as the transmission rate from susceptible to latent. We use the same rate because it takes some time for the vaccine to be effective, hence during that time the animals are susceptible to get infected with the virus.

The above assumptions and definitions lead the following FMD model with spatial dynamics:

$$\begin{cases} \dot{S}_i = -\beta_1(t)S_iI_i - \sum_{j\in\Omega_i}\beta_2(t)S_iI_j - \nu(t)S_i, \\ \dot{V}_i = \nu(t)S_i - \beta_1(t)I_iV_i + \sum_{j\in\Omega_i}\beta_2(t)I_jV_i - \mu(t)V_i, \\ \dot{L}_i = \beta_1(t)S_iI_i + \sum_{j\in\Omega_i}\beta_2(t)S_iI_j + \beta_1(t)I_iV_i + \sum_{j\in\Omega_i}\beta_2(t)I_jV_i - \kappa L_i, \\ \dot{I}_i = \kappa L_i - \alpha(t)I_i, \\ \dot{J}_i = \alpha(t)I_i, \\ \dot{P}_i = \mu(t)V_i. \end{cases}$$

where,

$$\Omega_i = \{1 \le j \le n : \text{county j is a neighbor of county i}\}.$$

Note that $\beta_1 > \beta_2$ since the contacts inter-county are higher than intra-county contacts.

We considered the parameters to be time dependent because it allows for implementing various control measures at different times [5]. $\beta_1(t)$ and $\beta_2(t)$ depend on time because the contact rate is higher before implementing movement restrictions. Similarly, $\nu(t)$ and $\mu(t)$ depend on time because vaccination is not implemented until after a few days of the initial and depending on the resources of the country. For simplicity, we are going to define these parameters with step function.

$$\beta_1(t) = \begin{cases} \beta_{1a} & t < \tau_m \\ \beta_{1b} & t \geq \tau_m \end{cases}$$

$$\beta_2(t) = \begin{cases} \beta_{2a} & t < \tau_m \\ \beta_{2b} & t \geq \tau_m \end{cases}$$

$$\alpha(t) = \begin{cases} \alpha_0 & t < \tau_\nu \\ \alpha & t \geq \tau_\nu \end{cases}$$

$$\nu(t) = \begin{cases} 0 & t < \tau_\nu \\ \nu & t \geq \tau_\nu \end{cases}$$

$$\mu(t) = \begin{cases} 0 & t < \tau_\nu \\ \mu & t \geq \tau_\nu \end{cases}$$

We let $\tau_m = 4$ which represents the epidemic day when movement restrictions were implemented and we define $\tau_\nu = 13$ as the time when vaccination started.

3 Basic Reproductive Number

The basic reproductive number, R_0, is a threshold quantity in epidemiological models, defined as the average number of secondary cases produced by a typical infected individual when the virus is introduced in a population of fully susceptible individuals [7]. In other words, R_0 measures how powerful the disease is in invading the population. When $R_0 > 1$ the disease progresses and if $R_0 < 1$ the disease dies out.

For spatial models, the computation of the the basic reproduction number, R_0, becomes a challange. In the analysis of the spatial model, we are able to find upper and lower bounds for R_0. We introduce a region in the complex plane where the R_0 lies. To do so, we implemented the second generator approach ([8],[9]). The next generation matrix is given by F and V, for our model F and V are given by

$$F = \begin{bmatrix} 0 & 0 & \beta_1 N_1 & \cdots & \beta_2 N_1 \zeta_{1j} \\ & \ddots & \vdots & & \vdots \\ 0 & 0 & \beta_2 N_m \zeta_{mj} & \cdots & \beta_1 N_m \\ 0 & 0 & 0 & & 0 \\ & \ddots & & \ddots & \\ 0 & 0 & 0 & & 0 \end{bmatrix}, V = \begin{bmatrix} k & 0 & 0 & 0 \\ & \ddots & & \ddots & \\ 0 & k & 0 & 0 \\ -k & 0 & \alpha & 0 \\ & \ddots & & \ddots & \\ 0 & -k & 0 & \alpha \end{bmatrix}, \text{ and}$$

$$V^{-1} = \begin{bmatrix} 1/k & & 0 & 0 & & 0 \\ & \ddots & & & \ddots & \\ 0 & & 1/k & 0 & & 0 \\ 1/\alpha & & 0 & 1/\alpha & & 0 \\ & \ddots & & & \ddots & \\ 0 & & 1/\alpha & 0 & & 1/\alpha \end{bmatrix}$$

Where,

$$\zeta_{ij} = \begin{cases} 1 & \text{if } j \in \Omega_i \\ 0 & \text{if } j \notin \Omega_i \end{cases}$$

In other words, if county j is a neighbor of county i then there will be a non-negative term in the corresponding entry, otherwise it is zero. Note that N_i for $1 \leq i \leq m$ is the total number of susceptible farms in county i. Now, we want to compute the next generation matrix, which is given by the product (FV^{-1}), hence

$$FV^{-1} = \begin{bmatrix} \frac{\beta_1}{\alpha} N_1 & \cdots & \frac{\beta_2}{\alpha} N_1 \zeta_{1j} & \frac{\beta_1}{\alpha} N_1 & \cdots & \frac{\beta_2}{\alpha} N_1 \zeta_{1j} \\ \vdots & & \vdots & \vdots & & \vdots \\ \frac{\beta_2}{\alpha} N_m \zeta_{mj} & \cdots & \frac{\beta_1}{\alpha} N_m & \frac{\beta 2}{\alpha} N_m \zeta_{mj} & \cdots & \frac{\beta_1}{\alpha} N_m \\ 0 & & 0 & 0 & & 0 \\ & \ddots & & & \ddots & \\ 0 & & 0 & 0 & & 0 \end{bmatrix}.$$

Following Diekmann et al. [7], the basic reproductive number is defined as the spectral radius of the next generation operator,

$$\mathcal{R}_0 = \rho(FV^{-1})$$

The previous definition for R_0 depends on the spectral ratio of a matrix. Let $A = FV^{-1}$, in order to compute R_0 we need to find the dominant eigenvalue of A. In doing so, we observe two major difficulties. The first difficulty is that the rows of A are determined by the location of the counties, and the entrees on each row is given by the number of neighbors. The second difficulty is that the degree of the characteristic polynomial depends on the number of counties hence it is not possible to find an explicit expression of the roots. However, we can give an approximation to R_0 using the following approach:

Theorem 1. (Gershgorin Circle Theorem 1965) *If A is a complex or real $n \times n$ matrix, and*

$$R_i = \sum_{j=1,\, i \neq j}^{n} |a_{ij}|,$$

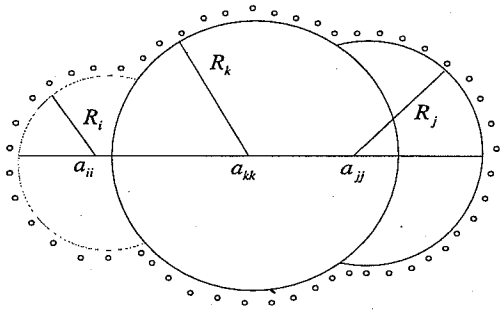

Figure 1: Feasible region of the $\mathcal{R}_0$.

then each eigenvalue of A is either in one of the disk

$$\{z : |z - a_{ii}| \leq R_i\}.$$

(the proof of this theorem can be found in most linear algebra books, see for example Brualdi et al. [4])

Using the idea from theorem 1 we can construct a region in the plane with m disk with centers and radii for each disk, D_k, is given by

$$Cr(D_k) = \frac{\beta_1}{\alpha} N_k \text{ and } \quad r(D_k) = \frac{1}{\alpha}(\beta_1 N_k + 2 \sum_{j \in \Omega_k} \beta_2 N_j)$$

where $k = 1, \ldots, m$, m the number of counties (see figure 1). In other words, the centers of the disks are given by the elements of the diagonal of A, the number of disks that the matrix A generates is twice the number of counties ($m = 2n$), and this number corresponds to the latent and infected classes.

Note that the entrees in A are nonnegative real numbers, thus we define d_k as the sum of the radii and the center of the disk k. d_k is well defined and has the following form:

$$\begin{aligned} u_k &= \frac{2}{\alpha}(\beta_1 N_k + \sum_{j \in \Omega_k} \beta_2 N_j) \\ l_k &= \frac{2}{\alpha}(\beta_1 N_k - \sum_{j \in \Omega_k} \beta_2 N_j) \end{aligned}$$

We define the bounds of the region as

$$\begin{aligned} M &= \max_{1\leq k\leq m} u_k\,, \quad \text{and} \\ m &= \min_{1\leq k\leq m} l_k\,. \end{aligned}$$

Hence, M is the upper bound and m is the lower bound, which implies that R_0 lies in that region. From the previous argument, we come to the following proposition,

Proposition 1. *There exist bounded region $\mathcal{D}$ in the plane such that $\mathcal{R}_0 \in \mathcal{D}$. In particular, if $M < 1$, then $\mathcal{R}_0 < 1$, and if $m > 1$, then $\mathcal{R}_0 > 1$*

3.1 Interpretation of the approximation of R_0

Since M and m depend on the density of the counties N_i, and the parameters α, β_1, and β_2 we can make some observations about R_0. The first one that on average the counties have the same number of farms,

$$\mathcal{R}_0 \approx M \approx m$$

We can also conclude that the worst case scenario for the epidemic will take place in the outbreaks originates in the county with the most farms and neighbors.

4 Caricature of the Model and Simulations

We construct a fixed, finite but large contact graph (ie an $N \times N$ square lattice). Each cell of the graph represents a county in Uruguay. It is important to emphasize that since there is almost no natural resistance to the disease and the disease is highly infectious, we can assume that once an infected animal appears on a given farm, soon a high percentage of all animals in that given farm are diseased, hence both the farm and the given county are now considered infected with FMD. A county is assumed to be immune once the vaccine is effective and the farm progresses to the protected class.

Since we are considering a spatial model, we define two rates of transmission β_1 and β_2 for inter-couty and intra-county transmission, respectively. Inter-county transmission is assumed to be homogenous while intra-county transmission occurs only in a neighborhood N_i. In the case of the square lattice, N_i is considered to be the von Neumann neighborhood.

For the simulations we choose the parameter values $\kappa = 0.28$ and $\alpha = 0.14$. We vary the vaccination rate of susceptible farms ν and the rate at which vaccinated farms achieve protective levels μ because we are interested in addressing how fast should vaccination be implemented and what level of potency should the vaccine have in order to achieve a smaller epidemic size. The graph is chosen as a 10×10 square lattice with static boundary conditions. We generate initial conditions in each cell (county) of the graph by adopting a normal distribution with mean 100 and variance 20. We also incorporate a time delay in order to account for the time dependent parameters.

4.1 The Number of Neighbors and the Final Epidemic Size

As suggested by the analysis and interpretation of R_0, the worst case scenario for an outbreak of foot-and-mouth disease is associated with the number of surrounding neighbors that an infectious site has. An infectious county has two neighbors if it is a county that is on the corner of the lattice (only four exists), three neighboring counties if the outbreaks start on the boundaries and four neighboring counties if the infectious county is in the center of the lattice. The purpose of these simulations is to illustrate the effect of the number of neighbors on the final epidemic size.

For the following simulation, we fixed the vaccination rate, $\nu = 0.25$, the rate at which vaccinated farms achieve protective levels $\mu = 0.14$ and we assumed that control measures did not take place until the fourth day (banned animal movement) and the thirteenth day (vaccination). In the case of four neighboring counties, the final epidemic size is 2,500 farms out of an initial size of 10,000 susceptible farms (see figure 2). In the case of the infected county having only three neighbors, the cumulative number of infected farms is about 1,800 out of an initial size of 10,000 (see figure 3). Once again it took approximately fifty days to achieve a final epidemic size. In this case, the number of vaccinated farms over the course of the epidemic is less than 4,000 farms of the total initial size. The last possible case is that the infected farms only has two neighbors. In this case, the final epidemic size turns out to be roughly 1,000 farms of the initial 10,000 farms (see figure 4). For this case, once again about 4,000 farms of the initial size get vaccinated.

As observed through the simulations, the final epidemic size decreases by 28% if the outbreak starts at a boundary county, and by 60% if it is a corner boundary. Hence, the position in the initial outbreak of foot-and-mouth disease plays an essential role in the final epidemic size.

4.2 Variation of Parameters

Vaccine can help contain the disease quickly if it is used strategically to create barriers between infected zones and disease free-zones. In FMD, vaccines are very effective and vaccinated animals develop sufficient immunity within a range of 4 to 8 days depending on the type of FMD virus and the type of vaccine used [16]. There are seven different types and more then 60 subtypes of FMD virus, and there is no universal vaccine against the disease [15]. Hence, it is a question of interest to vary the protection rate and vaccination rate and observe the impact of these variations in the final epidemic size.

4.2.1 The Effect of Vaccination Rate

During the 2001 outbreak of FMD in Uruguay, vaccination was not implemented until the thirteenth day of the epidemic. A natural question that arises is how would the final epidemic size differ had vaccination been implemented earlier and at a different rate? In FMD, vaccination is implemented after the first case is identified but the rate differs depending on the resources of the country. In this simulation we illustrate the effect of

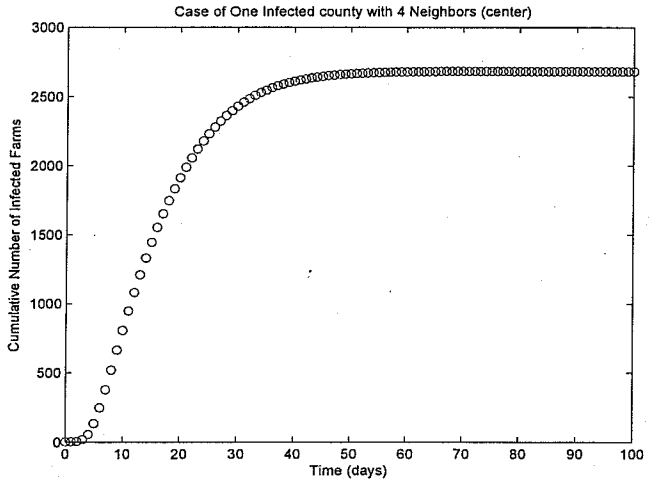

Figure 2: County with four neighbors

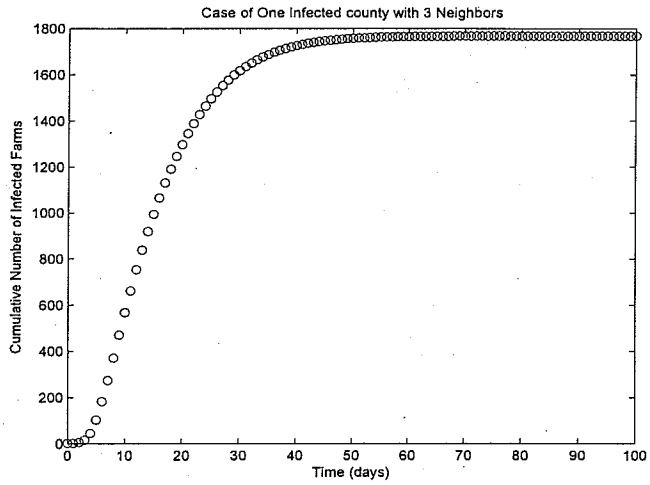

Figure 3: County with three neighbors

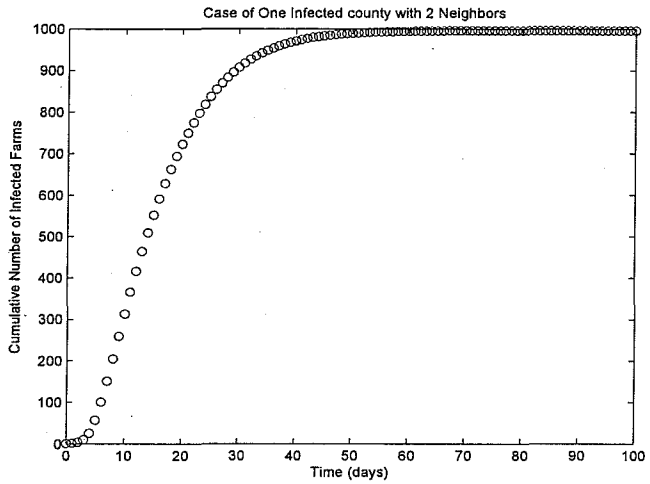

Figure 4: County with two neighbors

vaccinating the susceptible farms at various rates and determining the final epidemic size for each rate. We also capture the effect of implementing vaccination at various times throughout the epidemic.

In figure 5, we can observe the impact of vaccination as a control measure for FMD. With zero vaccination the final epidemic size is roughly 3000 cases. One must mention that although vaccination is not implemented as a control measure, animal movement is banned after the fourth day, hence the epidemic does not grow out of bounds. However it is important to notice that as soon as vaccination is implemented, then the final epidemic size decreases dramatically by 21%. Once the vaccination rate reaches 0.4, then the cumulative number of infected farms does not dramatically decrease. Hence, policy makers should not invest money in vaccinating at a higher rate because the final epidemic size will not change much.

Our interest also lies is looking at the time of vaccination implementation. When should the vaccination be implemented in order to reduce the final epidemic size? In the case of Uruguay, vaccination was implemented on the thirteenth day after the first reported case. However, movement restrictions were enforced after the fourth day. If officials had also implemented vaccination at the same time, then the cumulative number of infected farms would have decreased dramatically. The simulation shows how if vaccination is not executed as soon as the first case is identified, the cumulative number of infected farms increases by approximately 4.3% every two days (figure not shown). If vaccination is implemented on the thirteenth day, as it was in Uruguay, then the final epidemic size will increase by approximately 16%.

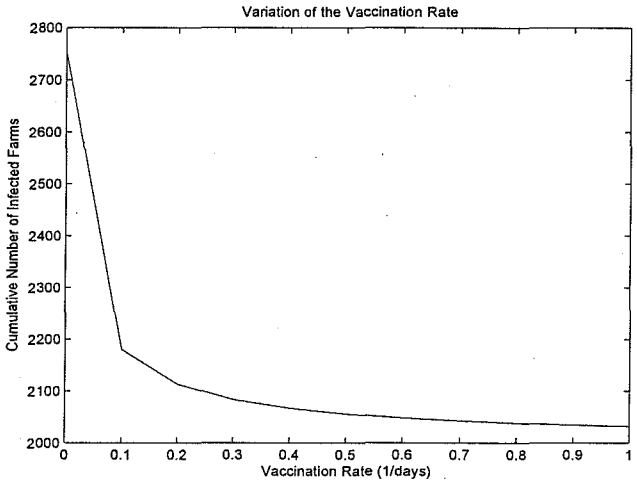

Figure 5: Effect of vaccination rate

4.2.2 The Effect of Protection Rate

Another aspect of the control measures implemented in Uruguay that is of interest to look at, specially since the data varies depending on the strain of FMD virus and the type of vaccination implemented, is the protection rate. In this simulation we illustrate the effect of varying the rate at which vaccinated farms achieve protective levels.

In figure 6, vaccination rate is set to $\nu = 0.25$. If the protection rate of the vaccination is 0, which is feasible since the vaccine takes a couple of days to boost the immune system depending on the virus and the type of vaccine used, then the final epidemic size is roughly 3000. However, if the vaccine is 100% protective then the cumulative number of infected farms reduces by 45%, leaving a final epidemic size of approximately 2000 farms.

4.2.3 The Impact of Vaccination Rate and Protection Rate on the Final Epidemic Size

In figure 7 we are interested in illustrating the effect of both the vaccination rate and the protection rate on the final epidemic size. From the previous simulations and arguments, we have been able to illustrate the role of both of these rates on decreasing the cumulative number of infected farms. The simulation shows that if both vaccination rate and protection rate are equal to zero, then the final epidemic size is 10,000, literally all the farms get infected since absolutely no control measures are being implemented. The graph shows that if there is a combination of both the vaccination rate and the protection rate then the final epidemic size decreases dramatically. It is important to point out the other extreme, which is a vaccination rate of 1 and a protection rate of 1, then the final epidemic size

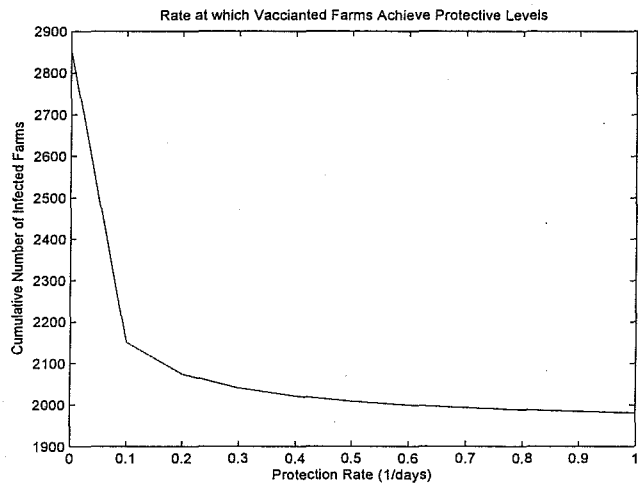

Figure 6: Effect of the efficacy of FMD vaccination on the final epidemic size

decreases by 8,000, a decrease of 80%.

5 Discussion

In this work, we explored the role of ring vaccination in controlling a foot-and-mouth disease epidemic. In order to control such an explosive disease, a combination of control measures must be implemented. In this work, we explored the combination of ring vaccination of susceptible farms, movement restrictions and isolation of infected farms. Movement restrictions and isolation proved to control better the epidemic when vaccination is also implemented. By introducing a vaccinating program, the cumulative number of infected farms drops by roughly 21%, and keeps dropping depending at the rate of vaccination. One interesting observation is that after a certain rate, (approximately 0.4), the final epidemic size will not change significantly. Hence, even if a country uses all their monetary resources in vaccinating susceptible farms at a faster rate, the cumulative number of infected farms will not decrease significantly. Therefore, it is not recommended for a country with limited resources, like Uruguay, to allocate all monetary resources in increasing the vaccination rate.

Another concern of policy makers is at what face of the epidemic should vaccination be implemented. Through this work, we are able to suggest that vaccination should be implemented as soon as the first case is confirmed. In doing so, the final epidemic size will decrease dramatically. If Uruguay had implemented vaccination two days earlier, the final epidemic size would have decrease by about 5%. Also if they had implemented

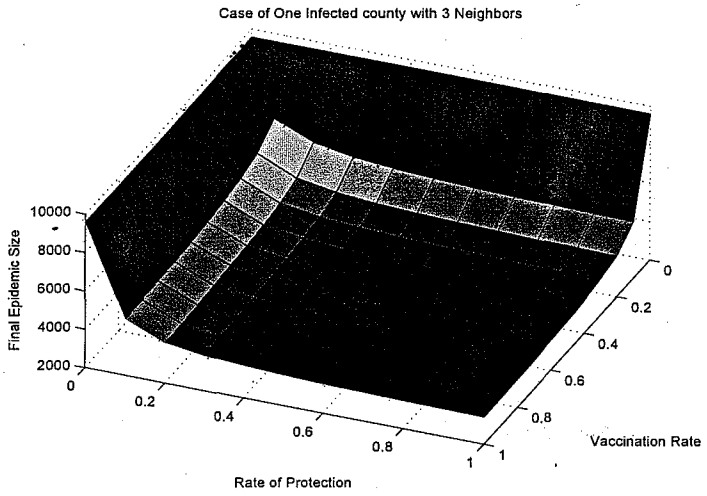

Figure 7: Impact of vaccination rate and protection rate on the final epidemic size

vaccination on the fourth day, along with animal movement, then the final epidemic size would have decreased by 12.5%. Hence, the time of vaccination implementation is crucial in determining the final outcome of the epidemic.

Ring vaccination is effecting in controlling a foot-and-mouth disease epidemic, however it must be combined with other control measures such as movement restrictions and isolation. Through this work, we were able to explore the efficacy of ring vaccination in controlling the epidemic. We conclude that ring vaccination is effective because for all of our simulations, we would end up vaccinating at most 50% of the total initial number of farms. However, depending on the potency of the vaccination, the time in days of the epidemic varies from 30 to 50 days. Uruguay implemented ring vaccination, however after a couple of days of adopting ring vaccination, mass vaccination was implemented. In order to avoid mass vaccination, Uruguay should have expanded the ring of vaccination.

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7 Appendix: Computation of the Next Generation Matrix

In our work we have a heterogeneous population of farms which are distinguishable by spatial position and can be grouped in n homogeneous compartments. Let

$$x = \begin{bmatrix} x_1 \\ \vdots \\ x_n \end{bmatrix}$$

be the number of farms on each compartment, i.e. $x_i > 0$ is the number of farms in county i, and the population is divided into n counties.

For clarity we sort the compartments so that the first m compartments correspond to the infected farms. The distinction between infected and uninfected compartments is determined from the epidemiological interpretation of the model and cannot be deduced from the structure of the equation alone [9]. Thus, the infected compartments are $L_1, \ldots, L_n$, and $I_1, \ldots, I_n$. Note that the dimension of x is $6n$ since we have six compartments in our model, and $m = 2n$ are the first entrees in x corresponding to the new infected classes. Therefore the vector x has the following form

$$x = (L_1, \ldots, L_n, I_1, \ldots, I_n, S_1, \ldots, S_n, V_1, \ldots, V_n, J_1, \ldots, J_n, P_1, \ldots, P_n)^T.$$

The *disease free equilibrium* (DFE) for this model is calculated by finding an equilibrium solution of (1) with $L_i = 0$, and $I_i = 0$ for all $i = 1, \ldots, n$ and without considering control-interventions. Hence the DFE solves the following system

$$\begin{aligned} \dot{S}_i &= -\beta_1(t) S_i I_i - \sum_{j \in \Omega_i} \beta_2(t) S_i I_j, \\ \dot{L}_i &= \beta_1(t) S_i I_i + \sum_{j \in \Omega_i} \beta_2(t) S_i I_j, \\ \dot{I}_i &= \kappa L_i - \alpha(t) I_i. \end{aligned}$$

Note that since $I_i = L_i = 0$, the value for S_i can be arbitrary, in particular, let S_i^* be the total number of farms in county i, i.e. $S_i^* = N_i$. Therefore the DFE without control-interventions is

$$x_0 = (0, \ldots, 0, 0, \ldots, 0, N_1, \ldots, N_n, 0, \ldots, 0, 0, \ldots, 0, 0, \ldots, 0)^T.$$

or in a simple form $x_0 = (0, 0, N_i, 0, 0, 0)^T$.

In order to compute $\mathcal{R}_0$, we need to distinguish new infections from all other changes in population. Let $\mathcal{F}_i(x)$ be the rate of appearance of new infections in compartment i, and $\mathcal{V}_i(x)$ be the rate of transfer of individuals. With the definitions above, the disease transmission model consists of the following system of equations:

$$\dot{x}_i = f_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x), \qquad i = 1, \ldots, n\,.$$

The decomposition of $f(x)$ into the components $\mathcal{F}$ and $\mathcal{V}$ is as follows. Progression from compartment L to compartment I, and compartment J are not considered to be new infections, only progression to compartment L is considered new infections. Hence,

$$\mathcal{F} = \begin{bmatrix} (\beta_1 I_i + \sum_{j\in\Omega_i} \beta_2 I_j)S_i + (\beta_1 I_i + \sum_{j\in\Omega_i} \beta_2 I_j)V_i \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix},$$

and

$$\mathcal{V} = \begin{bmatrix} \kappa L_i \\ -\kappa L_i + \alpha I_i \\ \beta_1 S_i I_i + S_i \sum_{j\in\Omega_i} \beta_2 I_j + \nu S_i \\ -\nu S_i + \beta_1 I_i V_i + \sum_{j\in\Omega_i} \beta_2 I_j V_i + \mu V_i \\ -\alpha I_i \\ -\mu V_i \end{bmatrix}.$$

The model consist of nonnegative initial conditions, and to ensure that *for each nonnegative initial condition there is a unique, nonnegative solution* the decomposition of $f(x)$ into the components $\mathcal{F}$ and $\mathcal{V}$ must satisfy the assumption (A1) through (A5) described in [9], where

$$\mathcal{V}^+(x) = \begin{bmatrix} \kappa L_i \\ \alpha I_i \\ \beta_1 S_i I_i + S_i \sum_{j\in\Omega_i} \beta_2 I_j + \nu S_i \\ \beta_1 I_i V_i + \sum_{j\in\Omega_i} \beta_2 I_j V_i + \mu V_i \\ 0 \\ 0 \end{bmatrix} \quad \text{and} \quad \mathcal{V}^-(x) = \begin{bmatrix} 0 \\ \kappa L_i \\ 0 \\ \nu S_i \\ \alpha I_i \\ \mu V_i \end{bmatrix}$$

Now, we want to know what happens to the population "near" the DFE x_0 (linearization around the equilibrium). If the population remains near to the DFE i.e., if the introduction of a few infected individuals does not result in an epidemic, then the population will return to the DFE according to the linearized system

$$\dot{x}_i = Df(x_0)(x - x_0)$$

where $Df(x_0)$ is the Jacobian matrix at the DFE x_0. The above decomposition of $f(x)$ allow us to partition the matrix $Df(x_0)$ as follow:

Lemma 2. *If x_0 is a DFE of (1), and $f(x)$ satisfy the assumption (A1) through (A5) described in [9], then the derivatives $D\mathcal{F}(x_0)$, and $D\mathcal{V}(x_0)$ are partitioned as*

$$D\mathcal{F}(x_0) = \begin{bmatrix} F & 0 \\ 0 & 0 \end{bmatrix}, \qquad D\mathcal{V}(x_0) = \begin{bmatrix} V & 0 \\ -C & B \end{bmatrix}$$

where F and V are the $m \times m$ matrices defined by

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0)\right] \qquad \text{and} \qquad V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0)\right] \qquad \text{with} \quad 1 \leq i, j \leq m.$$

Further, F is nonnegative, and V is nonsingular.

8 Appendix: How many neighbors?

We should note that if we have an $n \times n$ grid, where each cell in the grid represents a county, then it would be useful to know how many neighbors has a given county in the grid for all n.

Note for example, if $n = 4$ there are four counties with tow neighbors (corners), eight counties with three neighbors (sides), and four counties with four neighbors (centers). This suggest that if C is the set of all counties, we can form a *partition* $\mathcal{P}$ of C as follows:

$$\mathcal{P}(C) = \{C_2, C_3, C_4\},$$

where C_i denotes the set of counties with $i = 2, 3, 4$ neighbors.

Now, we observe that the number of elements of each C_i is

$$\begin{aligned} \#C_2 &= 4 \\ \#C_3 &= 4(n-2) \\ \#C_4 &= (n-2)^2, \end{aligned}$$

we can verify that

$$4 + 4(n-2) + (n-2)^2 = n^2$$

in other words, for a given n, the total number of counties in each class is in terms of n and check with the total number n^2 of counties in the grid.