



HAL
open science

A novel spatial and stochastic model to evaluate the within and between farm transmission of classical swine fever virus: I. General concepts and description of the model

B. Martínez-López, B. Ivorra, A.M. Ramos, J.M. Sánchez-Vizcaíno

► To cite this version:

B. Martínez-López, B. Ivorra, A.M. Ramos, J.M. Sánchez-Vizcaíno. A novel spatial and stochastic model to evaluate the within and between farm transmission of classical swine fever virus: I. General concepts and description of the model. *Veterinary Microbiology*, 2010, 147 (3-4), pp.300. 10.1016/j.vetmic.2010.07.009 . hal-00654950

HAL Id: hal-00654950

<https://hal.science/hal-00654950>

Submitted on 24 Dec 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Accepted Manuscript

Title: A novel spatial and stochastic model to evaluate the within and between farm transmission of classical swine fever virus: I. General concepts and description of the model

Authors: B. Martínez-López, B. Ivorra, A.M. Ramos, J.M. Sánchez-Vizcaíno



PII: S0378-1135(10)00344-5
DOI: doi:10.1016/j.vetmic.2010.07.009
Reference: VETMIC 4965

To appear in: *VETMIC*

Received date: 2-11-2009
Revised date: 7-7-2010
Accepted date: 15-7-2010

Please cite this article as: Martínez-López, B., Ivorra, B., Ramos, A.M., Sánchez-Vizcaíno, J.M., A novel spatial and stochastic model to evaluate the within and between farm transmission of classical swine fever virus: I. General concepts and description of the model, *Veterinary Microbiology* (2010), doi:10.1016/j.vetmic.2010.07.009

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

1 **A novel spatial and stochastic model to evaluate the within and between farm**
2 **transmission of classical swine fever virus: I. General concepts and description of the**
3 **model.**

4
5 **Martínez-López, B.^{a*}; Ivorra, B.^b; Ramos, A.M.^b; Sánchez-Vizcaíno, J. M.^a**

6
7 ^a VISAVET, Animal Health Department. Veterinary School. Complutense University of
8 Madrid. Av. Puerta de Hierro s/n. 28040, Madrid, Spain

9 ^b Applied Mathematics Department. Mathematics School. Complutense University of
10 Madrid. Plaza de Ciencias 3, 28040, Madrid, Spain.

11 * Corresponding author: Tel: +34 91 394 37 02; Fax: +34 91 394 39 08; E-mail address:
12 beatriz@sanidadanimal.info; Av. Puerta de Hierro s/n. 28040, Madrid, Spain.

13

14 **Abstract**

15

16 A new stochastic and spatial model was developed to evaluate the potential spread of
17 classical swine fever virus (CSFV) within and between farms, and considering the specific
18 farm-to-farm contact network. Within-farm transmission was simulated using a modified SI
19 model. Between-farm transmission was assumed to occur by direct contacts (i.e. animal
20 movement) and indirect contacts (i.e. local spread, vehicle and person contacts) and
21 considering the spatial location of farms. Control measures dictated by the European
22 legislation (i.e. depopulation of infected farms, movement restriction, zoning, surveillance,
23 contact tracing) were also implemented into the model. Model experimentation was
24 performed using real data from Segovia, one of the provinces with highest density of pigs in
25 Spain, and results were presented using the mean, 95% probability intervals [95% PI] and
26 risk maps. The estimated mean [95% PI] number of infected, quarantined and depopulated
27 farms were 3 [1, 17], 23 [0, 76] and 115 [0, 318], respectively. The duration of the epidemic
28 was 63 [26, 177] days and the most important way of transmission was associated with local
29 spread (61.4% of the infections). Results were consistent with the spread of previous CSFV
30 introductions into the study region. The model and results presented here may be useful for
31 the decision making process and for the improvement of the prevention and control
32 programmes for CSFV.

33

34 **Keywords:** classical swine fever; simulation model; disease spread; stochastic; decision tool

35

36 **1. Introduction**

37

38 Classical swine fever (CSF) is a highly contagious viral disease of domestic and wild
39 pigs which generates important economical losses in the affected regions. The disease is
40 caused by the CSF virus (CSFV), a *Pestivirus* belonging to the Flaviviridae family. Despite
41 the efforts to control and eradicate CSF, this disease remains endemic in many countries of
42 South and Central America, Africa and South-east of Asia and sporadic outbreaks have been
43 affecting 57% of the European countries from 1996 to 2008 (OIE, 2009a,b).

44 During a CSF epidemic, the spread of CSFV from an infected animal to other
45 susceptible ones may occur either by direct or indirect contacts. Direct transmission implies
46 animal-to-animal effective contact from an infectious animal to a susceptible one. Indirect
47 transmission requires an effective contact between a contaminated fomite (i.e. vehicle, insect,
48 material or people) and a susceptible animal. Historically, the movement of infected animals
49 and contaminated vehicles has been reported as one of the main routes of CSFV spread,
50 although other routes such as airborne spread, movement of people, use of infected semen or
51 feed, iatrogenic infection and mechanical vectors such as rodents, insects, birds or pets has
52 also been described as potential ways of transmission (De Vos et al., 2003). Nevertheless, the
53 spread patterns and magnitude and duration of a CSF epidemic change depending on the
54 epidemiological and demographic characteristics of the infected region and the timing and
55 effectiveness of the control measures applied. For this reason, it is difficult to extrapolate the
56 routes of infection and consequences of a CSF epidemic from one region to another.

57 The study of the potential spread patterns of CSFV into a region may help to identify risk
58 factors for disease spread and to improve the prevention and management of future outbreaks.
59 In CSFV-free areas, the only way to quantify the magnitude of potential epidemics and
60 evaluate the effectiveness of different control measures to be applied is to use epidemiologic
61 and mathematic models. These models are intended to simulate the potential spread of CSFV
62 into a region in order to evaluate effective measures to control disease and have a decision

63 support system to better manage real outbreaks. Recently, some models have been developed
64 to simulate the potential spread of CSFV into free regions such as Belgium (Staatkamp et al.,
65 1996; Ribbens et al., 2007), Germany (Stärk, 1998; Karsten et al., 2005a,b), The Netherlands
66 (Stegeman et al., 1999; Jalvingh et al., 1999) and Australia (Milne et al., 2008). Martinez et
67 al. (2009) also described a spatial stochastic model for Spain by using a commercial available
68 software (InterSpread Plus, Sanson et al. 1993). However, most of these models only focus
69 on the between-farm transmission of the CSFV, with poor assumptions regarding within-farm
70 transmission and, do not explicitly consider the specific farm-to-farm contact network into
71 the study region.

72 The study presented here, is intended to provide quantitative estimates of the magnitude
73 and duration of potential CSF-epidemics by using a stochastic and spatial model to simulate
74 both the within and between farm transmission and considering the specific farm-to-farm
75 contacts. The model would provide a decision-support system and results of this study will be
76 useful in the development of prevention and control strategies to better manage future CSFV
77 outbreaks.

78

79 **2. Material and Methods**

80

81 *2.1. General description of the model*

82 A spatial stochastic model, referred to as *Be-FAST* (Between -Farm -Animal Spatial
83 Transmission) Disease Model was developed to evaluate the daily spread of CSFV within
84 and between farms into a specific region.

85 At the beginning of the simulation ($t=0$) all farms were in the susceptible state (i.e.
86 non infected) except a randomly selected farm, called index case, which was assumed to have
87 one infected pig and was classified as infected. Then, during a time interval $[0, T]$, the within-

88 and between- farm daily CSFV-transmission process was simulated following the steps
89 described in sections 2.3 and 2.4. The process of random selection of the index case was
90 repeated 1,000 times to generate 1,000 different epidemics using the Monte Carlo method.

91 Control measures based on zoning, movement restriction, depopulation of infected
92 farms, increase of surveillance and tracing were also implemented into the model and can be
93 activated/deactivated in order to quantify their effectiveness to reduce the magnitude and
94 duration of the epidemic.

95 The main model outputs were the number of infected, quarantined and depopulated
96 farms and duration time of the epidemic. Quantification of CSFV farm-to-farm transmission
97 was evaluated by the computation of the risk of infection, the basic reproduction ratio and the
98 effective reproduction ratio. Risk of infection was defined as the number of times that a farm
99 became infected after the different simulated epidemics. Basic reproduction ratio , R_0 , was
100 defined as the expected number of secondary infections (i.e. effective contacts) arising from a
101 single infected farm during its entire infectious period under the assumption that all other
102 farms remain susceptible (naïve population). Effective reproduction ratio, R , was defined as
103 the amount of secondary infections caused by one infected farm in a not naïve population
104 (Anderson and May, 1991). Results were presented using mean and 95% prediction interval
105 (95% PI) and visual outputs were represented using graphs, epidemic curves and risk maps.

106

107 2.2. Farm data

108 Data available for each farm, identified as farm h , included the geographical location
109 of the farm (X_h and Y_h coordinates of the farm centroid), the number of pigs per farm (N_h), the
110 type of farm (T_h), the Integration group (INT_h), which refers to group of farms which share
111 material and vehicles and, the Sanitary Defence Association group (ADS_h) which refers to

112 group which share private veterinarians. The type of pig farms registered was farrowing,
 113 fattening, farrow-to-finish pig farms, artificial insemination centres and slaughterhouses.

114 Furthermore, pig shipments from farm-to-farm, number of pigs shipped, date of
 115 shipment and, farm of origin and destination of the shipment occurring from January 1st to
 116 December 31 of 2008 was also available.

117 Information on farm location allowed to simulate the between-farm transmission,
 118 accounting for the spatial heterogeneities within the study region.

119

120 2.3. *Within-farm CSFV transmission*

121

122 The CSFV spread within a particular pig farm h was modeled using a modified state
 123 transition model, in which a pig was characterized, for the sake of simplicity^a, to be in one of
 124 two states either susceptible (Sp) or infected (Ip). The transition from “susceptible” to
 125 “infected” state was governed by a stochastic SI model (Anderson and May, 1979), which is
 126 activated when the farm h reaches the state of “infectious (T_h)” (see Section 2.4). The number
 127 of susceptible $Sp_h(t)$ and infected $Ip_h(t)$ pigs at farm h at day t , was generated using a random
 128 variable following a Poisson distribution with mean of $\beta_h \frac{Sp_h(t)Ip_h(t)}{N_h(t)}$ where β_h is the
 129 transmission parameter set to 8.52, 1.85 or 5.18 depending if we consider farrowing, fattening
 130 or farrow-to-finish pig farms, respectively (Klinkenberg et al., 2002) (Table 1).

131

132 2.4. *Between-farms CSFV transmission*

^a Here, in order to reduce computational complexity, the infectious and clinical sign states were simulated at the farm level and the natural and disease mortality of pigs were assumed to be negligible.

133 CSFV transmission between farms was modeled by using a spatial and stochastic state
134 transition model with five mutually exclusive states: susceptible (S_h), infected (I_h), infectious
135 (T_h) and clinical signs (C_h).

136 More precisely: a farm was assumed to be in the “susceptible” state when no pig
137 within the farm is infected with CSFV. The “infected” state was assumed for a farm with at
138 least one infected pig (but none of them are still infectious for other pigs). The “infectious”
139 state was assumed for those farms with at least one pig reaching the latent period. Finally the
140 “clinical signs” state was assumed for those farms with at least one pig reaching the
141 incubation period. Farms in either infectious or clinical signs state were assumed to be a
142 potential source of infection to other pig farms.

143 The order of transition from one state to another was: $S_h \rightarrow I_h \rightarrow T_h \rightarrow C_h$. The
144 assumptions and parameters of the mathematical model regulating the transition from a
145 particular state to the next one are described in next subsections and table 1.

146

147 2.4.1 Transition from “susceptible” to “infected” farm state

148 The transmission of CSFV from farm-to-farm was modeled by considering both direct
149 and indirect contacts.

150 Transmission by direct contacts was assumed to occur by the movement of pigs from
151 farm h to farm k , at day t .

152 The movement from farm-to-farm was simulated by using the animal movement
153 network during 2008, which included 2,007,889 possible different movements. More
154 precisely, we simulate the number of movements at day t $SM(t)$ by considering a Poisson of
155 rate $M(t)$, where $M(t)$ is the number of movements occurring during 2008 at day t (Table 1)

156 For each simulated movement, a farm of origin h and a farm of destination k were
157 select by considering the following process. First, the number of movements m_{hk} from farm h

158 to farm k during 2008 was computed. In case of no movement between two farms during
159 2008, m_{hk} was set to 10^{-6} to account for movements not occurring during that particular year.
160 Finally, the probability of this movement to be selected is given by m_{hk}/MT where MT is the
161 total number of movements in the study region during 2008.

162 The number of pigs moved during a simulated movement occurring from farm h to
163 farm k at day t was computed as $n_{hk} * N_h(t)/N_h(0)$ where n_{hk} was the number of pigs moved
164 during 2008 between those farms and divided by m_{hk} . In case of no movement from farm h to
165 farm k during 2008 n_{hk} was set to the mean number of moved pigs from farm h during 2008.

166 Moreover, the probability of transmission per day from farm h to farm k by direct
167 contact depends on the number of infected pigs moved on the farm h where the shipment was
168 originated. The number of infected pigs moved from farm h to k , is obtained by combining
169 the number of infected pigs at time t on farm h where the shipment was originated, which is
170 given by the modified SI model described in Section 2.3, and a random number given by a
171 Poisson distribution which rate is the mean number of pigs shipped from farm h to farm k
172 during 2008. When farm h moves infected pigs to farm k the number of infected pigs at farm
173 h (I_{p_h}) is reduced whereas the number of infected pigs at farm k (I_{p_k}) increases.

174 Transmission by indirect contacts was assumed to occur by either movement of
175 vehicles transporting animals, vehicles transporting products (feed or slurry), movement of
176 people or local spread.

177 The number of contacts from farm-to-farm by vehicles transporting pigs was
178 simulated by using the animal movement contact network together with the simulation of
179 animal movements described above. The probability of transmission due to contact of a
180 contaminated vehicle transporting pigs was modeled using a Bernoulli distribution with mean
181 0.011 (Stegeman et al., 2002).

182 Contacts by vehicles transporting products from farm-to-farm were assumed to occur
183 only among those farms belonging to the same integration (INT_h) and with the assumption
184 that a vehicle can visit a maximum of 4 farms per day (CyL expert opinion, 2008^b) and can
185 only been infectious if previously has visited an infectious farm (i.e., a farm in state either T_h
186 or C_h). The number of contacts by vehicles transporting products per farm per day was
187 assumed to be Poisson distributed with a rate of 0.4 (Kartsen et al., 2005a). The probability of
188 CSFV introduction into a farm per contact with contaminated vehicles transporting products
189 was modeled using a Bernoulli distribution with mean 0.0068 (Stegeman et al., 2002).
190 More precisely, at a particular day and for each farm, we computed the number of vehicles
191 visiting a farm using the Poisson (0.4). Then, we grouped into a list the farms of a same
192 integration group that will be visited by vehicles, we recombined this list randomly and we
193 obtained the visit order. Finally, a vehicle was specified to visit each farm in the integration
194 group following the visit order until the fourth trip, then we consider a new vehicle starting
195 for the next farm in the list. An illustration of this process is explained in the following
196 example: at a particular day, considering an integrator group compound by farms 1, 2, 4, 6, 7,
197 10, 11, 13, 15 and 17 and, using Poisson (0.4), we obtain that farms 1, 2, 6, 10, 13 and 15 will
198 not receive vehicles; farms 4 and 7 will receive 1 vehicle; and farms 11 and 17 will received
199 2 vehicles. We create the list of farms visited by vehicles {4,7,11,11,17,17}, we recombine
200 this list randomly and we obtain {4,17,11,7,11,17}. A first vehicle will visit the four first
201 farms in this order: 4, 17, 11 and 7 and, a second vehicle will visit farms 11 and 17.

202 Transmission of CSFV by contact of people visiting farms was assumed to occur only
203 between farms belonging to the same ADS (ADS_h) and with the assumption that a person can
204 visit a maximum of three farms per day (CyL expert opinion, 2008) and can only been

^bExpert opinion elicitation performed for Foot-and-Mouth disease and classical swine fever with the Castile and Leon veterinary services, during November 5th 2008.

205 infectious if previously has visited an infectious farm. The number of contacts of people per
 206 farm per day was assumed to be Poisson distributed with a rate of 0.3 (Kartsen et al., 2005a).
 207 The probability of CSFV introduction into a farm per contact with contaminated persons was
 208 modeled using a Bernoulli distribution with mean 0.0065 (Stegeman et al., 2002). The same
 209 process used for integration group was applied.

210 Transmission of CSFV by local spread was assumed to occur to farms in proximity to
 211 infected farms by indirect contacts such as airborne spread or fomits. The probability of
 212 CSFV-infection by local spread from farm h to farm k per day, was modeled with the
 213 expression

$$214 \quad \frac{Ip_h(t)}{\bar{N}(t)} * LSM(h, k),$$

215 where $Ip_h(t)$ is the number of infected pigs at farm h at day t , $\bar{N}(t)$ is the mean number of pigs
 216 in all considered farms at day t and, $LSM(h, k)$ is the mean probability of infection due to local
 217 spread computed as a function of the distance between h and k built by interpolating the
 218 following combination of probability of infection per day and distance (meters): 0.014 at
 219 150m, 0.009 at 250m, 0.0038 at 500m, 0.0019 at 1000m and 0 at 2000m (Kartsen et al.,
 220 2005b).

221 If CSFV is introduced by any of the indirect contacts from farm h to farm k , the
 222 number of “infected” pigs in farm k (Ip_k) is increased by one.

223

224 2.4.2 Transition from “infected” to “infectious” state

225 The transition of a farm h from “infected” to “infectious” state depends on the latent
 226 period that was modeled using a Poisson distribution with mean of 7 days, assuming day 0 as
 227 the day of infection in farm h (Kartsen et al., 2005a).

228

229 2.4.3 Transition from “infectious” to “clinical signs” state

230 The transition of a farm h from “infectious” to “clinical signs” state depends on the
 231 incubation period that was modeled using a Poisson distribution with mean of 21 days after
 232 the beginning of the infectious state in farm h (Kartsen et al., 2005a).

233

234 2.5. Detection of disease

235 Detection of disease was simulated differently before and after detection of the first
 236 infected farm (i.e. index case). Before detection of the index case, disease was assumed to be
 237 detected by observation of clinical signs on farms, whereas after detection of the index case,
 238 disease was assumed to be detected either by clinical signs or serological tests.

239 The probability of detection per day based on clinical signs before detection of the
 240 index case was modeled using a Bernoulli distribution with mean 0.03 (Kartsen et al., 2005b).

241 After detection of the index case this probability was modeled using a Bernoulli distribution

242 with mean $0.98 \left(\frac{Ip_h(t)}{N_h(t)} \right)$ for farms within the control zone, $0.95 \left(\frac{Ip_h(t)}{N_h(t)} \right)$ for farms within the

243 surveillance zone (CyL expert opinion, 2008) and 0.06 for farms outside control and

244 surveillance zones (Kartsen et al., 2005b) (see Section 2.6). The probability of detection

245 based on serological tests was assumed to consider a sample size large enough to detect a

246 seroprevalence of 10% within the farm with a confidence of 95% (MAPA, 2006).

247

248 2.6. Control measures

249 Measures applied in the model to control disease were those defined in the European
 250 and Spanish legislation to control CSF (CyL expert opinion, 2008), which were based on
 251 zoning; restriction of movements of animals, vehicles and people; depopulation of farms
 252 detected as infected; increase of surveillance, which implies increase on the probability of

253 detection of an infected farm, and; tracing of the historical (<60 days) incoming or outgoing
254 contacts in the detected farm.

255

256 2.6.1. Zoning

257 Control (<3 km radius) and surveillance (<10 km radius) zones were defined around a
258 farm detected as infected, and movement restrictions were applied to farms within those
259 radius during a time period of 30 and 40 days, respectively. Overlapping of control and
260 surveillance zones after detection of new outbreaks in the area was allowed in the model.

261

262 2.6.2. Movement restrictions

263 Probability of restriction of animals, vehicle and people movements on the detected as
264 infected farm, were assumed to be Bernoulli distributed with a mean of 0.99, 0.95 and 0.80,
265 respectively. Those values were 0.95, 0.90 and 0.70, respectively, for the farms within the
266 control and surveillance zones. Furthermore, after each detection, movement restrictions were
267 applied for the rest of the pig farms in the study region outside control and surveillance zones
268 for a period of 90 days following a Bernoulli distribution with a mean of 0.4 (CyL expert
269 opinion, 2008).

270

271 2.6.3. Depopulation

272 The depopulation of a farm detected as infected was assumed to occur after a random
273 time period with probabilities 0.11 at day 0, 0.58 at day 1, 0.2 at day 2, 0.06 at day 3, 0.04 at
274 day 4, 0.004 at day 5, 0.003 at day 6 and 0.0015 at day 7 and 8 (Elbers et al., 1999). The
275 maximum number of farms to be depopulated per day was assumed to be Poisson distributed
276 with mean of 20 farms (CyL expert opinion, 2008). If this limit is reached the farm will be
277 depopulated the day after. A depopulated farm would be not susceptible or infectious until its

278 repopulation. The repopulation of the depopulated farm occurs after a period that was
279 modeled using a Poisson distribution with a rate of 90 days (CyL expert opinion, 2008). The
280 number of susceptible animals used to repopulate the farm was the same number of animals
281 present on farm at the beginning of the simulation, $N_h(0)$.

282

283 2.6.4. *Tracing*

284 Tracing activities involved the process to identify contacts leaving or entering a farm
285 detected as infected. The objective of tracing is to identify potentially infectious contacts
286 which may have introduced disease into the farm or spread disease to other farms. The
287 probability of tracing an animal, vehicle or people movement was assumed to be Bernoulli
288 distributed with mean 0.99, 0.70 and 0.40 respectively (CyL expert opinion, 2008). Tracing
289 was applied for animal, vehicle and people contacts occurring <60 days before detection of
290 the infected farm, with a probability to escape from this control that follows a Bernoulli law
291 with mean 0.01 (CyL expert opinion, 2008). Serological test were used to detect disease in all
292 traced farms. The maximum number of farms to be traced per day was assumed to be Poisson
293 distributed with mean of 60 farms (CyL expert opinion, 2008). If this limit is reached the
294 farm will be traced the day after.

295

296 2.7. *Model experimentation*

297 Segovia, one of the most important areas of pig production in Spain which was
298 affected by the 1997-1998 CSF-epidemic in Spain and for which data were available, was
299 used to illustrate the model performance. Registration of pig farms and notification of animal
300 movements is mandatory by the Spanish legislation, so all pig farms and pig movements in
301 Segovia region were assumed to be registered. During 2008, Segovia registered 1,400 pig
302 farms and 1,108,415 pigs, and there were 10,468 movements. The 49.6% of the farms were

303 classified as farrow-to-finish, 36.4% fattening, 13.6% farrowing and 0.35% artificial
304 insemination centres. CSF is an exotic disease for the Spanish pig population and no CSF
305 vaccination is performed into the country. Therefore, it was assumed that all pig farms were
306 susceptible to CSFV infection (i.e. naive population). The input variables of the model were
307 estimated using real data provided by the Regional Government of Castile and Leon (CyL)
308 and the expert opinion of CyL Veterinary Services obtained in November 5, 2008.

309 We consider two experiments, one without control measures, denoted by NM and the
310 other with all control measures described in section 2.6. and denoted by WM. The maximum
311 time interval in the NM experiment was set to $T=100$ days, whereas no maximum time
312 interval was set for the WM experiment. In both cases, we run 1000 simulations.

313 The model and the statistical analysis were performed using MatLab interface
314 (Ver.7.5.0.342 R2007b-The MathWorks Inc.) on a Pentium 4 of 3.4 Ghz with 2Gb and needs
315 64000 seconds for the NM case and 20000 seconds for the WM case. Maps were developed
316 using ArcGIS 9.2 (ESRI).

317

318 *2.4. Model verification and sensitivity analysis*

319 The experiments with and without control measures were repeated several times to
320 assure consistency of results. Furthermore, the maximum time interval in the experiment
321 without control measures was changed to $T=200$ and $T=365$ and the dynamic of the epidemic
322 was evaluated.

323 The large number of input variables used in the model formulation and the little information
324 available on many of these variables make necessary the application of an extensive and
325 detailed sensitivity analysis to identify the influence of each variable on the model outcomes.
326 This is the reason why a complete sensitivity analysis, together with validation of the model
327 using data from the 1997-1998 CSFV-epidemic in Segovia, will be presented in a second

328 manuscript entitled “A novel spatial and stochastic model to evaluate the within and between
329 farm transmission of classical swine fever virus: II. Sensitivity analysis and validation” (to be
330 submitted). Nevertheless, in this paper we present a preliminary sensitivity analysis to test the
331 overall sensitivity of the model and to evaluate the value of input variables for which
332 uncertainty may be high (those obtained by expert opinion). Those inputs obtained by expert
333 opinion were systematically varied from minimum and maximum values equal to,
334 respectively, a 10% reduction and a 10% increase in the base value of the variable, while
335 keeping constant on their base values all other variables. A percentage of change smaller than
336 10% in outputs was considered evidence of lack of influence of input variables in model
337 results.

338

339 **3. Results**

340

341 *3.1. Within-farm transmission*

342 The mean spread of CSFV within a farm reaching the infectious state (i.e. after the
343 latent period) was observed to occur very fast, mainly for the farrowing farms (Figure 1). As
344 a result, 80% of the animals were infected at day 8, 11 and 23 for the farrowing, farrow-to-
345 finish and fattening farms, respectively.

346

347 *3.2. Magnitude and duration of CSFV epidemic without control measures*

348

349 The estimated mean and 95% PI of infected farms in the experiment without control
350 measures were 7 [1, 33], 32 [1, 138] and 234 [2, 705] for the simulations with maximum time
351 interval of 100, 200 and 365 days, respectively. The main sources of transmission were local
352 spread and vehicles transporting products (feed, slurry, etc) which were responsible of 62.4%

353 [0, 100] and 21.1% [0, 100] of the infections, respectively. The movement of people, animal
354 movements and vehicles transporting animals were responsible of the 9.6% [0, 85.6], 6.8%
355 [0, 50] and 0.1% [0, 1] of the infections, respectively.

356

357 *3.3. Magnitude and duration of CSFV epidemic with control measures*

358

359 The estimated mean and 95% PI number of infected farms, quarantined farms in the
360 control zone and quarantined farms in the surveillance zone in the experiment with control
361 measures were 3 [1, 17], 23 [0, 76] and 115 [0, 318], respectively. The peak of infections is
362 reached at day 47 (Figure 2). The duration of the epidemic was 63 [26, 177] days.

363 The most important way of transmission was local spread which account for 61.4%
364 [0, 100] of the infections. Other ways of transmission were the movement of vehicles
365 transporting products (21.3%, [0, 100]), movement of animals (8.8%, [0, 100]), people
366 contacts (8.5%, [0, 100]) and vehicles transporting animals (0.1%, [0, 1]).

367 The median distance (meters) from an infected farm to the 10 nearest farms was 1.64
368 times smaller (median = 436, 95% PI [20; 2485]) than the distance from a non infected farm
369 to the 10 nearest farms (median = 713, 95% PI [711, 719]).

370 The mean basic reproduction ratios (R_0) for farrowing, farrow-to-finish and fattening
371 farms were 2.98 [0-15.25], 3.43[0-19.00], 1.72 [0-10.00], respectively. The mean effective
372 reproduction ratios (R) were 2.05 [0-12.5], 1.79 [0-10.55], 1.33 [0-8.00], respectively. Risk
373 values for those farms were 1.66 [0, 8.25], 1.72 [0, 8.00] and 1.62 [0, 7.00], respectively.

374 Artificial insemination centres registered an R_0 and R of 0.2 [0, 0.9], and a risk value of 0.8
375 [0, 1.9]. Slaughterhouses had an R_0 and R of 0.05 [0, 0.12], and a risk value of 89.52 [0,
376 398.20]. Spatial distribution of the effective reproduction ratio and risk values for Segovia
377 region is presented in Figure 3.

378

379 *3.4. Sensitivity analysis*

380 Model results were not very sensitive to changes in input parameters (<10% of
381 change). Only 1% of the simulations present an increase in the maximum duration of the
382 epidemic (those lasting more than 600 days) (Figure 2).

383

384 **4. Discussion**

385 The *Be-FAST* model presented here allows to stochastically simulate the potential
386 within- and between- farms spread of CSFV, to quantify the magnitude and duration of a
387 CSFV epidemic and to identify areas at high risk for the introduction and spread of the
388 disease.

389 This model incorporates two important improvements compared with other previous
390 models based on InterSpread and described by Karsten et al., (2005a,b) and Jalvingh et al.,
391 (1999).

392 The first one is the ability to explicitly model the within-farm CSFV spread, which
393 also modulates the between-farm transmission of the virus. Traditionally, the infectivity
394 within a farm was considered to be constant from the day of infection till depopulation of the
395 farm. However, the number of animals infected on the farm changes over time, due to within-
396 farm spread and, consequently, the probability of a farm to transmit CSFV to other farms by
397 direct or indirect contacts also changes. Moreover, the within-spread is usually different
398 depending on the type of farm considered, because modifications in structure and
399 demographics within the farm substantially change the contact patterns among individuals
400 (Klinkenberg et al., 2002). The model presented here is the first one that incorporates the
401 explicit simulation of the within-farm spread dynamics in the different types of pig farms
402 (Figure 1).

403 The second improvement is the introduction of the real farm-to-farm contact network.
404 Previous studies assumed a mean number of contacts for all farms, without considering the
405 farm size or the production system on farm (Karsten et al., 2005a). The model presented here
406 distinguishes not only the contacts patterns between different types of farms (i.e. farrowing,
407 farrow-to-finish, fattening and artificial insemination centers), like in the study of Jalvingh et
408 al., (1999), but also, the specific individual farm-to-farm trade patterns.

409 Two other differences of the *Be-FAST* disease model are the explicit consideration of
410 the limited resources for depopulation measures and the repopulation of farms after
411 depopulation/disinfection. Most of the models assumed that all infected farms would be
412 depopulated the day after detection of infection, no matter the number of farms to be
413 depopulated. Similarly, no repopulation of the depopulated farms was assumed during the
414 epidemic. These assumptions, which seem reasonable for small epidemics, may not be
415 realistic in large epidemics, where capacities for slaughtering will be exceeded, delaying the
416 time to depopulation and where depopulated farms will be repopulated increasing the
417 susceptible population. The consequence of those simplifications is an underestimation of the
418 magnitude and duration of the simulated epidemics, and may certainly impact the reliability
419 of the model results, as it has been discussed by Karsten et al. (2005a) and Jalvingh et al.,
420 (1999).

421 Model results showed a relative small magnitude and duration of the epidemic in the
422 scenario with control measures, with an average of 3 infected farms and 63 days of epidemic
423 duration, which was similar to the 1-5 infected farms and 21-60 of duration obtained by
424 Karsten et al. (2005a).

425 Local spread and vehicles were found to be important components in disease
426 transmission in both experiments, with- and without-control measures, being consistent with
427 Dutch studies (Crauwels et al., 2003; Stegeman et al., 2002). This was an expected result as

428 most of pig farms in Segovia region are located in high density areas. Movements of animals
429 from farm-to-farm helped to introduce the virus in remote CSFV-free areas, hindering the
430 control of the epidemic.

431 Areas with high number of incoming infections (i.e. Risk of introduction) were related
432 to those areas with high number of outgoing infections (i.e. effective reproduction ratio)
433 (Figure 3). Furthermore, those areas were relatively constant in both the experiment without-
434 and with- control measures, although with an important reduction in the experiment with
435 control measures. These findings involve that the risk of introduction and spread of disease is
436 concentrated in the same regions and, therefore, allocation of preventive and control
437 measures in those areas may allow to meaningfully reduce the number of infections. Other
438 interesting result was the high risk value of the slaughterhouses (Risk= 89.52). This implies
439 that slaughterhouses were likely to receive high number of infected animals during an
440 epidemic and may be good places to centralize efforts to increase sensitivity of the
441 surveillance programs in a CSFV epidemic.

442 Spatial and stochastic models are complex and time consuming from a computational
443 point of view; however, results usually are more realistic and adjusted to the region of study,
444 offering a useful tool for policy makers. One of the most important shortcomings when
445 developing complex epidemic models is the data quality and the potential high computational
446 time needed to run the simulations and obtain the stochastic results. Fortunately, for this
447 study high quality data was provided by Castile and Leon region, allowing to explicitly
448 include into the model the farm demographics (i.e. production type, farm size), farm location
449 (geographical coordinates) and the complex time-space network of direct and indirect
450 contacts in the study region. However, in order to reduce the high computational time needed
451 to obtain results, it was also necessary to implement some simplifications and assumptions in
452 the model. Maybe one of the most important simplifications was to simulate the latent period

453 (i.e. transition between infected to infectious) at a farm level instead of at the animal level.
454 This assumption allowed to simplify the within-herd transmission process by using an SI
455 (Susceptible-Infectious) instead of the more complex SEIR (Susceptible-Exposed-Infectious-
456 Removed) model. Various simulations were run to compare both approaches (using the SI
457 and the SEIR within-farm model), and results showed that the SI allowed to reduce almost
458 40% of the computation time without significantly affecting (<5% change) the model
459 outcomes. Because time is very important for decision making when using a model as a
460 decision support tool during an epidemic, authors decide to keep the simple SI within-farm
461 spread model to reduce the computational time.

462 The parameterization of the model was based on the epidemiological characteristics of
463 the disease obtained from previous studies and expert opinion of the Regional Animal Health
464 Authorities. Most of the parameterization was based on scientific publications related to
465 recent outbreaks in regions which circumstances and conditions were similar to the Spanish
466 ones (Kartsen et al., 2005a,b; Klinkenberg et al., 2002; Stegeman et al., 2002). However, no
467 published data was available for some parameters such as restriction of movements, capacity
468 of depopulation per time period, time to repopulation and, the probability of tracing a
469 movement, and expert opinion was needed to obtain values that could be adapted to the study
470 region. Because the value of the input parameters, particularly those obtained by expert
471 opinion, may have associated high variability and uncertainty, sensitivity analysis was
472 conducted to specifically quantify the nature and magnitude of change in the outcomes when
473 varying those initial values. Sensitivity analysis demonstrated the overall robustness of the
474 parameters used in the *Be-FAST* model, showing that variations in the values of the
475 parameters evaluated did not significantly (<10%) affect model outcomes (Figure 2).
476 Nevertheless, the performance of every single parameter and their influence on the model
477 outcomes will be presented in detail in a future manuscript, as well as the influence of aspects

478 such as farm size or farm location (i.e. high/low animal density areas). Validation using data
479 from 1997-1998 CSFV-epidemic in Segovia region of Spain will be also presented in detail
480 in this future publication.

481 The methods and results presented in this study may be useful for developing
482 programs and contingency plans for the prevention and control of CSFV in Segovia.
483 However, the results of simulations of the model must always be interpreted with caution for
484 making decisions. The assumptions and the uncertainties associated with some model
485 parameters should be evaluated as well as the influence that the unpredictability of human
486 behavior can have on the network of contacts and business relationships. It should be
487 considered that the results presented here, with data from Segovia, are indicative of the
488 performance of the model, and in no case should be extrapolated directly to other Spanish
489 regions or countries, where demographic conditions, contact patterns and management of the
490 epidemic may substantially differ. However, the transparent nature of the model, with clear
491 definition of each parameter and the values used, makes easy to adapt it to other regions or
492 countries, after some appropriate adjustments on the input values. Furthermore, it would be
493 interesting to instigate collaborations with other international research groups in order to have
494 access to unpublished data and to study a potential broader application of the model.

495

496 Future research would be focus on the evaluation of the current and alternative (such
497 as vaccination) control measures to be applied and the economical impact of a CSFV-
498 epidemic.

499

500 **5. Conclusion**

501 The model described here allows to stochastically simulate the potential within- and
502 between- farms spread of CSFV, considering the spatial heterogeneities and the real farm-to-

503 farm contact network into a specific region. Methods and results presented here may be
504 useful for the decision making process and for the improvement of the prevention and control
505 programmes for CSFV.

506

507 **Acknowledgements**

508

509 The project was funded in part by the project MTM2008-04621 of the Spanish
510 Ministry of Science and Innovation, the Universidad Complutense de Madrid (Research
511 group 910480), the Regional Government of Castile and León Region (JCyL) and the
512 Spanish Ministry of Environment and Rural and Marine Affairs (MARM). We gratefully
513 acknowledge the assistance of Olga Minguéz and her team (JCyL) for providing data and
514 assistance in the interpretation of the results and the two anonymous reviewers for their
515 useful comments and suggestions.

516

517 **Conflict of interest**

518 None of the authors of this manuscript has personal or financial relationship with
519 people or organizations that could influence or bias the work and results presented in this
520 paper.

521

522 **References**

523 Anderson, R.M., May, R.M., 1979. Population biology of infectious diseases: Part I. *Nature*.

524 280, 361-367.

525 Anderson, R.M., May, R.M., 1991. *Infectious Diseases of Humans*. Oxford, U.K.: Oxford

526 University Press.

- 527 Crauwels, A.P.P.; Nielen, M.; Elbers, A.R.W.; Stegeman, J.A.; Tielens, M.J.M., 2003.
528 Neighbourhood infections of classical swine fever during the 1997-1998 epidemic in
529 the Netherlands. *Prev. Vet. Med.*, 61, 263-277.
- 530 De Vos, C.J., Saatkamp, H.W., Huirne, R.B., Dijkhuizen, A.A., 2003. The risk of the
531 introduction of classical swine fever virus at regional level in the European Union: a
532 conceptual framework. *Rev. Sci. Tech.*, 22, 795-810.
- 533 Elbers, A.T.W., Stegeman, A., Moser, H., Ekker, H.M., Smak, J.A., Pluimers, H., 1999. The
534 classical swine fever epidemic 1997-1998 in the Netherlands: descriptive
535 epidemiology. *Prev. Vet. Med.*, 42, 157-184.
- 536 Jalvingh, A.W., Nielen, M., Maurice, H., Stegeman, A.J., Elbers A.R.W., Dijkhuizen, A.A.,
537 1999. Spatial and stochastic simulation to evaluate the impact of events and control
538 measures on the 1997–1998 classical swine fever epidemic in The Netherlands. I.
539 Description of simulation model, *Vet. Microbiol.*, 42, 271–295.
- 540 Kartsen, S., Rave, G., Krieter, J., 2005a. Monte Carlo simulation of classical swine fever
541 epidemics and control I. General concepts and description of the model. *Vet.*
542 *Microbiol.*, 108, 187-198.
- 543 Kartsen, S., Rave, G., Krieter, J., 2005b. Monte Carlo simulation of classical swine fever
544 epidemics and control II. Validation of the model. *Vet. Microbiol.* 108, 187-198.
- 545 Klinkenberg, D., De Bree, J., Laevens, H., De Jong, M.C.M., 2002. Within- and Between-pen
546 transmission of Classical Swine Fever Virus: a new method to estimate the basic
547 reproduction ration from transmission experiments. *Epidemiol. Infect.*, 128, 293-299.
- 548 MAPA, 2006, Manual práctico de operaciones en la lucha contra la peste porcina clásica
549 (PPC). 121 pages. Available at:
550 <http://rasve.mapa.es/Publica/InformacionGeneral/Documentos/Manuales/Manual%20>
551 [PPC%202006.pdf](http://rasve.mapa.es/Publica/InformacionGeneral/Documentos/Manuales/Manual%20PPC%202006.pdf)

- 552 Martínez-López, B., Perez, A.M., Sánchez-Vizcaíno, J.M., 2009. Evaluation of the potential
553 spread and effectiveness of control measures for Classical Swine Fever into Spain by using a
554 spatial and stochastic model. 12th International Symposium on Veterinary Epidemiology and
555 Economics (ISVEE), 10-14 August, 2009, Durban, South Africa.
- 556 Milne, G., Fermanis, C., Johnston, P., 2008. A mobility model for classical swine fever in
557 feral pig populations. *Vet. Res.*, 39, 53.
- 558 OIE 2009b. WAHID. Available at: <http://www.oie.int/wahis/public.php?page=home>
- 559 OIE, 2009a. Handistatus II. Available at: <http://www.oie.int/hs2/report.asp?lang=en>
- 560 Ribbens, S., Dewulf, J., Koenen, F., Maes, D., de Kruif, A., 2007. Evidence of indirect
561 transmission of classical swine fever virus through contacts with people. *Vet*
562 *Rec.*, 160, 687-690.
- 563 Saatkamp, H.W., Dijkhuizen, A.A., Geers, R., Huirne R.B.M., Noordhuizent, J.P.T.M.,
564 Goedseels, V., 1996a. Simulation studies on the epidemiological impact of national
565 identification and recording systems on the control of classical swine fever in
566 Belgium. *Prev. Vet. Med.*, 26, 119-132
- 567 Stärk, K.D.C., 1998. Systems for the prevention and control of infectious diseases in pigs.
568 PhD thesis. EpiCentre. Massey University, New Zealand.
- 569 Stegeman, A., Elbers, A.R.W., Smak, J., de Jong, M.C.M., 1999. Quantification of the
570 transmission of classical swine fever virus between farms during the 1997-1998
571 epidemic in The Netherlands. *Prev. Vet. Med.*, 42, 219-234.
- 572 Stegeman, J.A., Elbers, A.R.W., Bouma, A., De Jong, M.C.M., 2002. Rate of inter-farm
573 transmission of classical swine fever virus by different types of contact during the
574 1997-8 epidemic in The Netherlands. *Epidemiol. Infect.*, 128, 285-291.
- 575

576 **Table and Figure captions**

577

578 Table 1. Assumptions and parameters used within the *Be-FAST* CSFV- model.

579

580 Figure 1. Dynamic of within-farm CSFV-transmission in the fattening, farrow-to-finish and
581 farrowing farms.

582

583 Figure 2. Epidemic curve showing the range of the number of infected farms per day in the
584 experiment with control measures (dark grey) and when 10% of perturbation of the input
585 variables is applied (light grey).

586

587 Figure 3. Spatial distribution of the incoming infections (i.e. Risk of introduction) (TOP) and
588 outgoing infections (i.e. effective reproduction ratio) (BOTTOM) obtained in the *Be-FAST*
589 CSFV-model in Segovia region for the experiment without control measures (LEFT) and
590 with control measures (RIGHT). Therefore, Figure 3a represents the spatial distribution of the
591 incoming infections without control measures, Figure 3b the incoming infections with control
592 measures, Figure 3c the outgoing infections without control measures and Figure 3d the
593 outgoing infections with control measures.

Table 1.

Parameter	Value	Reference
Within-farm transmission parameter for farrowing pig farms	$\beta_h = 8.52$	Klinkenberg et al., 2002
Within-farm transmission parameter for fattening pig farms	$\beta_h = 1.85$	Klinkenberg et al., 2002
Within-farm transmission parameter for farrow-to-finish pig farms	$\beta_h = 5.18$	Klinkenberg et al., 2002
Number of pig movements from farm h to farm k at day t	Poisson $[M(t)] * m_{hk} / MT^{(1)}$	CyL data
Number of pigs moved during a simulated movement from farm h to farm k at day t	$n_{hk} * N_h(t) / N_h(0)^{(2)}$	CyL data
Probability of infection by animal contacts due to a movement from farm h to farm k at day t	Poisson $[M(t)] * m_{hk} / MT * n_{hk} * Ip_h(t) / N_h(0)^{(3)}$	Klinkenberg et al., 2002
Probability of infection by contact with vehicles transporting infected animals	Bernoulli [0.011]	Stegeman et al., 2002
Maximum number of visits that a vehicle can do per day	4	CyL expert opinion, 2008
Number of contacts with vehicles transporting products per farm at day t	Poisson [0.4]	Kartsen et al., 2005a
Probability of infection by contacts with vehicles transporting products	Bernoulli [0.0068]	Stegeman et al., 2002
Maximum number of visits that a person can do per day	3	CyL expert opinion, 2008
Number of contacts with people per farm at day t	Poisson [0.3]	Kartsen et al., 2005a
Probability of infection by contact with people	Bernoulli [0.0065]	Stegeman et al., 2002
Probability of infection by local spread at day t	$\frac{Ip_h(t)}{N(t)} * LSM(h, k)$	Kartsen et al., 2005b
Latent period (transition from infected to infectious state)	Poisson [7]	Kartsen et al., 2005a
Transition from infectious to clinical signs state	Poisson [21]	Kartsen et al., 2005a

Probability of detection based on clinical signs at day t before detection of the index case	Bernoulli [0.03]	Kartsen et al., 2005b
Probability of detection based on clinical signs at day t outside the control and surveillance zones	Bernoulli [0.06]	Kartsen et al., 2005b
Probability of detection based on clinical signs at day t in the control zone	Bernoulli $\left[0.98 \left(\frac{I_{p_h}(t)}{N_h(t)}\right)\right]$	CyL expert opinion, 2008
Probability of detection based on clinical signs at day t in the surveillance zone	Bernoulli $\left[0.95 \left(\frac{I_{p_h}(t)}{N_h(t)}\right)\right]$	CyL expert opinion, 2008
Probability of detection based on serological test	Bernoulli [0.95]	MAPA, 2006
Radius (duration) of the control zone	3 km (30 days)	MAPA, 2006
Radius (duration) of the surveillance zone	10 km (40 days)	MAPA, 2006
Probability of restriction of animal movements on the detected as infected farm	Bernoulli [0.99]	CyL expert opinion, 2008
Probability of restriction of vehicle movements on the detected as infected farm	Bernoulli [0.95]	CyL expert opinion, 2008
Probability of restriction of people movements on the detected as infected farm	Bernoulli [0.80]	CyL expert opinion, 2008
Probability of restriction of animal movements within the control and surveillance zone	Bernoulli [0.95]	CyL expert opinion, 2008
Probability of restriction of vehicle movements within the control and surveillance zone	Bernoulli [0.90]	CyL expert opinion, 2008
Probability of restriction of people movements within the control and surveillance zone	Bernoulli [0.70]	CyL expert opinion, 2008
Duration of the restriction of movements outside the control and surveillance zones	90 days	CyL expert opinion, 2008
Probability of restriction of movements outside the control and surveillance zones	Bernoulli [0.4]	CyL expert opinion, 2008
Probability to depopulate a detected as infected farm	Table [prob,day]: [0.11,0], [0.58,1], [0.2,2], [0.06,3],	Elbers et al., 1999

	[0.04,4], [0.004,5], [0.003,6], [0.0015,7] and [0.0015,8]	
Maximum number of farms to be depopulated at day t	Poisson [20]	CyL expert opinion, 2008
Time to repopulation of a depopulated farm	Poisson [90]	CyL expert opinion, 2008
Probability of tracing an animal movement	Bernoulli [0.99]	CyL expert opinion, 2008
Probability of tracing a vehicle movement	Bernoulli [0.70]	CyL expert opinion, 2008
Probability of tracing a people movement	Bernoulli [0.40]	CyL expert opinion, 2008
Period of time to consider when tracing historical incoming or outgoing contacts	60 days	CyL expert opinion, 2008
Probability of not tracing an animal, vehicle or people movement	Bernoulli [0.01]	CyL expert opinion, 2008
Maximum number of farms to be traced at day t	Poisson [60]	CyL expert opinion, 2008

⁽¹⁾ $M(t)$ = number of movements occurring during 2008 at day t ; m_{hk} = number of movements from farm h to farm k during 2008; MT = total number of movements in the study region during 2008

⁽²⁾ n_{hk} = number of pigs moved between farm h and k during 2008; $N_h(t)$ = number of pigs on farm h at time t .

⁽³⁾ $I_p(t)$ = number of infected pigs on farm h at time t .

Figure 1
[Click here to download high resolution image](#)

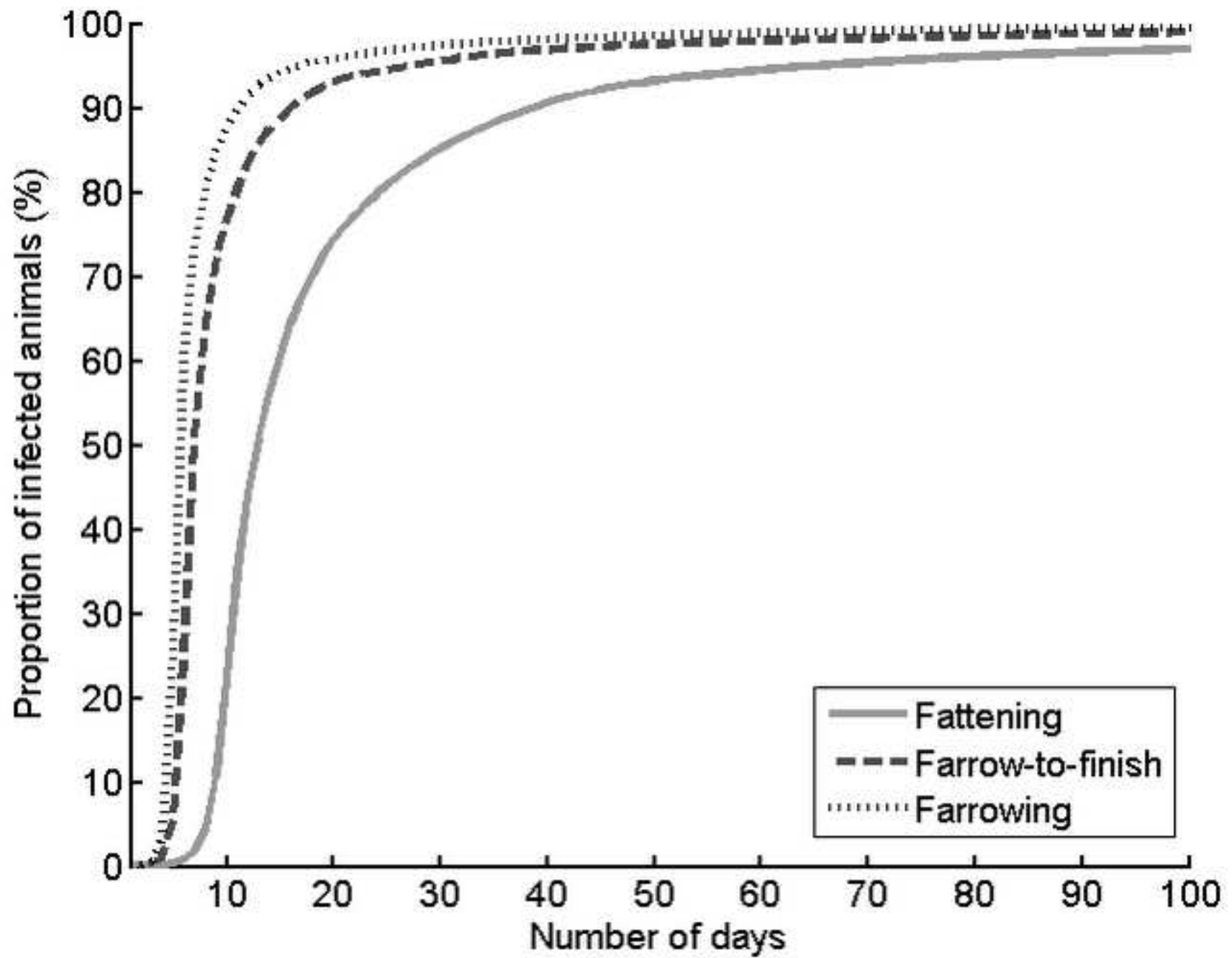


Figure 2
[Click here to download high resolution image](#)

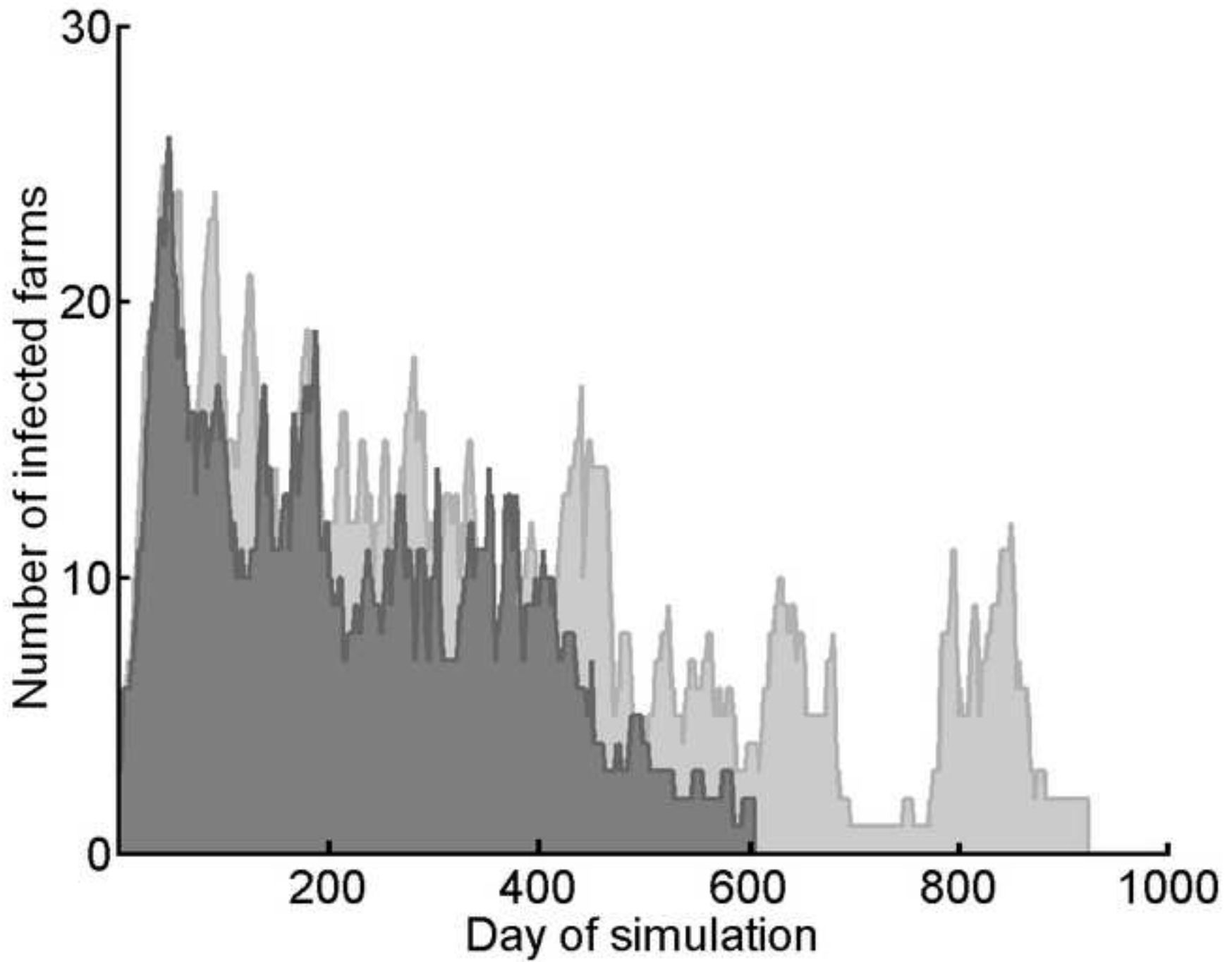


Figure 3
[Click here to download high resolution image](#)

