



Quantitative risk assessment of foot-and-mouth disease introduction into Spain via importation of live animals

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Received 31 July 2007; received in revised form 22 February 2008; accepted 5 March 2008

Abstract

Spain has been a foot-and-mouth disease (FMD)-free country since 1986. However, the FMD epidemics that recently affected several European Union (EU) member countries demonstrated that the continent is still at high risk for FMD virus (FMDV) introduction, and that the potential consequences of those epidemics are socially and financially devastating. This paper presents a quantitative assessment of the risk of FMDV introduction into Spain. Results suggest that provinces in north-eastern Spain are at higher risk for FMDV introduction, that an FMD epidemic in Spain is more likely to occur via the import of pigs than through the import of cattle, sheep, or goats, and that a sixfold increase in the proportion of premises that quarantine pigs prior to their introduction into the operation will reduce the probability of FMDV introduction via import of live pigs into Spain by 50%. Allocation of resources towards surveillance activities in regions and types of operations at high risk for FMDV introduction and into the development of policies to promote quarantine and other biosecurity activities in susceptible operations will decrease the probability of FMD introduction into the country and will strengthen the chances of success of the Spanish FMD prevention program.

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Keywords: Foot-and-mouth disease (FMD); Risk analysis; Live animal imports; Spain

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1. Introduction

Foot-and-mouth disease (FMD) is a highly infectious disease of cloven-hoofed animals that causes severe economic losses to infected countries and regions. FMD remains endemic in many areas of the world and only 59 countries are considered to be free from the disease by the Office International des Epizooties (OIE, 2007c). Trade restrictions imposed to non-FMD-free regions have helped most European Union (EU) member countries to maintain their FMD-free status since the disease was first eradicated from the continent in 1992. However, the risk for FMD virus (FMDV) introduction into the EU is still high, as demonstrated by the recent epidemics in Italy (1993), Greece (1996, 2000), United Kingdom (2001), Ireland (2001), France (2001), and the Netherlands (2001) (Maragon et al., 1994; Kesby, 2002; Chmitelin and Moutou, 2002; Davies, 2002; Griffin and O'Reilly, 2003).

Social and economic consequences of some FMD epidemics have been devastating for EU member countries. For example, the economic cost of the FMD epidemic that affected the United Kingdom (U.K.) in 2001 was estimated to be approximately \$5.8 billion in agriculture and food and \$5.1 to \$6.0 billion in tourism-related business (Thompson et al., 2002). Because the economy of Spain is highly dependent on industries that would be vastly affected by an FMD epidemic, introduction of FMDV into Spain would certainly have a broad impact on the social and economic stability of the country. Spain is the second largest pig, sheep, and goat producer among the 25 EU member countries (FAOSTAT, 2007). Livestock production supplies over US\$13.4 billion to the country's economy; almost one third of this amount (US\$4 billion) is contributed by the revenues obtained from meat and dairy products exports (MAPA, 2005a,b). Furthermore, with an annual average profit of US\$45.2 billion, Spain is the leading country of the EU in tourism (MITYC, 2006).

Movement of animals is considered to be the main risk factor for the introduction of many infectious diseases, including FMD, into disease-free areas (Horst et al., 1999; Gilbert et al., 2005; Bigras-Poulin et al., 2006; Green et al., 2006; Kiss et al., 2006). For this reason, since 1972 (Directiva 72/462/CEE) EU legislation allows for the import of live animals only from FMD-free regions. However, the combination of a free animal trade policy and the relatively short distances between EU countries, makes the EU particularly vulnerable to the spread of the disease before the diagnosis of an epidemic. This vulnerability was evidenced in 2001, when in the lapse of a few days FMD spread from the U.K. into the Netherlands, the Republic of Ireland, and France (Chmitelin and Moutou, 2002).

Quantitative estimates of the risk, the spatial variation in the risk, and the factors associated with the risk for FMDV introduction into a country are a prerequisite for the development of differential policies for prevention and eventual control of epidemics. Several risk analyses of FMD introduction have been conducted for EU countries (MacDiarmid, 1993; Morley, 1993; Yu et al., 1997; Horst et al., 1999; Moutou et al., 2001; Hartnett et al., 2007). However, no study assessing the risk of FMDV introduction into an EU member country via legal import of livestock from another EU country during the silent phase of an epidemic has been recently, i.e., after the FMD-epidemics in the EU in 2001, published in the peer-reviewed literature.

The goal of this paper was to estimate the probability of an FMD epidemic occurring in Spain as a consequence of the introduction of live animals into the country from another EU member country. The geographical variation, the association with livestock demographics, the relative contribution of different susceptible animal species, and the impact that increasing biosecurity measures in agricultural operations would have on the risk of FMDV introduction have also been estimated. The null hypotheses tested here were that the risk of FMDV introduction into Spain via

live animals is homogeneously distributed throughout the country and that susceptible species are equally associated with the risk of entrance. The results reported in this study will contribute to the success of the FMD prevention program in Spain by helping to guide the allocation of human and financial resources toward geographical areas at a higher risk for FMD, and in the control and monitoring of factors that contribute significantly to the risk of FMDV introduction into the country.

2. Methods

2.1. General approach

The design of the risk assessment was divided into six consecutive steps (Miller et al., 1993): (1) definition of the unit of analysis, (2) model formulation, (3) definition of distributions for input variables, (4) estimate of the likelihood of hazard occurrence, (5) analysis of results and experimentation, and (6) model environment and software.

2.2. Definition of the unit of analysis

Spain is divided into 17 territorial entities called autonomous communities. Autonomous communities are subsequently divided into 50 smaller administrative units called provinces. We have considered a province as the unit of analysis for this assessment for three reasons:

- (i) Granularity: the province is the smallest unit of aggregation for which data are collected, organized, and compiled in Spain.
- (ii) Spatial heterogeneity of the data distribution: the number of imported animals and animal density differ considerably among provinces. Therefore, we expect that both the probability of introducing FMD-infected animals and the probability of spread will substantially differ among provinces.
- (iii) Decision making process: control and prevention measures are primarily installed at the province level in Spain. For this reason, results and recommendations originated from this study will be more useful for the Spanish administration if they are articulated at the province level rather than at a smaller unit of aggregation.

2.3. Model formulation

The probability of introduction of FMDV into Spain via the import of susceptible species (pigs, cattle, sheep and goats) during 1-year period was estimated as the sum of the probabilities of introducing the disease into every province from each of the 18 EU member countries that export animals to Spain.

The probability of introduction and effective contact with a susceptible animal of at least one FMD-infected animal via the legal import of live animals of susceptible species s , from country c into the Spanish province g , $P(I_{cgs})$ was modeled as a binomial process of the form:

$$P(I_{cgs}) = 1 - (1 - p_{cgs})^{n_{cgs}},$$

where n_{cgs} is the number of animals of species s imported from country c into province g and the probability p_{cgs} that an infected animal was introduced into province g and effectively contacts a susceptible animal is a conditional probability that was estimated as the product of five

Table 1

Equations, assumptions, and sources of information used to formulate and to parameterize a model to assess the risk of foot-and-mouth disease virus introduction into Spain

Notation	Variable description	Parameterization	Source of information
n_{cgs}	Number of animals of species s imported from country c into the Spanish province g	Normal (μ_{cgs} , σ_{cgs})	Model equations
μ_{cgs}	Expected value of n_{cgs}	NA	Spanish Foreign Trade Statistics Database (2007) FAOSTAT (2007)
σ_{cgs}	Square root of the average squared deviation from the mean	$\sqrt{\frac{\sum (x-\bar{x})^2}{n}}$	
p_{cgs}	Probability of an infected animal being introduced into province g and effectively contacting a susceptible animal	$\prod_{i=1}^5 P(A_i)$	Model equations
$P(A_1)$	Probability that country c becomes infected in the lapse of 1 year	Gamma (α_c , β)	OIE (2007a,b)
α_c	Probability of having at least one undetected FMD epidemic in country c during the period of time β	E_c/t_c	Model equations
E_c	Number of FMD epidemics reported from country c during the period of time t to the OIE	NA	OIE (2007a,b)
t_c	Period of time for which information regarding the occurrence of FMD epidemics was available at the OIE website for each particular country c	NA	OIE (2007a,b)
$P(A_2)$	Probability that an infected animal x survives the infection	Pert (minimum, most likely, maximum)	Morley (1993)
$P(A_3)$	Probability that animal x was exported from country c into Spanish province g before detection	Beta ($\alpha 1_c$, $\alpha 2_c$); $\alpha 1_c = NI_c + 1$ $\alpha 2_c = NT_c - NI_c + 1$	Vose (1997)
NI_c	Number of animals in country c expected to be infected before the detection of the epidemic	$U_c \times H_c \times P_{H_c}/NT_c$	Model equations
U_c	Number of undetected FMD outbreaks	Pert (minimum, most likely, maximum)	Bouma et al. (2003) and Morris et al. (2001)
H_c	Average herd size in country c	$H_c = NT_c/NH_c$	FAOSTAT (2007)
P_{H_c}	Intra-herd prevalence	Pert (minimum, most likely, maximum)	Thurmond and Perez (2006)
NT_c	Population of susceptible animals in country c	Normal (μ_{cgs} , σ_{cgs})	FAOSTAT (2007)
NH_c	Total number of herds in country c	Normal (μ_{cgs} , σ_{cgs})	FAOSTAT (2007)
$P(A_4)$	Probability that animal x enters a Spanish premises	Pert (minimum, most likely, maximum)	Murray and Johnson (1998), Malena et al. (2006) and Knowles (1998)
$P(A_5)$	Probability that animal x transmits the disease to other susceptible animal in the premises	$1 - (P_q \times P_d)$	Model equations
P_q	Probability of doing quarantine	Beta ($\alpha 1_q$, $\alpha 2_q$)	Luis Romero, Spanish Ministry of Agriculture, expert opinion
P_d	Probability of detection during quarantine	Beta ($\alpha 1_d$, $\alpha 2_d$)	Luis Romero, Spanish Ministry of Agriculture, expert opinion

NA = not applicable.

independent events: the probability that country c becomes infected in the lapse of 1 year $P(A_1)$; the probability that the infected animal x survives the infection $P(A_2)$; the probability that animal x was exported from country c into the Spanish province g before detection $P(A_3)$; the probability that animal x reaches an agricultural operation $P(A_4)$; and the probability that animal x transmits the disease (i.e., establishes an effective contact) to another animal in the agricultural operation $P(A_5)$. Table 1 summarizes the equations and sources of information used to estimate the values of parameters considered in the formulation of the model.

2.4. Definition of distributions for input variables

2.4.1. Number of animals imported [n_{cgs}]

The number of animals of species s imported from country c into province g (n_{cgs}) was modeled using a normal distribution with parameters μ_{cgs} and σ_{cgs} , where μ_{cgs} is the number of animals of species s imported from country c into the Spanish province g during 2005, which is the most recent year for which information was complete and available (Spanish Foreign Trade Statistics Database, 2007). σ_{cgs} is the square root of the average squared deviation from the mean number of animals of species s imported into Spain in year y , where y varies from 1 to 6 (2000 through 2005). Thus, σ_{cgs} provides an estimate of uncertainty in the value of n_{cgs} .

2.4.2. Country-specific probability of infection [$P(A_1)$]

The probability of occurrence of an FMD outbreak was modeled for each of the 18 EU countries that export animals to Spain using a gamma distribution with parameters α_c and β (Vose, 2000; Defra, 2004), where α_c is the probability of having at least one undetected FMD

Table 2
Country-specific mean probabilities of foot-and-mouth disease (FMD) epidemics in European Union member countries assumed in the formulation of a risk assessment of FMD-virus introduction into Spain

Country	Number of epidemics reported between 1996 and 2006	Year of the last FMD epidemic reported before 1996	Mean probability of infection
Austria	0	1981	0.024
Belgium	0	1976	0.020
Czech Republic	0	1975	0.019
Denmark	0	1983	0.026
France	1	1981	0.047
Germany	0	1988	0.032
Greece	2	1994	0.097
Hungary	0	1973	0.018
Ireland	1	1941	0.019
Italy	0	1993	0.036
Latvia	0	1987	0.031
Lithuania	0	1982	0.025
Netherlands	1	1984	0.053
Poland	0	1971	0.017
Portugal	0	1984	0.027
Romania	0	1973	0.018
Slovakia	0	1973	0.018
United Kingdom	1	1981	0.047

epidemic in country c during the period of time β , which is the period of time considered in the assessment ($\beta = 1$), and that has been estimated here as:

$$\alpha_c = \frac{E_c}{t_c},$$

where E_c is the number of FMD epidemics reported from country c during the period of time t to the OIE (OIE, 2007a), assuming that the maximum number of epidemics that will occur in a country per year equals 1, and t_c is the period of time for which information regarding the occurrence of FMD epidemics was available at the OIE website (OIE, 2007a,b) for each particular country c . The value of t_c varied among EU countries depending on the year when the last FMD epidemic prior to 1996 occurred. For example, the last FMD epidemic in the Netherlands and in Germany prior to 1996 occurred, respectively, in 1984 and 1988. Additionally, one FMD epidemic was reported in the Netherlands after 1996. Thus, values of $E_{\text{Netherlands}} = 2$, $E_{\text{Germany}} = 1$, $t_{\text{Netherlands}} = 22$ and $t_{\text{Germany}} = 18$ were assumed (Table 2).

2.4.3. Probability of survival to FMD-infection [$P(A_2)$]

The probability that FMD-infected animals survive to the infection was modeled using a Pert distribution, where the maximum probability of survival was assumed to be 1 (corresponding to mild strains with nil mortality rate) and minimum and most likely probabilities were 0.80 and 0.98, respectively (Morley, 1993).

2.4.4. Probability of exporting into Spain [$P(A_3)$]

The probability of exporting an infected animal x from country c into province g before the detection of the epidemic and the restriction of animal movement was modeled using a beta distribution with parameters α_{1c} and α_{2c} , where $\alpha_{1c} = \text{NI}_c + 1$, and $\alpha_{2c} = \text{NT}_c - \text{NI}_c + 1$ (Vose, 1997), with NI_c denoting the number of animals in country c expected to be infected before the detection of the epidemic, and NT_c indicating the population of susceptible animals in country c . NI_c was estimated as the product of the number of outbreaks that are expected to occur before the epidemic is detected and movements from country c are banned (undetected outbreaks), the average herd size in the country, and the expected intra-herd FMD prevalence, divided by the number of animals in country c (NT_c). The expected number of undetected outbreaks (U_c) was assumed to be Pert distributed, with minimum, most likely, and maximum values of 1 (at least one undetected outbreak corresponding to the index case in country c), 11 (based on the experience of the Netherlands in 2001, Bouma et al., 2003), and 29 (based on the experience of the U.K. in 2001, Morris et al., 2001), respectively. The average herd size (H_c) was estimated as the ratio between NT_c and the total number of herds (NH_c). NT_c and NH_c were assumed to be normally distributed, with parameters μ_c equal to the total number of animals and herds in the country in 2005 (FAOSTAT, 2007), and parameters σ_c estimated similarly to the procedure described for the estimates of the number of animals imported, respectively. The intra-herd prevalence (P_{H_c}) was assumed to be Pert distributed, with a maximum value of 1, which typically occurs in less than 2 weeks after exposure, a minimum value of 0.05, which is the expected intra-herd prevalence at 4 days post-infection under a scenario of low transmission rate, and a most likely value of 0.9, which is the expected intra-herd prevalence when 10% of the infected animals show clinical signs, considered in previous studies as a condition that will likely result in the identification and reporting of the outbreak by the herd owner (Thurmond and Perez, 2006).

2.4.5. Probability of entering into an agricultural operation [$P(A_4)$]

There is no movement of animals from foreign countries to Spanish slaughterhouses, and therefore all imported animals are expected to be introduced into an agricultural operation. We expect that $P(A_4)$ will solely depend on the probability that the animal does not die during the shipment, which was modeled as Pert distributed with minimum, most likely, and maximum values of 0.05%, 0.27%, and 9.2%, respectively for pigs (Murray and Johnson, 1998); 0.004%, 0.007%, and 0.024% for cattle (Malena et al., 2006); and 0.007%, 0.01% and 0.031% for sheep (Knowles, 1998).

2.4.6. Probability of establishing an effective contact [$P(A_5)$]

The probability of establishing an effective contact was modeled as 1 minus the product of the probability that shipped animals are quarantined at the agricultural operation before contacting other susceptible animals and the probability that the infected animal is detected during the quarantine. There are no estimates of the number of agricultural premises that quarantine animals prior to their introduction into the operation available. However, official veterinarians with extensive access to information collected in the field believe that only 10% of pig premises and 2% of ruminant premises quarantine animals in Spain with a conservative assumption of 95% confidence that those figures are no higher than 15% and 10%, respectively (Luis Romero, Head of the Epidemiology Section, Spanish Ministry of Agriculture, MAPA, personal communication). Thus, the probability that animals are quarantined prior to their introduction into the herd (P_q) was modeled using a beta distribution with parameters $\alpha 1_q = 130.71$ and $\alpha 2_q = 15.41$ for pigs and $\alpha 1_q = 42.11$ and $\alpha 2_q = 1.83$ for other susceptible species. Because quarantine lasts between 30 and 60 days, it is expected that infected animals will likely develop evident clinical signs during the quarantine period. However, certain FMDV strains may result in mild disease in infected animals, particularly when the infected animal species are adapted to the strain or if they are sheep, which are intrinsically less likely to develop clinical signs than other species. The probability of detection of infected animals during the quarantine (P_d) was modeled using a beta distribution with parameters $\alpha 1_d = 1.33$ and $\alpha 2_d = 34.16$ for cattle and pigs, and $\alpha 1_d = 15.03$ and $\alpha 2_d = 2.55$ for sheep and goats. These parameters reflect the belief that, most likely, infected cattle and pigs will be detected during the quarantine in 99% of the cases with 95% confidence that the probability of detection is not less than 90%, and that infected sheep and goats will be detected during the quarantine in 10% of the cases with 95% confidence that the probability of detection is not greater than 40% (Luis Romero, Spanish Ministry of Agriculture, MAPA, personal communication).

2.5. Analysis of results and model experimentation

Because of the large number of variables used on the formulation of the model and of the difficulty in estimating the value of many of these parameters in the field, sensitivity analysis is an important process in the identification of the nature and extent, if any, in which each particular variable is likely to influence the outcomes of the model. The sensitivity of the model to each of the input variables was estimated using a two-stage procedure. On a first stage, the standardized regression coefficient β_i of the association between the input parameter i and the species-specific probability of FMDV introduction into Spain was computed to identify variables most likely to influence the outcomes of the model ($\beta \geq 0.1$). On a second stage, parameters most likely to influence the outcomes of the model ($\beta \geq 0.1$) were assessed using a one-way sensitivity analysis and a balanced design. The first stage is computationally less intense than the second stage.

However, the second stage is formally more appropriate than the first stage because of the possible influence that correlation and dependence between and among the input variables may have on the computation of the values of β . Therefore, the second stage of the sensitivity analysis was used to identify whether the estimates of β obtained from the first stage may have been influenced by correlation and dependence among the variables used to formulate the model.

For the first stage of the sensitivity analysis, the value of β_i was calculated as:

$$\beta_i = b_i \left(\frac{SD_{xi}}{SD_{yi}} \right),$$

where b_i was the regression coefficient of the association between the species-specific probability of FMDV introduction into Spain estimated using multiple linear regression analysis, i.e., accounting for the association between the outcome and other input variables; and SD_{xi} and SD_{yi} were, respectively, the standard deviations of the input parameter and the outcome estimated in 10,000 runs of the model. Therefore, β_i represents the change in the species-specific probability of FMDV introduction into Spain associated with a change of one standard deviation in the value of the input variable i . Estimates of $\beta < 0.1$ were considered evidence of lack of sensitivity of the model to the variable.

For the second stage of the sensitivity analysis, a balanced design and a one-way sensitivity analysis was used to assess the association between parameters with $\beta \geq 0.1$ and the species-specific probability of FMDV introduction into Spain, which were estimated in the first stage of the sensitivity analysis. The value of each parameter with $\beta \geq 0.1$ was systematically varied in eight steps from minimum and maximum values equal to, respectively, a 20% reduction and a 20% increase in the base value of the variable, while keeping constant on their base values all other variables. The values of the standardized regression coefficient, which were denoted as β'_i , associated with changes on the values of the parameters assessed using this balanced design was subsequently computed for each parameter i and compared with the values of β_i estimated on the first stage of the sensitivity analysis. Similar values of β_i and β'_i , as indicated by variation of $< 10\%$ at the first decimal level of precision, were considered evidence of lack of influence of correlation and dependence among and between variables in the results of the sensitivity analysis.

The association between the probability of FMDV introduction into a province and the animal density and number of animals in the province was estimated by computing the Spearman's R values (R_s). The assessment of the association between risk for FMDV introduction and animal density and number of animals in the province was not considered part of the sensitivity analysis because those variables were not used for the model formulation. Computation of R_s rather than β was preferred in order to differentiate those results from the results of the sensitivity analysis. The impact of increasing biosurveillance measures in the probability of introduction of FMDV into Spain was estimated by calculating the increase in the proportion of premises that quarantine animals necessary to decrease the probability of FMDV introduction by 50%.

2.6. Model environment and software

The model was run 10,000 times using a Monte Carlo approach implemented on a commercial software (@Risk version 4.5.5 and PrecisionTree version 1.0.9, Professional Edition[®], Palisade Corporation, 1996–2007) on Microsoft Excel (Microsoft[®] Office Professional Edition, 2003). Maps displaying the risk of FMDV introduction per province, categorized using percentiles as negligible (0), very low (under percentile 0.25), medium (percentile 0.25–0.50), high (percentile 0.50–0.75), and very high (percentile 0.75–1) were created using ArcMap 9.1 (ESRI[®], 2005).

3. Results

The mean probability of FMDV introduction into Spain via import of live animals per year was estimated as 2.36×10^{-2} , with a 95% PI of $(7.37 \times 10^{-6}, 1.61 \times 10^{-1})$, which corresponds to approximately one outbreak every 40 years. The probability of FMDV introduction through import of pigs [mean: 1.31×10^{-2} , 95% PI of $(1.76 \times 10^{-8}, 1.08 \times 10^{-1})$] was 1.34 times higher than the probability of introduction through sheep and goats [mean: 9.80×10^{-3} , 95% PI of $(5.03 \times 10^{-8}, 8.22 \times 10^{-2})$] and 9.42 times higher than the probability of introduction via cattle [mean: 1.39×10^{-3} , 95% PI of $(3.15 \times 10^{-7}, 1.09 \times 10^{-2})$].

The minimum probability of introduction of FMDV into Spain was estimated for the province of Cadiz (mean: 6.01×10^{-9}). The highest probabilities were estimated for the provinces of Lleida (7.85×10^{-3}), Girona (4.74×10^{-3}), Teruel (2.82×10^{-3}), Barcelona (1.84×10^{-3}), and Huesca (1.35×10^{-3}). These five provinces concentrate 76.4% of the overall probability of FMDV introduction into Spain. Pigs, cattle and sheep and goats were estimated as the most likely route of entry for FMDV in 45.8%, 37.5%, and 16.7% of the provinces, respectively (Fig. 1). Two provinces, Almeria and Baleares, did not import live animals and for that reason, the risk of FMDV introduction estimated in this study was nil.

The probability of FMDV introduction via live animals imports was mostly affected ($\beta \geq 0.1$) by the probability of infection in the Netherlands (pigs, $\beta = 0.762$), Czech Republic (cattle, $\beta = 0.478$), France (sheep and goats, $\beta = 0.405$), Portugal (cattle, $\beta = 0.157$), and Italy (sheep and goats, $\beta = 0.110$) (Table 3). Similar values ($\beta_i = \beta'_i$ at the first decimal of precision) were estimated for all of the five parameters i for which values of $\beta \geq 0.1$ were estimated on the first

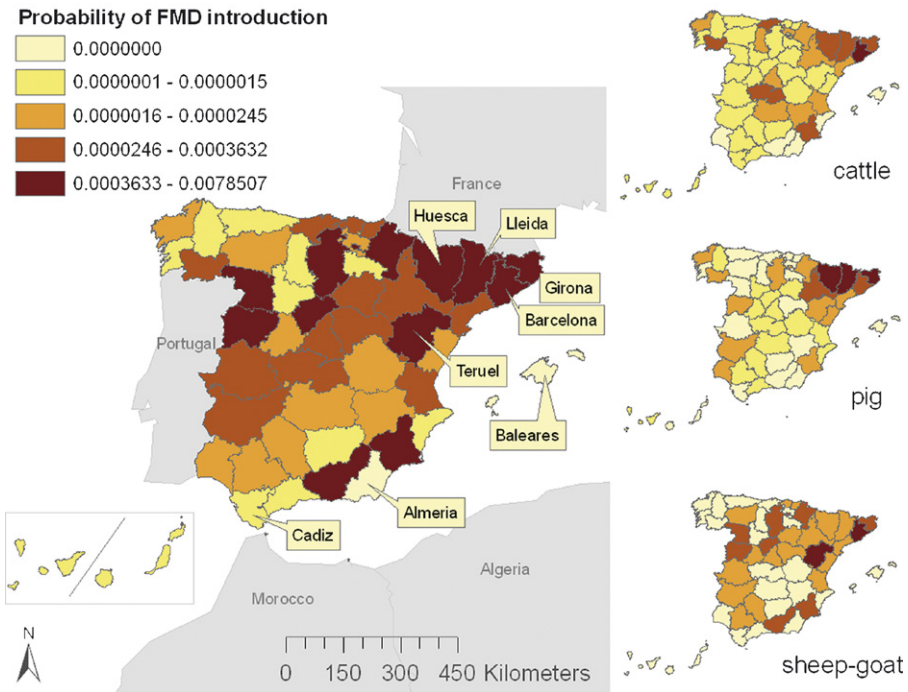


Fig. 1. Mean predicted probability of foot-and-mouth disease (FMD) introduction into Spain via importation of live animals (main figure) and discriminated by susceptible species (small figures).

Table 3
Standardized regression coefficients (β_i)^a of the simulated stochastic inputs

Input parameter ^b	Output		
	$P(I)_{\text{cattle}}$	$P(I)_{\text{pig}}$	$P(I)_{\text{sheep-goat}}$
$P(A_1)_{[\text{Netherlands}]}$	c	0.762	c
$P(A_1)_{[\text{Czech Republic}]}$	0.478	c	c
$P(A_1)_{[\text{France}]}$	c	c	0.405
$P(A_1)_{[\text{Portugal}]}$	0.157	c	c
$P(A_1)_{[\text{Italy}]}$	c	c	0.110

^a Only parameters accounting for more than 10% of change in the output are presented.

^b See Table 2 for parameter description.

^c Less than 10% of change in the output.

stage of the sensitivity analysis, suggesting that the estimates of β_i were not affected by dependence and correlation among and between input parameters.

The probability of FMDV introduction was to some extent correlated with the number ($R_s = 0.56$; $P < 0.01$) and density ($R_s = 0.50$; $P < 0.01$) of livestock, with the number ($R_s = 0.54$; $P < 0.01$) and density ($R_s = 0.45$; $P < 0.01$) of pigs, and with the number ($R_s = 0.37$; $P = 0.01$) and density ($R_s = 0.31$; $P = 0.03$) of sheep and goats, but not with the number ($R_s = 0.24$; $P = 0.10$) and density ($R_s = 0.12$; $P = 0.43$) of cattle in the province.

The probability of FMDV introduction into Spain decreased by 50% when the proportion of premises that quarantine pigs increased from 0.1 to 0.58. An increase in the proportion of operations that quarantine ruminants from 0.02 to 0.56 was necessary to decrease the probability of FMDV introduction into Spain by 50%.

4. Discussion

The probability of FMDV introduction into Spain was estimated to be more likely to occur via importation of live pigs than through importation of other species susceptible to FMDV infection. Many of the pig imports in Spain originate from countries such as the U.K. or the Netherlands, where FMD epidemics have been reported recently. This observation explains, at least partially, the finding that pigs are the susceptible species that impose the highest risk for FMDV introduction into Spain. Imported pigs are typically piglets that are fattened and slaughtered in Spain with the objective of supplying local markets. Major fattening operations and slaughterhouses are located in the north-eastern region of the country, in provinces among those estimated to be at the highest risk for FMDV introduction (MAPA, 2005a). Introduction of foreign animal diseases into north-eastern Spain via importation of live pigs has occurred in the past, as demonstrated by the Classical Swine Fever epidemics that affected Lleida in 1997–1998 and in 2001–2002 (Allepuz et al., 2007). Lleida was also estimated in our study to be the province at the highest risk for FMDV introduction into Spain. Moreover, some of the provinces estimated here to have the highest risk for FMDV were also among those at the highest risk for FMDV introduction in 2001, when susceptible livestock was shipped from Mayenne (France) and Surrey (U.K.) into operations in Barcelona and Teruel, respectively, only a few days before an FMD epidemic was reported in the region of origin of the imported animals (MAPA, 2001).

Interestingly, species other than pigs were estimated to be the most likely route of FMDV introduction into more than half of the provinces. Locations of major ruminant operations, markets, and slaughterhouses are dispersed in Spain (MAPA, 2005a,b). For that reason, the

province of destination for imported cattle, sheep, and goats is more variable than for imported pigs, resulting in a higher spatial heterogeneity of the predicted risk (Fig. 1). Subsequently, if FMDV was introduced into Spain via importation of infected ruminants, prediction of the specific province where the index case would be located is much more uncertain, than if FMDV was introduced by imported live pigs.

The low correlation between the probability of FMDV introduction into Spain and the number and density of susceptible species in the province ($R_s < 0.6$) suggests that knowledge of the value of these parameters alone is not sufficient to predict the risk of FMDV introduction into Spain. Producers in certain provinces with a relatively low number and density of susceptible animals may be more likely to import livestock than producers in other regions, which is expected to result in a higher risk for FMDV introduction. Factors other than the number and density of animals that may increase the predilection of farmers in certain provinces to import susceptible livestock into their premises include proximity to international borders, the number of international ports of entry for livestock, cultural and ethnic links with neighboring countries, and the degree and extent of intensification of production.

Estimates presented here were mainly sensitive only to the probability of infection in the Netherlands ($\beta = 0.762$, Table 3), probably due to a combination of a recent history of FMD (Bouma et al., 2003) and a high number of animals annually shipped into Spain. Free-trade policy applied by EU-member countries and characteristics of livestock production in Spain, which is highly dependent on supply of animals for fattening and slaughtering, makes the country particularly vulnerable to the introduction of FMD and other major livestock diseases. Techniques and strategies aimed at increasing the temporal sensitivity of animal disease surveillance systems would certainly result in an increased probability of early detection and prevention of FMD spread in Europe.

The risk for FMDV introduction into a region is certainly proportional to the number of animals annually imported. Because the main destination of livestock imported into Spain is fattening operations, an increase in the number of breeding and farrow-to-finish operations in the country will reduce the risk of FMDV introduction into Spain associated with the dependence of the country on foreign supply of live animals. The risk of FMDV introduction into Spain may also be substantially reduced by increasing the level of biosecurity in agricultural operations. Increases in the proportion of pigs and ruminant premises that quarantine animals to 0.58 and 0.56, respectively, were estimated to result in a 50% reduction in the probability of FMDV introduction into Spain. These figures represent, respectively, 5.8- and 28-fold increases in the current proportion of operations that quarantine animals prior to their introduction into Spanish premises. For this reason, a reduction in the risk of FMDV introduction via an increase in the proportion of operations that quarantine animals would be more easily achieved in pig operations, compared with cattle and small ruminant premises. Because the risk of FMDV introduction into Spain was more strongly associated with pig imports, and reaching critical levels in the proportion of premises that quarantine animals would be more realistically achieved in pig premises, the results presented here encourage the development of policies in Spanish, directed to promote the practice of quarantine and other biosecurity measures, particularly in pig operations, as an effective means of reducing the risk of introduction of FMD and other foreign animal diseases into Spain.

To the best of the authors' knowledge, this is the first quantitative assessment of the risk of FMDV introduction into an FMD-free country via legal importation of livestock, discriminated by susceptible species introduced, country of origin and province of destination. Although a moderate risk for FMDV introduction into Russia and Europe was estimated from Georgia,

Armenia, and Azerbaijan, the risk for the introduction could not be quantified (Moutou et al., 2001). Other earlier approaches assumed that livestock does not represent a risk because import of susceptible live animals into FMD-free countries from countries that are not FMD-free is typically prohibited (Pharo, 2002). Earlier assessments of FMDV introduction into FMD-free areas were mostly based on the risk posed by legal (USDA, 2002) or illegal (Defra, 2004; Hartnett et al., 2007) importation of meat. The authors have noted, however, that three of four EU countries that were affected by FMD in 2001 were believed to be infected by the legal importation of livestock unknown to be FMD-infected at the time of the shipment (Chmitelin and Moutou, 2002). Consistently with this observation, the mean risk of FMDV introduction into Spain estimated here was higher than the mean risk associated with illegal importation of meat into the U.K. (Hartnett et al., 2007). An earlier risk assessment for FMDV introduction into the Netherlands estimated that the highest risk was associated with the silent phase of an FMD epidemic in other European countries (Horst et al., 1999). The results presented here support the conclusion emerging from the Dutch study, in the sense that reinforcing the sensitivity of overseas surveillance systems is an effective strategy to reduce the risk for FMDV introduction into one's own country. Animal movements are numerous, frequent, and rapid within the EU due to the combination of a supportive legislation in place, short distances, and a highly developed communication network. These observations and findings suggest that accuracy of the risk assessments of FMDV introduction conducted by EU-member countries would greatly be improved by taking into consideration the risk associated with importation of infected livestock during the silent phase of an epidemic. Discrimination of the risk by imported species and province of destination and use of sensitivity analysis, which were not considered on other risk assessments published in the peer reviewed literature, were useful means of exploring the association between risk and factors associated with the risk for introduction in Spain.

The values of certain parameters necessary to quantify the risk of FMDV introduction associated with legal importation of livestock into Spain were unknown. The approach used here was to quantify the uncertainty by assuming distributions for the values of the parameters. Most likely, minimum, and maximum values used to build the distributions were derived from historical data series that were made available to us, from data published in the peer reviewed literature, and from the knowledge and beliefs from people with experience in the field and with access to a large amount of field data. The analysis of the sensitivity that the model outcomes have to variations in the value of the model inputs provides an estimate of how important lack of reliable or objective information related with the true value of critical parameters may have had on the model results. The influence that parameters for which values were derived from experts knowledge and beliefs on the results of the risk assessment presented here was nil ($\beta < 0.1$). Therefore, the authors believe that the model results were unlikely to be affected by lack of information on the value of those particular inputs. Certainly, the finding that the outcomes of the model were mostly ($\beta > 0.1$) affected by the variations in prevalence of the disease in countries from where Spain imports a large number of animals has been interpreted by the authors as an indicator of the biological sound of the model formulation and parameterization.

A very well known principle of modeling indicates that the quality and validity of the conclusions depend on the quality and validity of the information and assumptions used to formulate the model. The authors believe that the formulation and parameterization of the risk assessment presented here was rational and biological sound considering the state of the knowledge and availability of information at the time when the model was formulated. The authors would like to highlight, however, that the model is not intended to predict the future and that results will remain up to date only if conditions and parameters values assumed in the

formulation process persist. Because quality of available information, state of the scientific knowledge, and values of the parameters used to fit the model are continuously evolving, the risk assessment presented here should be periodically revised in order to update the estimates and improve the quality of the conclusions.

The methodological approach and conclusions presented here will be useful in helping Spain to develop policies to prevent the risk for FMDV introduction and mitigate the consequences of an FMDV incursion into the countries.

5. Conclusion

The results presented here suggest that directing surveillance activities to provinces at higher risk for FMDV introduction and increasing the number of agricultural premises that quarantine animals are critical factors necessary to prevent the introduction of FMDV into Spain. Differential allocation of human and financial resources to policies that promote these activities and considering the spatially and species-specific differential risk estimated here will contribute to the success of the national FMD prevention and control program.

Acknowledgements

The project was funded in part by the Spanish Ministry of Agriculture, Fisheries and Food (MAPA), the Spanish Ministry of Education and Science (MEC), the Spanish Organization of Agricultural Insurances (ENESA), and the U.S. Armed Forces Medical Intelligence Center. We gratefully acknowledge the assistance of Drs. Tirso Yuste, ENESA, and Luis Romero, MAPA, for providing data and assistance in the interpretation of the results.

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