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A simulation model for the potential spread of foot-and-mouth disease in the Castile and Leon region of Spain

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ABSTRACT

A spatial stochastic model was used to simulate the spread of a foot-and-mouth disease (FMD) epidemic in the Castile-and-Leon (CyL) region of Spain. The model was fitted using information available on premises demographics and on assumptions for animal movements, indirect contacts, and airborne exposure. Control measures dictated by Spanish and European Union regulations constituted a reference strategy to which six alternative control strategies were compared. For the reference strategy, the median (95% PI) numbers of infected, depopulated, and quarantined premises were 141 (2–1099), 164 (4–1302), and 334 (31–2059), respectively. Depopulation and vaccination of premises within a radius of <1 km and <3 km, respectively, around infected premises significantly (p-value < 0.001) decreased the number of infected premises, compared to the reference scenario. Results presented here will contribute to the revision, design, and implementation of contingency plans and programs for prevention and control of FMD epidemics in Spain.

1. Introduction

Foot-and-mouth disease (FMD) is a highly infectious disease of cloven-hoofed animals, including cattle, pigs, sheep, and goats, and causes important economic losses to infected countries and regions (James and Rushton, 2002). FMD is endemic in many regions of the world and the potential introduction of FMD virus (FMDV) remains a significant threat for FMD-free countries (Leforban and Gerbier, 2002), such as Spain, which has been free of FMD since 1986. The numerous and repeated FMD epidemics experienced by European Union (EU) member countries over the last 15 years (Davies, 2002; Bouma et al., 2003; Griffin and O'Reilly, 2003; Chmitelin and Moutou, 2002, DEFRA, 2007) and the recent introduction of other exotic diseases into Spain (Rodriguez et al., 1992; Bech-Nielsen et al., 1995; Allepuz et al., 2007) have increased concerns of the Spanish government and of stakeholders about the potential introduction of FMD into Spain (Anonymous, 2006, 2007).

Currently, Spain is the second largest producer of pigs, sheep, and goats and the sixth largest producer of cattle among the 25 EU countries. Animal agriculture contributed \$17.4 billion to the Spanish economy in 2005 (MAPA, 2005). Thus, an FMD epidemic will likely have severe consequences for the Spanish economy, including restrictions on trade and losses for many livestock-related industries and for tourism. Because the disease has not been reported in Spain for over 20 years, there is a lack of understanding of how and where FMD might spread given the geographical distribution of farms and dynamics of animal movements in the country. Such information would be a prerequisite for planning effective means of preventing and controlling FMD epidemics in Spain. In the absence of controlled experiments on natural disease, models can be used to simulate hypothetical epidemics, based on assumptions about

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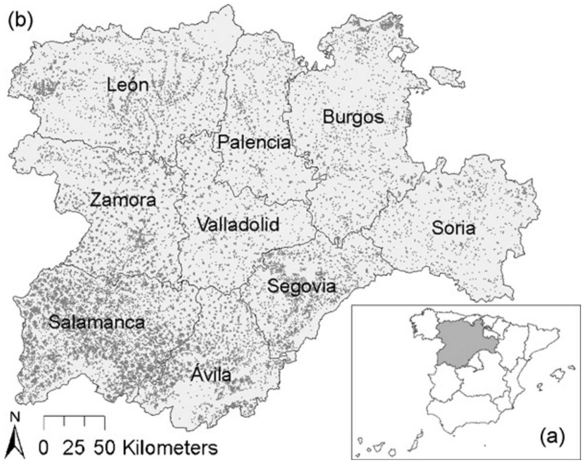

Fig. 1. Geographic distribution of animal premises in the Castile and Leon (CyL) region of Spain in 2005. (a) Map of Spain showing the location of the CyL in dark grey. (b) Distribution of foot-and-mouth disease (FMD)-susceptible livestock premises in the nine provinces of CyL.

disease transmission, and to identify features of animal management or demographics or of control strategies that could amplify or retard an epidemic. Knowledge of such features could be applied to design of control and prevention programs. Several of these types of models have been developed to predict spread of an FMD epidemic and to assess the effects of different control strategies in FMD-free countries (Garner and Lack, 1995; Durand and Mahul, 2000; Bates et al., 2003a,b; Sanson et al., 1993; Le Menach et al., 2005; Morris et al., 2001; Kobayashi et al., 2007). No studies, however, have been reported that offer a model for the potential spread of FMD, or that estimate the potential magnitude of an FMD virus incursion, in Spain.

The objectives of the study here were to estimate the potential magnitude and duration of an FMD epidemic, to identify areas likely to be at highest risk of having FMD, and to compare the potential effectiveness of alternative control measures in the Castile-and-Leon (CyL) region of Spain, which is heavily engaged in animal agriculture. Results will contribute to improved contingency planning for control strategies, should there be an FMD epidemic in Spain.

2. Materials and methods

2.1. Study region and data

The CyL region was selected for study because it represents a major area for animal agriculture in Spain (MAPA, 2005) and because data were available for premises locations and animal movements. CyL is one of 17 autonomous communities in Spain (Fig. 1), with nine administrative areas, referred to as provinces, each of which is divided into smaller administrative areas, referred to as municipalities (Table 1). The CyL region could be considered to be at a high risk of FMD introduction and potential spread because the region has a high animal density and the extensive system for animal movement would likely foster transmission of FMD, as observed in previous epidemics (MAPA, 1952–1965, MAPA, 1966–1987) and as suggested by a recent risk assessment study (Martínez-López et al., 2008).

Information used here consisted of premises (n = 70,015) and animal movement (n = 299,225) data obtained from the CyL Livestock Production Department for 2005. Premises data included a unique premises identifier, the point location of the premises centroid, the municipality and province where the premises was located, and the type and number of susceptible species on the premises. Animal movement data included premises of origin, premises of destination, date of the movement, and number of animals moved.

2.2. Model description and formulation

A modified stochastic spatial disease state transition model was used to simulate the hypothetical spread of FMD within CyL. The formulation of the model, referred to as the InterSpread model (InterSpread Plus version 1.048.3. Copyright ©Massey University, 2003), has been described elsewhere (Sanson et al., 1993, 1999, 2006a,b; Morris et al., 2001; Bigras-Poulin, 2003). Briefly, each premises was assumed to exist in only one of the five mutually exclusive herd-based disease transition states of susceptible, undetected subclinical infection, undetected clinical infection, detected infection, and depopulated. The susceptible state, $S_{i(t)}$, included premises with animals that were susceptible to FMD virus-infection and that were not infected with FMD virus and that had not ever been infected with the virus or vaccinated for FMD. The undetected subclinical infection state, $I_{i(t)}$, included premises with at least one infected animal and no evidence of clinical disease on any of the infected animals and no diagnosis being reported. The undetected clinical infection state, $Cl_{i(t)}$, included premises with at least one infected animal with clinical signs of FMD and no diagnosis of FMD being reported. The detected infection state, $D_{i(t)}$, included premises with infected animals showing clinical signs of FMD and a reported diagnosis of FMD. The depopulated state, $Dp_{i(t)}$ was one for which all individuals on the premises had been destroyed, infectious material had been removed, and cleaning and disinfection had been completed so that the premises could no longer be considered infected/infectious. FMDV spread from premises i to premises j was assumed to occur by the movement of infected animals or by local spread, which considered possible short distance airborne spread or transmission by indirect contacts with contaminated materials or fomites. The likelihood of a premises transitioning from one state to another was estimated by use of variables that were parameterized using data collected from the literature or through elicitation of expert opinion (Table 2), which was referred to as the baseline parameterization of the model. There were no local data available in Spain to justify the maximum extension of local spread. The epidemiological conditions of the FMD epidemic that affected the UK in 2001 are arguably more similar to those that one would expect in CyL, than any other FMD epidemic for which information may be available. Consequently, local spread was limited to $\leq$3 km, which is a value used by others, based on empirical evidence collected in the UK in 2001

Table 1
Administrative divisions and animal demographics of the Castile and Leon (CyL) region of Spain in 2005.

Province	Area (km^2)[a]	Number of municipalities	Number of veterinary officials[b]	Number of premises[c]	Density of animals[d] (animals/km^2)
Ávila	8050	248	78	9615	99.19
Burgos	14,022	424	75	4603	62.07
León	15,570	216	94	12,887	60.69
Palencia	8052	191	50	2423	69.21
Salamanca	12,349	363	90	18,980	142.30
Segovia	6796	210	45	5587	285.25
Soria	10,303	184	40	1919	82.64
Valladolid	8110	225	61	3273	115.06
Zamora	10,561	248	67	10,728	135.06
Total	**93,813**	**2309**	**600**	**70,015**	**107.42**

[a] *Source*: National Statistics Institute.
[b] Including veterinary inspectors and livestock controllers.
[c] Only premises with FMD-susceptible animals. Source: CyL animal premises database.
[d] Only FMD-susceptible animals. *Source*: CyL animal premises database.

(Keeling et al., 2001; Ferguson et al., 2001; Sanson et al., 2006b).

Control measures assumed by the model in the 'reference scenario' were those required by Spanish and European Union regulations (MAPA, 2006) (Table 2). These were depopulation of infected premises, restriction of movements in a 10 km buffer zone, and tracing of incoming and outgoing movements.

2.3. Simulation of FMD cases

Simulation of the hypothetical spread of FMD was performed by randomly selecting (without replacement) a premises as the first infected premises from which the epidemic would spread, and referred to here as the *index case*. Random selection was repeated 199 times over the entire region of CyL to produce 200 different locations for index cases. For each index case, 100 epidemics were simulated beginning on the day the index case became infected. The magnitude of the epidemic was characterized for each of the 200 index case epidemic simulations by the median and 95% probability intervals (PI 95%) of the number of infected premises, of the number of depopulated premises, of the number of quarantined premises in the protection zone, and of the duration of the epidemic. The median time to detection also was computed. The procedure was conducted for the reference scenario and for each of the six scenarios in which alternative control measures were applied.

The probability of infection (P_j) of each premises j was estimated for the reference scenario as the proportion of model runs ($n = 20{,}000$) in which premises j had become infected. An isopleth map of P_j was created by using an inverse distance weighting (IDW) algorithm (Isaaks and Srivastava, 1989) to compute for each single location i, a weighted average (W_i) of the value of P_j such that nearby premises were weighted more heavily in the predictions than distant premises. The value of W_i was computed as:

$$W_i = \frac{\sum_{j=1}^{n} P_j / d_{ij}^{p}}{\sum_{j=1}^{n} 1/d_{ij}^{p}}$$

The value of p, which is a weighting factor that modifies the relative influence of premises j on predicted locations i so that the relation is not necessarily proportional, was computed as the value that minimized the root-mean-squared prediction error at premises j. The IDW was computed and maps were created using ArcMap 9.1. (ESRI©, 2005).

2.4. Alternative control measures

Epidemic duration and magnitude estimated for six alternative control scenarios based on variations of preventive depopulation and vaccination strategies (Table 3) were compared to those estimated for the reference control scenario. A Kruskal–Wallis test and box plots were used to test for statistical significance in the median number of infected premises, in the median number of depopulated premises, and in the median duration of the epidemic estimated for each strategy and index case ($n = 200$).

2.5. Sensitivity analyses

The sensitivity of the model to the number of index cases ($n = 200$) used here was tested by computing the variation in the number of infected premises obtained by the addition of every index case, from a minimum of 1 up to a maximum of 200 index cases. Stabilization in the number of predicted infected premises was considered evidence that the number of index cases was sufficient to produce robust predictions of the model.

Sensitivity analysis was also used to quantify the influence that selected input variables had on the model outcomes for the reference scenario. Selected input variables and changes applied to the baseline parameterization were (1) time from detection to depopulation of an infected premises (+2 days, +5 days); (2) maximum number of premises that could be depopulated per day (−50%); (3) probability of transmission by local spread (−50%, −20%, +20%, +50%); and probability of success in implementation of movement restrictions for premises (4) in the detected infection state (−20%), (5) within the control and surveillance zones (−20%), and (6) outside the control and surveillance zone (−20%). The magnitude of 100 epidemics simulated for each of the 10 sensitivity-scenarios was compared to the magnitude of the epidemic estimated for

Table 2
Variables and assumptions used to parameterize the transmission of foot-and-mouth disease (FMD) on a simulation model of FMD spread in the Castile and Leon (CyL) region of Spain.

Parameter description (InterSpread name)	Value	Source
Section 1. Movement of animals		
Average number of cattle and pig shipments sent from premises-to-premises per day (number use farm column)	Poisson (λ_i)[a]	CyL data
Average number of sheep and goat shipments sent from premises-to-premises per day (number per time period)	Poisson ($\lambda = 0.02$)	CyL data
Average number of cattle, sheep and goat shipments sent from premises-to-market per day (number per time period)	Poisson ($\lambda = 0.003$)	CyL data
Average number of cattle, sheep and goat shipments sent from market-to-premises per day (number per time period)	Poisson ($\lambda = 0.002$)	CyL data
Probability that a cattle, sheep, or goat shipment reaches a specific distance (movement distance)	Lookup table: 0.7731 from 0 to <64 km, 0.192 from 64 to <128 km, 0.0283 from 128 to <192 km, 0.0054 from 192 to <256 km and 0.0012 from 256 to <320 km.	CyL data
Probability that a pig shipment reaches a specific distance (movement distance)	Lookup table: 0.7260 from 0 to <72 km, 0.2160 from 72 to <144 km, 0.0453 from 144 to <216 km, 0.00976 from 216 to <288 km and 0.00294 from 288 to 360 km.	CyL data
Probability that a premises receives a shipment (destination probability [source farm class][b] and destination farm weighting column)	$W_j/\sum W_j$; where W_j is the number of shipments received per premises j and per day	CyL data
Probability that a premises becomes infected from an incoming animal shipment if the source premises is infected (probability of transmission)	Constant = 1	Bigras-Poulin (2003)
Section 2. Local spread		
Probability that a premises becomes infected as a consequence of local spread at a given day after onset of clinical signs at the source premises (probability of transmission)	Lookup table: from 0 to 1 km: 0.007 at day 0, 0.012 at days 1 and 2, 0.009 at day 3; from 1 to 2 km: 0.002 at day 0, 0.003 at day 1, 0.004 at day 2 and 3; from 2 to 3 km: 0 at day 0, 0.001 at days 1, 2 and 3.	Sanson et al. (2006b)
Section 3. Infectivity		
Probability that at least one animal in an infected premises shows clinical signs at a given day after infection (time to clinical signs)	Lookup table: 0 at day 1, 0.035 at day 2, 0.158 at day 3, 0.333 at day 4, 0.772 at day 5, 0.789 at day 6, 0.825 at day 7, 0.877 at day 8, 0.912 at day 9 and 10, 0.947 at day 11, 0.965 at day 12 to 15, 0.982 at day 16 and 1 from day 17 in advance.	Sanson et al. (2006a)
Probability that a cattle, sheep or goat premises becomes infectious at a given day after infection (infectivity [animal type])	Lookup table: 0.174 from day 1 to day 4, 0.391 from day 5 to day 8, 0.652 from day 9 to day 11, 0.869 from day 12 to day 17, 1 from day 18 in advance	Sellers and Daggupaty (1990)
Probability that a pig premises becomes infectious at a given day after infection (infectivity [animal type])	Lookup table: 0 at day 1, 0.5 from day 2 to day 7, 0.8 from at day 8, 1 from day 9 in advance	Sellers and Daggupaty (1990)
Section 4. Zones		
Duration of the 3 km radius control zone (duration)	30 days	MAPA (2006)
Duration of the 10 km radius surveillance zone (duration)	40 days	MAPA (2006)
Section 5. Resources for depopulation		
Number of premises that can be depopulated per day during the first 15 days after the detection of the index case (farms per time period)	50	Expert opinion[c]
Number of premises that can be depopulated per day after 15 days of detection of the index case (farms per time period)	100	Expert opinion[c]
Section 6. Movement restriction		
Probability of imposing successful movement restrictions to infected-and-detected premises (probability movement restricted)	0.98	Expert opinion[c]

Table 2 (*Continued*)

Parameter description (InterSpread name)	Value	Source
Probability of imposing successful movement restrictions to premises within the control and surveillance zones (probability movement restricted)	0.95	Expert opinion[c]
Probability of imposing successful movement restrictions to premises other than those infected-and-detected or located within the control and surveillance zones (probability movement restricted)	0.7	Expert opinion[c]
Section 7. Surveillance		
Number of days between the date when a premises is placed under surveillance and the date of first visit to the herd, before the detection of the index case (visit delay)	Poisson ($\mu = 1$)	Expert opinion[c]
Number of days between the date when a premises is placed under surveillance and the date of first visit to the herd, after the detection of the index case (visit delay)	Poisson ($\mu = 0.5$)	Expert opinion[c]
Number of days between two consecutive visits to a farm that has been placed under surveillance (visit frequency)	Poisson ($\mu = 7$)	Expert opinion[c]
Duration of the surveillance on a particular premises (visit duration)	Poisson ($\mu = 30$)	Expert opinion[c]
Time between the date when a visit to the premises took placed to the date when the premises will be detected as infected, relative to the time to onset of clinical signs on the premises, before detection of the index case (delay to detection)	Poisson ($\mu = 1$)	Expert opinion[c]
Time between the date when a visit to the premises took placed to the date when the premises will be detected as infected, relative to the time to onset of clinical signs on the premises, after detection of the index case (delay to detection)	Poisson ($\mu = 0.5$)	Expert opinion[c]
Probability of an infected premises being detected as infected at a given visit before the detection of the index case (detection probability)	Pert (min, most likely, max = 0.85, 0.9, 0.95)	Expert opinion[c]
Probability of an infected premises being detected as infected at a given visit after the detection of the index case (detection probability)	Pert (min, most likely, max = 0.95, 0.99, 1)	Expert opinion[c]
Section 8. Tracing (on/off premises)		
Probability of forgetting or missing the trace of a cattle or pig shipment (probability movement forgotten)	0.001	Expert opinion[c]
Probability of forgetting or missing the trace of a sheep or goat shipment or a shipment from/to a market (probability movement forgotten)	0.01	Expert opinion[c]
Time required to trace a cattle and pig shipment (tracing delay)	Pert (min, most likely, max = 0, 1, 2)	Expert opinion[c]
Time required to trace a sheep or goat shipment or a shipment from/to a market (tracing delay)	Pert (min, most likely, max = 1, 2, 3)	Expert opinion[c]

[a] Lambda is the average number of shipments sent per premises and per day (each premises has a specific Poisson distribution).
[b] Shipments were possible only between premises with animals from the same species.
[c] Expert opinion of Castile and Leon Veterinary Services, November 5, 2008.

the baseline parameterization of the reference scenario. Similar results (<10% variation in the magnitude of the epidemics) were considered evidence of robustness of the model to variations in the input variables.

The randomly selected index cases ($n = 200$) were the same for the reference scenario, for the alternative control measures, and for the sensitivity analysis.

3. Results

3.1. Magnitude and duration of the FMD epidemic estimated for the reference scenario

The median (95% PI) number of infected premises was 141 (2–1099), which corresponds to 0.2% (0.002%, 1.56%)

Table 3
Alternative control strategies applied to control foot-and-mouth disease (FMD) on a simulation modeling exercise of FMD spread in the Castile and Leon region of Spain.

Alternative measure	Description
1. Preventive depopulation	Depopulation of premises that received shipments from infected-and-detected premises
2. Vaccination within a <3 km radius	Vaccination[a] of premises within a 3 km radius around infected-and-detected premises
3. Vaccination within a <5 km radius	Vaccination[a] of premises within a 5 km radius around infected-and-detected premises
4. Vaccination within a <3–10 km radius	Vaccination[a] of premises within a 3 to 10 km radius around infected-and-detected premises (Stärk, 1998)
5. Depopulation of premises within a <1 km	Depopulation of premises within a 1 km radius around infected-and-detected premises
6. Depopulation of premises within a <3 km	Depopulation of premises within a 3 km radius around infected-and-detected premises

[a] Immunity reached by vaccinated animals was assumed to be 0% from day 0 through day 3, 35% from day 4 through day 6, 96% from day 7 through day 13, 99% from day 14 through day 21, and 100% since day 21 post-vaccination (Salt et al., 1998; Golde et al., 2005).

of the total number of FMD-susceptible premises in CyL (n = 70,015). The median number of depopulated and quarantined premises was 164 (4, 1302) and 334 (31, 2059), respectively. The median time to detection and duration of the epidemic was 17 (12, 69) and 82 (11, 188) days, respectively.

Many (49.6%) of the FMD-infected premises were pig farms, whereas the remaining 27.6%, 16.28%, and 6.53% infected premises corresponded to cattle, sheep, and goat or mixed herds, respectively.

Local spread accounted for 68.9% of the infected premises in the reference scenario. Similarly, premises-to-premises and market-to-premises movements accounted for 25.4% and 5.7% of the infected premises, respectively.

Pig premises were the source of 56.0% of the infections, whereas cattle, sheep and goat, and mixed farms were the source of 22.8%, 14.8%, and 6.4% of the infections, respectively.

Areas at high risk of FMD infection were estimated for the 9 provinces of CyL, with the largest number of high-risk areas predicted for the northern and western regions (Fig. 2).

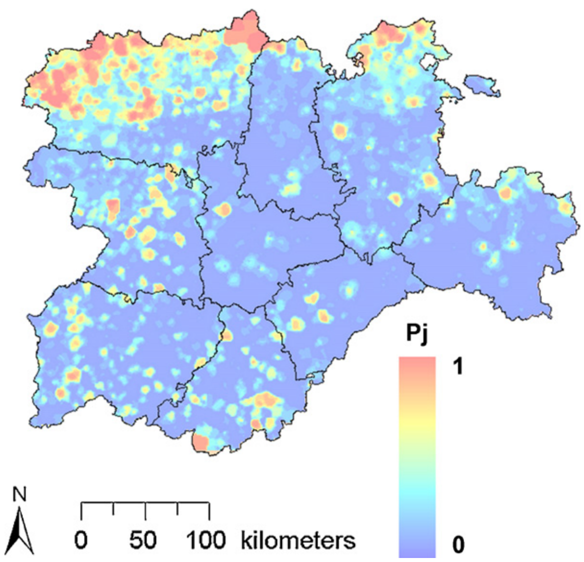

Fig. 2. Inverse distance weighting estimates of the predicted probability of foot-and-mouth disease (FMD) infection (Pj) estimated with a simulation model of FMD spread in the Castile and Leon region of Spain.

3.2. Alternative control measures

Preventive depopulation of premises within radii of <1 km and <3 km around an infected premises resulted in a median 78% decrease of the magnitude of the FMD epidemic (Fig. 3a) compared to the reference control scenario. Preventive vaccination of premises within radii of <3 km and <5 km around infected premises resulted in a 55% decrease in the number of infected premises. The number of infected premises in the scenarios of preventive depopulation of premises within radii of <1 km and <3 km and vaccination within radii of <3 km and <5 km were significantly smaller than those estimated for the reference scenario (Kruskal–Wallis chi-square = 147.27, p-value < 0.001; chi-square = 146.29, p-value < 0.001, chi-square = 134.26, p-value < 0.001 and chi-square = 137.46, p-value < 0.001, respectively). Preventive depopulation of premises that received shipments from infected-and-detected premises and vaccination within a radius of 3–10 km did not significantly reduce the number of infected premises estimated for the reference scenario (Kruskal–Wallis chi-square = 0.04, p-value = 0.844 and chi-square = 3.68, p-value = 0.06, respectively).

Preventive depopulation strategies significantly decreased the number of infected premises compared with the preventive vaccination measures (Kruskal–Wallis chi-square = 97.17, p-value < 0.001). The probability of infection (P_j) was smaller with preventive depopulation within a <3 km radius (median = 0; 95% PI = 0–0.26), compared with preventive depopulation within a <1 km radius (median = 0.02; 95% PI = 0–0.32); similarly, vaccination within <3 km yield to values of Pj that were slightly smaller than those computed for the <5 km radius of vaccination (Fig. 3b). As a consequence of such small variation, no significant differences were found between preventive depopulation within a radius of <1 and <3 km (Kruskal–Wallis chi-square = 0.003, p-value = 0.956) and between preventive vaccination within radius of <3 km and <5 km (Kruskal–Wallis chi-square = 2.78, p-value = 0.1).

The largest reduction in the number of depopulated premises (53.3%), compared to the reference scenario was achieved when preventive vaccination of premises within radii of <3 km and <5 km around infected premises and depopulation within radii of <1 km and <3 km around an infected premises were simulated (Kruskal–Wallis chi-square = 192.40, p-value < 0.001). Preventive depopulation of premises within radii of <1 km and <3 km around

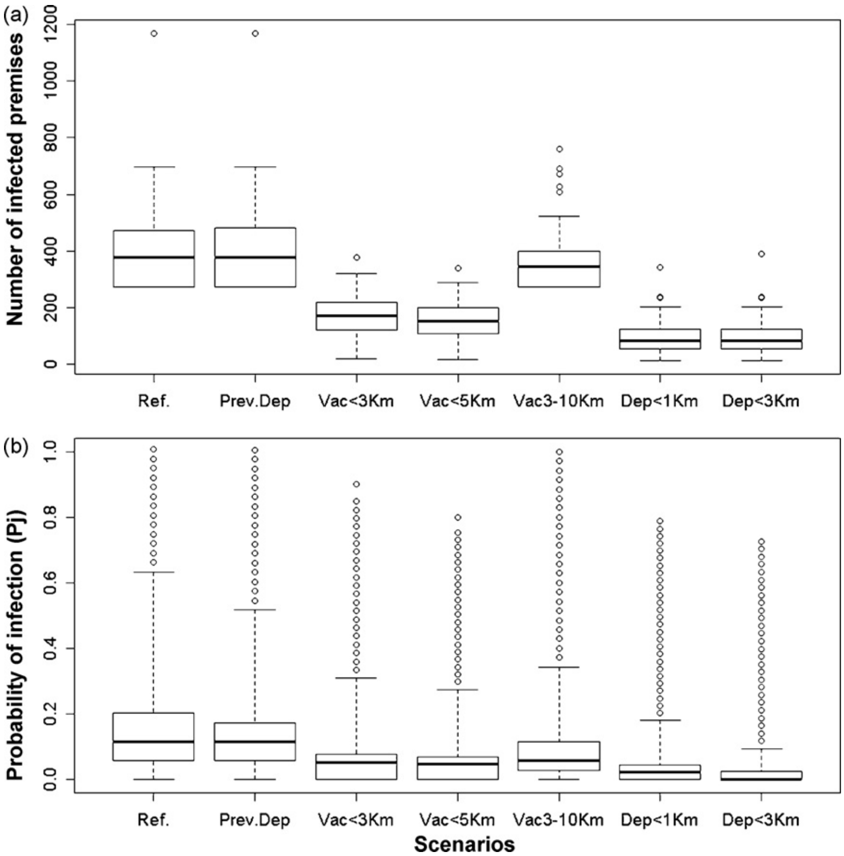

Fig. 3. Box plot of the number of infected premises (a) and the probability of infection (b) estimated for the reference control scenario, which was parameterized according to current Spanish legislation, and six alternative control scenarios in a simulation exercise of foot-and-mouth disease (FMD) spread in the Castile and Leon region of Spain. Ref = reference scenario; Prev. Dep = depopulation of premises that received shipments from infected-and-detected premises; Vac < 3 km = vaccination within a radius of <3 km; Vac < 5 km = vaccination within a radius of <5 km; Vac3–10 km = vaccination within a radius from 3 to 10 km; Dep < 1 km = preventive depopulation within a radius of <1 km; Dep < 3 km = preventive depopulation within a radius of <3 km.

an infected premises also resulted in the largest reduction (65.6%) of the number of quarantined premises (Kruskal–Wallis chi-square = 84.58, p-value < 0.001). Other output measures were not significantly different compared to the reference scenario (Kruskal–Wallis chi-square = 1.99, p-value = 0.737).

3.3. Sensitivity analyses

The estimated number of infected premises was constant after the selection of 160 index premises and addition of more index premises did not affect the model results (Fig. 4), suggesting that the number of index premises used

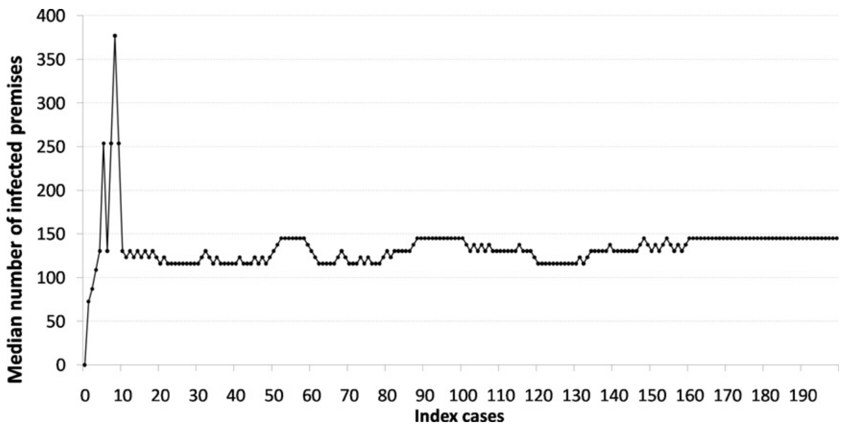

Fig. 4. Variation in the estimated median number of infected premises obtained by the addition of every index case, from a minimum of 1 up to a maximum of 200 index cases.

here ($n = 200$) was sufficient to estimate the expected distribution of an hypothetical FMD epidemic in CyL.

The model was sensitive to changes in the parameterization of the local spread and movement restriction in the surveillance and control zones. A 50% increase in the proportion of local spread resulted in increments of 73.6%, 53.3%, and 53.0% in the number of infected, depopulated, and quarantined premises, respectively. A 20% decrease in the probability of successful restriction of animal movements within the control and surveillance zones produced an increase of 26.4%, 22.9%, and 59.1% in the number of infected, depopulated, and quarantined premises, respectively.

The model was robust (<10% variation) to other changes in the input variables.

4. Discussion

Results of the simulation model presented here suggest that control measures specified in the Spanish and EU legislations are not the most effective strategy to control FMD spread in the event of a potential epidemic in CyL. Preventive vaccination of premises within a radius of <3 km and preventive depopulation of premises within a radius of <1 km around an infected premises were more effective in controlling a hypothetical FMD epidemic than depopulation of infected premises. This finding suggests that Spanish regulations should be reviewed in order to consider the implementation of strategies that may be more effective in controlling an FMD epidemic than those currently in place. Preventive vaccination and preventive depopulation within radii of <5 km and <3 km, respectively, did not result in significant reductions of the magnitude of the epidemics, compared to vaccination and depopulation within <3 km and <1 km, respectively. This observation suggests that increments in the size of the vaccination or depopulation zones are not cost-effective control strategies for FMD in the region.

Preventive vaccination and depopulation of premises are control strategies aimed at reducing the number of susceptible and infectious animals, respectively, within the infected region, which will ultimately lead to the reduction of the transmission rate of the disease. The higher effectiveness that preventive vaccination and preventive population strategies had in controlling an hypothetical FMD epidemic in CyL, compared to depopulation of infected premises only, may be explained, at least in part, by the highly infectious nature of FMD. Because the FMD virus is expected to rapidly spread through densely populated areas, such as CyL, it is possible that depopulation of infected-and-detected herds may not be sufficient to prevent the spread of the disease into susceptible premises before the infectious herd could be detected and depopulated. However, preventive vaccination or preventive depopulation of premises at high risk of being infected will eventually result in the reduction of effective contacts between infectious and susceptible herds. Subsequently, on average, the numbers of quarantined and depopulated herds were lower when preventive vaccination or preventive depopulation was applied compared to depopulation of infected herds only.

Certainly, the decision of applying either or both preventive depopulation or vaccination to control an FMD epidemic is not exempt of controversy and discussion (Toma et al., 2002; Schoenbaum and Disney, 2003). Among the negative implications that preventive vaccination may have, compared to preventive depopulation, are the nature, extent, and duration of the trade restrictions that will be imposed to the country, the extension of the period required to recover the FMD-free status, and the requirement of having available a sufficiently large number of vaccine doses with a strain formulation that is effective in raising protective immunity against the specific strain that caused the epidemic. In turn, culling a large number of animals may have a negative impact on the public opinion and logistics of preventive depopulation, including sacrifice, removal, and disposal of the livestock, may be overwhelming and difficult to handle for the veterinary services, particularly in those areas populated by a high density of susceptible animals. Alternatively, preventive vaccination and culling of vaccinated animals, which is a control strategy that has been applied in The Netherlands in 2001 (Bouma et al., 2003), may contribute to reduce disease spread when epidemiological, logistic, or social conditions prevent the immediate application of depopulation strategies (Woolhouse et al., 2001). Despite the social, economical, and political implications that implementation of either or both preventive vaccination and preventive depopulation may have in Spain, results of the study here suggest that any of those measures will result in a significant reduction of the magnitude of a hypothetical FMD epidemic in CyL, compared to depopulation of infected premises alone. Consequently, development of a contingency plan that considers the application of such measures will likely improve the ability of Spanish veterinary services to prevent and control FMD incursions in the region.

The probability of FMDV infection (P_j) was concentrated in the northwestern region of CyL, in which the probability of infection approximated values as high as 1 for some premises (Fig. 2). Unfortunately, not data on type of farm was available to us and for that reason, it was not possible to assess whether this high risk was associated with particular characteristics of the index farms and/or of the farms in the region. However, and although not specifically assessed here, one may speculate that this finding may be explained, at least in part, by a combination of large numbers of markets and of farms with >1 animal species (mixed farms), high frequency of incoming and outgoing movements, and relatively high density of farms (>3 farms per km^2) in that region.

Airborne spread (Daggupaty and Sellers, 1990; Donaldson and Alexandersen, 2002; Gloster et al., 2003) and long range transmission such as that resulted through the movement of contaminated vehicles were not considered in the model here because the data necessary to model those potential routes were not available to us. The impact of such simplification is uncertain, although one can speculate that it has resulted in an underestimation of the rate of virus transmission and, consequently, in the number of predicted infected farms. Noteworthy, however, the magnitude and duration of the FMD epidemic simulated here was similar to those

Table 4
Number of foot-and-mouth disease (FMD)-infected premises and duration of FMD epidemics reported from field observations and estimated through simulation modeling.

Country	Infected premises	Duration of the epidemic	Reference
Simulation modeling			
Spain	141 (2–1099)	82 (11–188)	This study
Australia			Garner and Lack (1995)
Northern Victoria	36 (18–54)	100 (67–133)	
Northern New South Wales	29 (15–43)	78 (56–100)	
Midlands	25 (10–40)	53 (38–68)	
U.K.	3604 (2966–3974)	193 (192–195)	Morris et al. (2001)[a]
USA	46 (1–148)	71 (25–109)	Bates et al. (2003b)
Korea	15 (1–130)	58 (1–60)	Yoon et al. (2006)[a]
France	2050 (1810–2300)	+200	Le Menach et al. (2005)
Epidemics			
Taiwan (1997)	6147	121	Yang et al. (1999)
The Netherlands (2001)	26	38	Bouma et al. (2003)
U.K. (2001)	2030	±240	Savill et al. (2006)
Irlanda (2001)	1	33	Griffin and O'Reilly (2003)
France (2001)	2	10	Chmitelin and Moutou (2002)
Argentina (2001)	2126	266	Perez et al. (2004)
Uruguay (2001)	2057	121	Sutmoller and Olascoaga (2002)
Korea (2002)	16	52	Yoon et al. (2006)
UK (2007)	8	40	Cottam et al. (2008)

[a] Estimated using InterSpread.

estimated through simulation modeling in Australia, the U.S.A., and Korea, as suggested by the overlapping confidence intervals of predictions and observations, and also similar to those observed in FMD epidemics recently reported in The Netherlands (2001), Korea (2002), Ireland (2001), France (2001), and U.K. (2007) (Table 4). However, simulation exercises conducted in the U.K. and France, and FMD epidemics reported in Taiwan (1997), the U.K. (2001), Argentina (2001), and Uruguay (2001) resulted in a significantly larger duration and magnitude compared to those estimated here. In addition to the observation that in the model here airborne spread and long range transmission were not considered, it is also possible that such difference may be related, at least in part, with the time-to-detection of the index case assumed and observed in those simulation exercises and epidemics. The time to detection of the FMD epidemic assumed for CyL was, on average, 17 days, which is similar to those assumed and observed in simulation exercises and epidemics that resulted in magnitudes and durations similar to those estimated here. Conversely, at least 3 weeks, and possibly more, lasted between the introduction of the virus and detection of the index case in Taiwan (1997), U.K. (2001), Argentina (2001), and Uruguay (2001), which resulted in larger magnitudes and duration of the epidemics. In the absence of recent experiences of FMD epidemics in Spain, time-to-detection of the index case assumed here was obtained through the consultation of members of the national veterinary service. However, if official expectations are not met in terms of the delay until detection of the epidemic, it is possible that an FMD incursion will result in larger magnitude and longer duration than those estimated here. In such scenario, it is also possible that the effectiveness of the strategies simulated here will also be affected.

Model results were sensitive to the parameterization of the local spread and to the probability of successful restriction to animal movements. Following the detection of the index case, animal movements are banned and disease transmission is mainly determined by local spread. Therefore, it is not surprising that local spread and probability of successful restriction of animal movements were influential parameters of the model. Local spread was estimated to be an important mechanism for FMD virus spread here, likely, as a consequence of a combination of the high density of pig premises in the region and the recognized capacity of pigs to produce FMD virus aerosols. This finding is consistent with previous simulations that suggested an important role for local transmission in the spread of FMD outbreaks (Morris et al., 2001; Bouma et al., 2003; Le Menach et al., 2005). Consequently, many of the premises that, on average, were infected in the simulation here were pig farms. However, ability of the FMD virus to infect specific animal species is highly dependent on the specific serotype and strain causing the epidemic. For example, in the FMD epidemic that affected Taiwan in 1997, only pig premises were infected, whereas in Argentina in 2001, most of the FMD outbreaks corresponded to cattle herds (Yang et al., 1999; Perez et al., 2004). Species-specific susceptibility and virulence of the virus was not modelled here; however, sensitivity of model results to the probability of local spread suggests that the magnitude and duration of an FMD epidemic in CyL will likely be highly influenced by the characteristics of the specific virus strain causing the epidemic. Susceptibility of model results to the effectiveness of the quarantine imposed by the veterinary services suggests that animal movement is an important component of the spread of FMD epidemics (Schley et al., 2009; Green et al., 2006). Moreover, failure to identify the initial outbreaks and promptly implement the appropriate control measures have been proposed to explain, at least in part, the large size of the FMD epidemics that affected the UK in 1967/68 (Hugh-Jones, 1976) and 2001 (Davies, 2002), Taiwan in 1997 (Yang et al., 1999), and Argentina in 2001 (Perez et al., 2004). The results presented here are consistent with those empirical observations and with the results of previous modelling exercises, which suggest that early identification of the initial outbreaks is a critical factor for preventing large FMD epidemics (Chmitelin and Moutou, 2002; Bates et al., 2003b). Our findings stress the importance of conducting simulation exercises to maximize the ability of the veterinary service to early detect and to quickly implement and enforce control measures in the face of an FMD epidemic.

5. Conclusion

Preventive depopulation or preventive vaccination at, respectively, <1 km and <3 km radii around infected premises, were more effective in controlling the spread of FMD epidemics in CyL than the strategy currently approved by the Spanish legislation. Implementation of any of those strategies will likely enhance the ability of the veterinary services to control a hypothetical FMD epidemic in the region. However, use of vaccination to control a hypothetical FMD epidemic will extend the period required to recover the free status of the country, resulting on a larger impact than the depopulation of neighboring (<1 km radius) premises. For that reason, and under certain epidemiological conditions, depopulation may be more beneficial than vaccination for controlling FMD epidemics in EU countries that heavily rely on exporting livestock products such as Spain.

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