

Supplementary Online Material

to

The role of movement restrictions and pre-emptive destruction in the emergency control
strategy against CSF outbreaks in domestic pigs

submitted by

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Supplement A – Explanatory Simulations – Figure S1

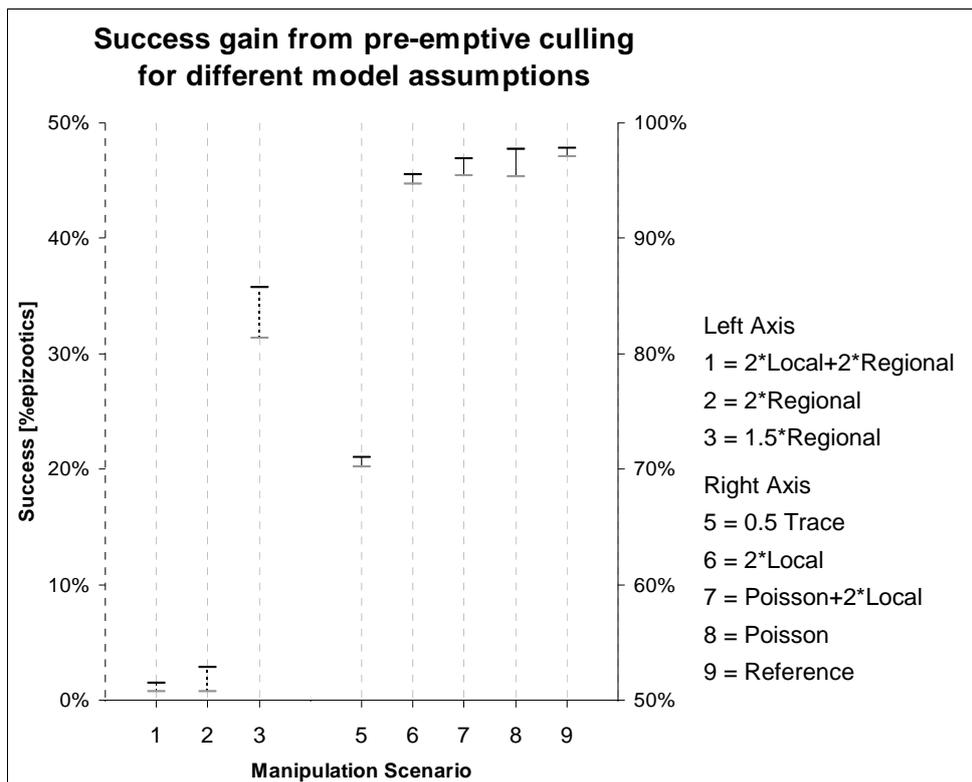
Supplement B – Model Flow Chart

Supplement C – Model Parameters & Standard Reference

Supplement D – Model Documentation

Supplement A – Explanatory simulations

Figure S1: Difference in success between standstill only scenario and application of standstill in combination with pre-emptive culling.

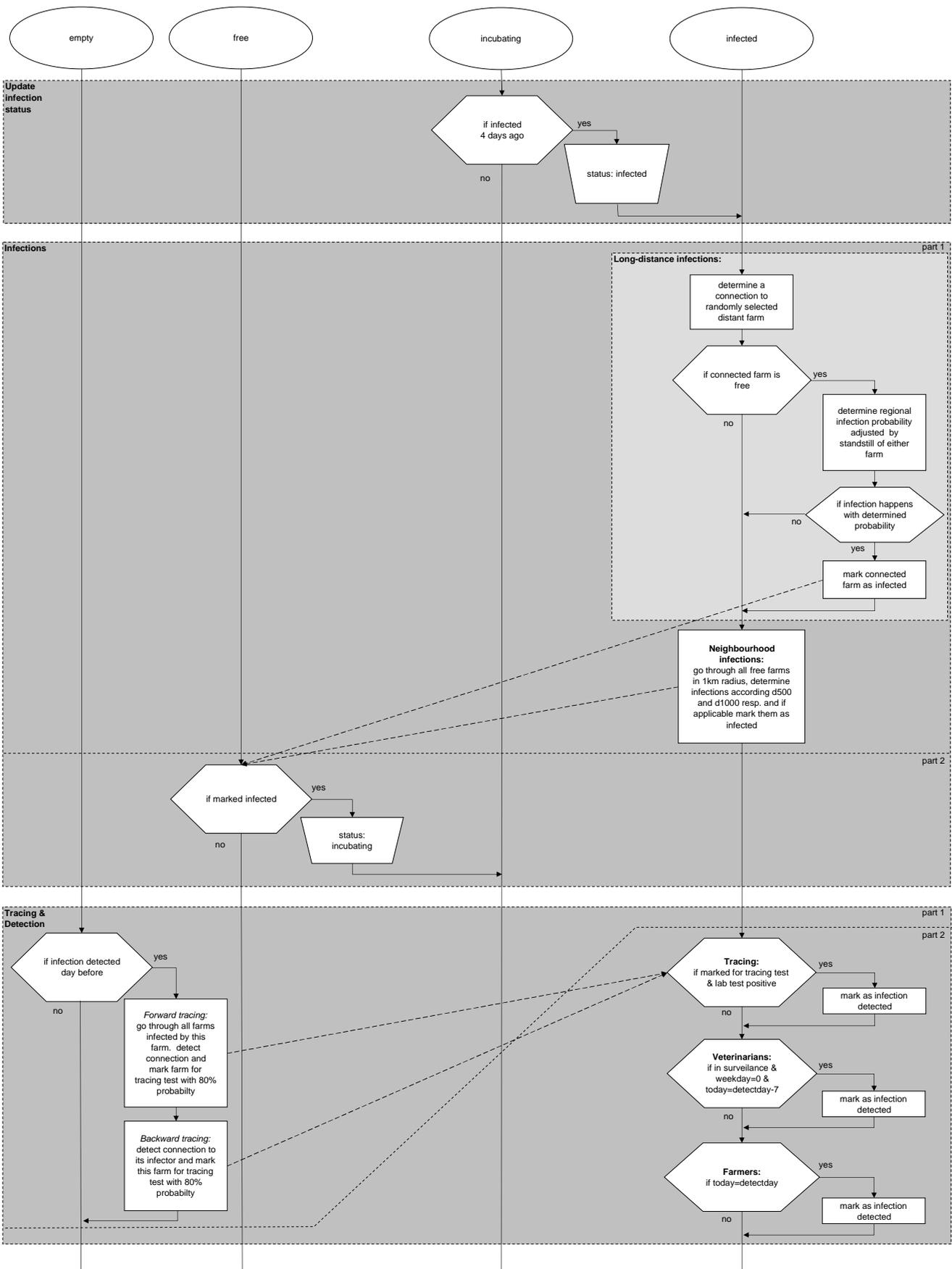


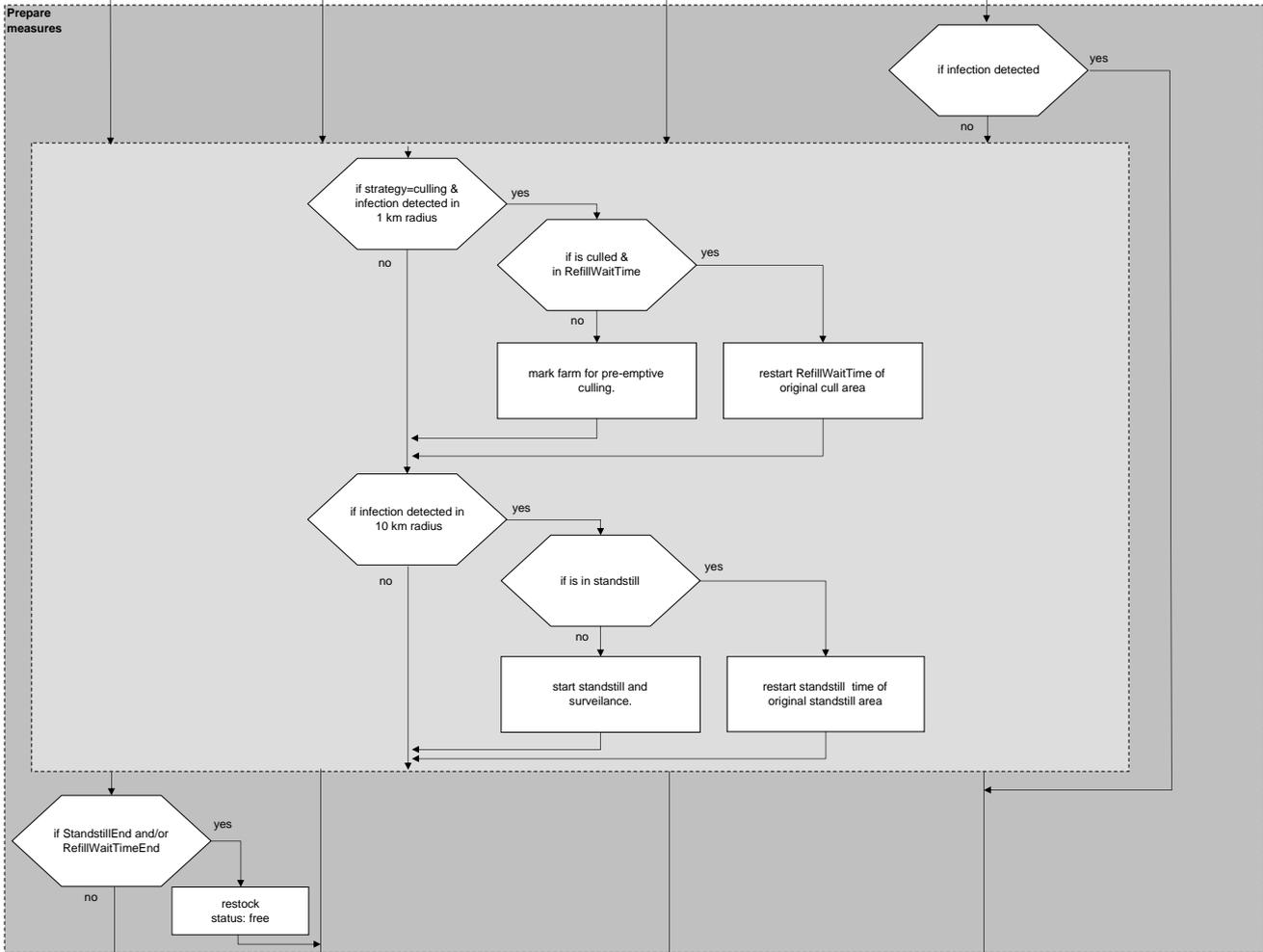
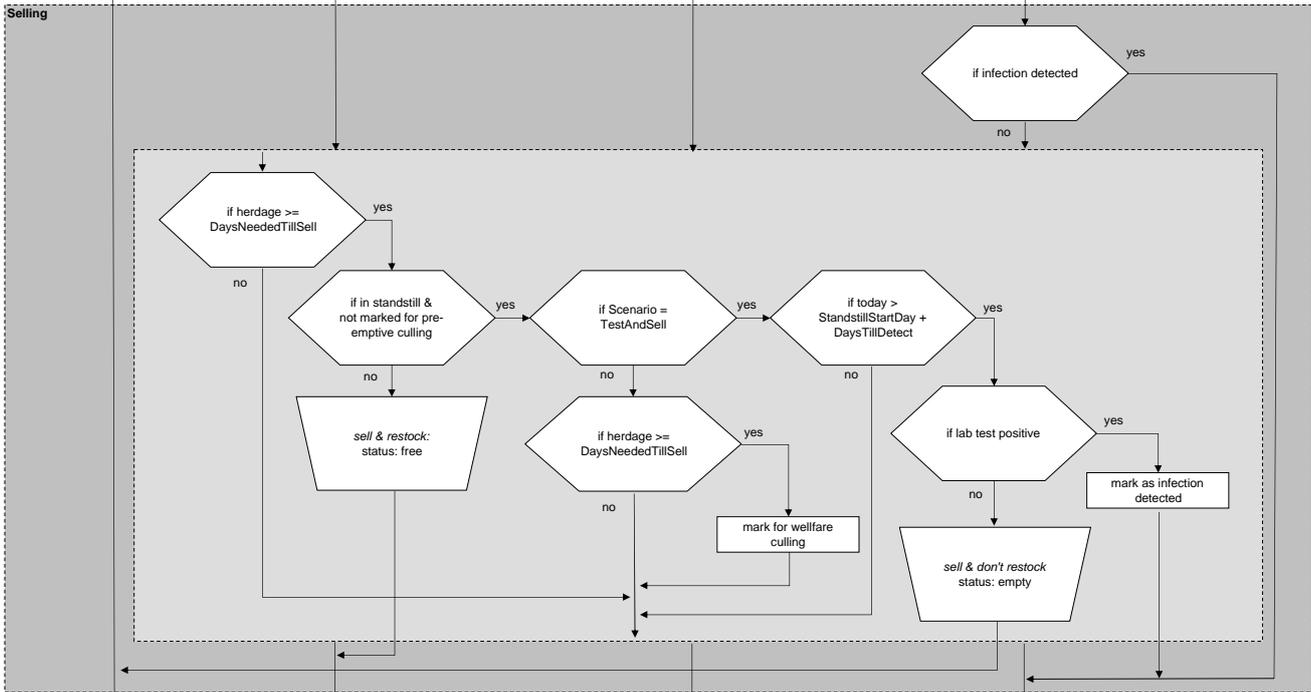
Basic assumptions or parameterisations according to literature were tested with regards to the main result that strict standstill contributes dominant to the success of the emergency strategy combining stamping-out, standstill zoning and pre-emptive culling of neighbourhoods of detected outbreaks. Figure S1 shows the pair wise outcome of twice 150 repetitions simulated assuming standstill efficiency of 80% (i.e. 80% of regional transmissions originating from or targeting to the standstill area are randomly discarded). Eight alternative assumptions are shown on the x-axis as manipulation scenarios. Per scenario the two horizontal sticks represent the success proportion with standstill only (grey stick) and the corresponding simulations where pre-emptive culling was applied (black stick). Scenarios 1-3 are plotted on the left axis while 5-9 refer to the right axis.

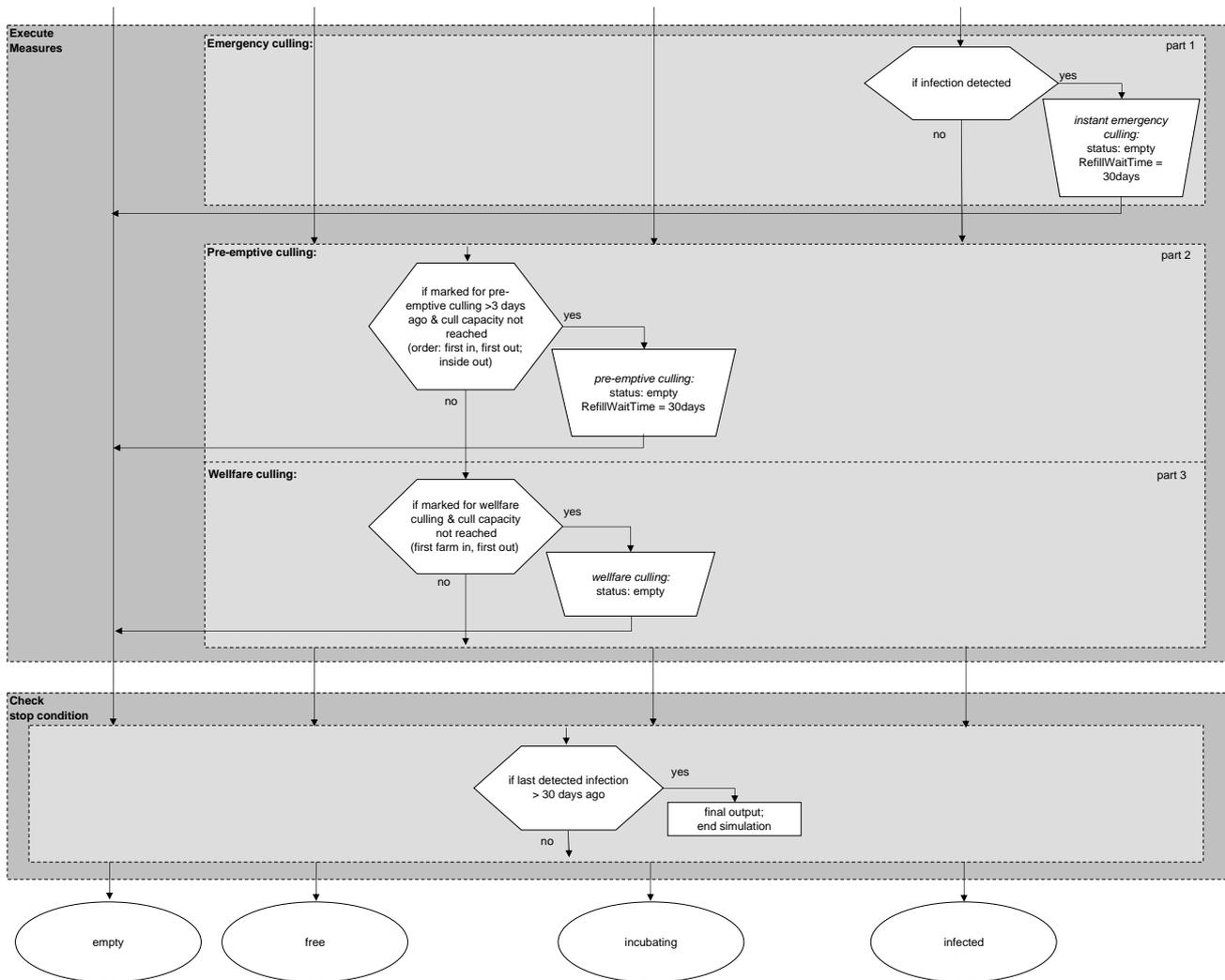
Left axis: 1 – Doubled intensity of local AND regional transmission; 2 – Doubled intensity of regional transmission (Mangen et al. 2002); 3 – Medium increased intensity of regional transmission.

Right axis: 5 – Halved efficiency of backward and forward tracing; 6 – Doubled intensity of local transmission (Mangen et al. 2002); 7 – Doubled intensity of local transmission AND Poisson distributed daily frequency of events; 8 – Poisson distributed daily frequency of events (Jalvingh et al. 1999; Karsten et al. 2005); 9 – Reference (Harvey et al. 2007; Stegeman 1999b).

Supplement B – Model Flow Chart







Supplement C – Model Standard Parameters & Reference

Parameter	Parameter values	Source	Explanation
HerdDensity	1 & 3	Scenario Bernard et al. 1999	<u>Average</u> herd density per sq km
PigsPerHerd [#]	1000	Bernard et al. 1999	<u>Average</u> pig number per herd
DaysNeededTillSell	120	Meuwissen et al. 1999	Time till finishing/slaughter of finisher pigs above 40 days old
Disease & Transmission			
HerdIncubationDays	4	e.g. Jalvingh et al. 1999	Herd starting to be infectious (days)
D500 [#]	0.003813242	Stegeman et al. 2002	Local infection probability per herd less than 500m apart of an infectious herd
D1000 [#]	0.001110579	Stegeman et al. 2002	As before but between 500m & 1000m
RegionalInfectProb [#]	0.073	<u>Reverse</u> <u>parameterised</u> Stegeman et al. 1999	Probability per day per infectious herd to cause an infection (Fit: observed secondary infections per HRP)
RegionalMaxInfectDist [#]	50	Scenario	Maximum distance of regional transmission
RegionalMeanInfectDist [#]	10	<u>Reverse</u> <u>parameterised</u> Jalvingh et al. 1999	Mean of distance distribution (neg.exp.) (Fit: observed transmission distances)
Detection			
MinFarmerDetectTime [#]	21	Klinkenberg et al. 2005	Lower limit of detection (days; farmer's suspicion)
MaxFarmerDetectTime [#]	55	Klinkenberg et al. 2005	Upper limit of detection (days; farmer's suspicion)
FirstDetectDelay	14	Klinkenberg et al. 2005	Delay during high risk period (days)
TestDaysTillDetect	4 days	EFSA 2009 (mean of interval)	rt-RTPCR positive given infection (days); earlier testing will be false negative
TestSensitivity	100%	EFSA 2009	Sensitivity of the applied test after TestDaysTillDetect days post infection
TestSample	census	EFSA 2009	census test, all animals, pooled
TracingEfficiency [#]	0.8	Assumption	Probability to establish a regional infection sourcing from & targeting at the herd
Standstill			
StandstillRadius	10km	Scenario (see Table 1)	Radius of standstill zone established around every detected outbreak (km)

StandstillDuration	30days	Directive 2001/89/EC	Minimum duration of standstill per assigned area (realisation may be longer if involved in continued outbreak detection)
StandstillDelay	1	Expert knowledge	Time after detection before standstill is established (days)
StandstillEfficiency [#]	100%	Scenario (see Table 1)	Probability to suppress regional infections
Surveillance			
SurveillanceRadius	10	Directive	Radius of surveillance zone (km)
SurveillanceDetect Reduction	7	e.g. Klinkeberg et al. 2005	Shortens time till detection at regular visit of an expert (days; 1 visit per week)
Pre-emptive Culling			
CullRadius	1km	Scenario (see Table 1)	Radius of pre-emptive culling (km)
CullDelay	3	Stegeman et al. 1999; EFSA 2009	Time after detection (days) until first animal is pre-emptively culled; may be delayed by limited capacities
CullCapacityPerDay	7500	Scenario (see Table 1)	Animals per day including destruction and disinfection (stamping-out + pre-emptive culling + welfare slaughter)

[#] Parameter used to specify stochastic processes. See Model Documentation – Design Concepts for details (Suppl. D)

Supplement D – Model Documentation

CSFMM – Classical Swine Fever Management Model

The following documentation details the structure of the model as implemented in C++ programming language. The description orients to the ODD protocol (Overview, Design, Details) for documentation of complex models (Grimm et al., 2006. A standard protocol for describing individual-based and agent-based models. *Ecol.Modell.* 198, 115-126) and extends the OD parts already provided in the manuscript.

Purpose

The CSFMM was developed to evaluate different aspects of CSF-outbreak management by simulating the geographical spread of the infection on a “landscape” of pig herds. The formulation of model rules on how the disease spreads through an area as well as on how different management measures interfere with this spread is determined by the existing expert concepts. The simulation tool collates the relevant expert rules on the very grainy basis thus the outbreak dynamics seen in the model are emerging bottom-up from the conceptual model input. The main purpose of the modelling initiative is to test suggested management concepts or control schemes given the state-of-the-art knowledge on the disease.

Overview

The CSFMM is a spatially explicit, stochastic, state-transition model comparable to several similar models (Bates et al., 2003; Garner and Beckett, 2005; Harvey et al., 2007).

The model construction orients to the approach of the more generic NAADSM (Harvey et al., 2007). The description was prepared to parallel the model documentation of these authors to enhance comparability although the CSFMM was not a reimplementations of the former and its focus is exclusively on CSF management problems.

The model is organised in an object-oriented manner to enhance efficient alterations according to simulation protocols on the level of control activities and their interaction.

In CSFMM, disease spread occurs between pig herds at specified locations, and is dependent on relative locations and distances between herds. After introduction of the virus into the herd, the infection follows a predictable cycle over time, moving the herd from one disease state to the next. This cycle may be interrupted by intervention of disease control mechanisms. Stochastic decisions drive all processes within the model for which empirical probability distributions are reported (i.e. detection, spread, testing).

The components and input parameters of the model are described in the following sections: Section organisation, Section disease, Section spread, Section disease detection, Section tracing out, Section control measures, Section priorities of actions and Section costs.

Organisation

Entities, state variables, scales

The CSFMM was formulated with two hierarchical entities: herd and landscape.

The low-level entities are individual herds and the transmission of the infection is followed on the herd level (cf. units in (Harvey et al., 2007)). Animals inside a herd are reflected by

numbers and within herd spread follows deterministic epidemic dynamics (e.g. (Klinkenberg et al., 2003).

The state variables of the herd entities that are stochastically pre-assigned during initialisation are its geographical position (x,y coordinates; random distribution), and its size (stocking number; see eq.1). Additionally, each herd is assigned an initial age (time since last restocking).

Disease state variables reflect the herd's CSF status (susceptible, infected, infectious), and whether it is involved in the outbreak (detected or not detected, number of infected or sero-converted animals) or any control activity (standstill zone, surveillance zone, pre-emptive culling, vaccination, tracing or testing).

The herd size is assumed to be static: herd size is not altered by the movement of animals. Only when a herd is destroyed or not restocked the number of animals will be affected (i.e. herd gets empty). Finished herds [**Par**: DaysNeededTillSell] are instantaneously restocked assuming slaughter of all pigs and disinfection i.e. the age and infection features are reset.

The second level entity is the landscape (simulation area) that maintains information on the whole population, the density and the actual stage of control measures (i.e. outbreak detected, or final success). The landscape is initialised at the beginning of each simulation by distributing a number of herds per sq km [**Par**: HerdDensity] and the realisation of an average herd size [**Par**: PigsPerHerd] following the distribution:

$$\text{eq.1} \quad \text{Herd size} = \text{PigsPerHerd}/4 + \text{random number between } 0 \text{ and } 1.5 * \text{PigsPerHerd}$$

(e.g.: if PigsPerHerd=1000; then herd size is between 250 and 1750)

Scheduling

The model steps forward in time by one day. On each simulation day, a regular sequence of processes is scheduled by the landscape:

Init: Generate farm landscape (herds with age, position, size)

Update Status: Increment of the disease and vaccination status of each single herd.

Pass Infection: Evaluate potential transmission to next herds (regional and local)

Detect Infection: Test every infected herd whether detected today

Sell: Handle finished finisher herds (welfare or pre-tested slaughter);

Make Priorities: Organise scheduling of control measurements (culling, vaccination & testing);

Start Measure: Perform control measures along the schedule up to daily capacity;

Check Stop Condition: Eradication; or lift-up etc. (depends on experiment)

Stop: Output and Statistics

Within process operations are performed synchronously for all related herds (i.e. resulting changes in status of a herd does not affect the process itself during one day).

At the end of the simulation run the overall statistics are prepared.

Design Concepts

Emergence: The model is designed and parameterised to allow emergence of dynamics on the level of epizooty from simple and expert approved epidemiological details – rule-based modelling approach.

Stochasticity: Most dynamic processes are modelled stochastic. The reason is high uncertainty about very particular realisations for e.g. herd assemblages, daily disease transmission pathway and temporal order, detection distribution, traceability of the infection network, human compliance with regulations.

Table 1: Overview of stochasticity components of the CSFMM

Process/Mechanism	Distribution	Parameter(s)
Locations of herds	2D uniform(0;p)	p: AreaSize
Stocking size (eq.1)	Uniform(1/4*p; 7/4*p)	p: PigsPerHerd
Detection by clinics	Uniform(p _u ;p _o)	p _u : MinFarmerDetectTime p _o : MaxFarmerDetectTime
Regional transmission - Distance (eq.2b)	Negative Exponential(p ₁) Censored at p ₂	p ₁ : RegionalMeanInfectDist p ₂ : RegionalMaxInfectDist
- Infection given contact	Bernoulli(p)	p: RegionalInfectProb
Regional transmission - Standstill effect	Bernoulli(p)	p: StandstillEfficiency
Local infection - up to 500m	Bernoulli(p ₁)	p ₁ : D500
- up to 1000m	Bernoulli(p ₂)	p ₂ : D1000
Traceability of infection network	Bernoulli(p)	p: TracingEfficiency

Submodels (ordered by schedule)

Disease

Disease dynamics within the basic entity (herd)

When a susceptible herd is infected, it transits instantaneously to incubating, and further to infectious according to the parameter describing herd incubation [**Par**: HerdIncubDays]; e.g. when an infected herd is assumed to be able to cause infections itself. When infected herd switches to infectious the infectious animal population of the herd is seeded randomly with 2-4 infectious pigs. Further growth of the infectious respective recovered cohort follows standard exponential growth with random increments [**Par**: EpidemicGrowthRate], i.e. for

each virus positive pig one comes up with daily rate of 0.0822 (parameterised according to (Klinkenberg et al., 2003)).

The course of the disease in an infected herd is not altered by re-infection (i.e. no super-infections are modelled). Technically, a herd that receives an infection (e.g. by animal transport) could be regarded as immediately infectious. Treating newly infected herds as incubating, however, reflects the fact that most of the animals in the herd still need to progress through the early state of the infection.

Transmission

According to the literature the model differentiates the known modes of CSF transmission (Staubach et al., 1997; Stegeman et al., 2002; Ribbens et al., 2004): Distance dependent or local transmission refers to all processes that cause decreasing risk by distance in the vicinity of an outbreak herd (e.g. insects, children, farmer's movement etc.) and is usually attributed to surroundings up to 500-1000m (Staubach et al., 1997; Stegeman et al., 2002). Distance independent or regional transmission refers to routes by which the risk of transmission does not depend on this distance (Lorry or service personal moving around (Ribbens et al., 2004)). Any infected herd that is no longer incubating is assumed infectious i.e. is capable of spreading disease.

Local transmission:

Local transmission summarizes distance dependent transmission events. These are associated to any neighbourhood transportation of the virus making the infection risk continuously decreasing by distance from the source.

According to the analysis by Stegeman et al. (2002) two parameters for local transmission are used (Table 1): An infectious herd passes the infection either of its neighbours according to a Bernoulli probability up to 500m [**Par:** D500] and further up to 1000 meters [**Par:** D1000]. Local transmissions are recorded as such but cannot be identified during tracing investigations.

Regional transmission:

Regional transmission simulates distance independent virus transport (Staubach et al., 1997) or "direct contact" spread (Harvey et al., 2007). The scale of the transmission events is "regional" i.e. they may cover large parts of the pig area without decreasing final risk of infection.

The regional transmission occurs from an infectious source herd according to a twofold random procedure: First, on each simulation day, a distance is randomly drawn from the regional distance distribution (either negative exponential with specified mean [**Par:** RegionalMeanInfectDist] or uniform; and up to a specified maximum distance [**Par:** RegionalMaxInfectDist] but beyond 1000m. Distances are calculated according to the Euclidean metric.

If uniform:

$$\text{eq.2a } \text{Distance} = 1 + \text{uniform}[0;1] * (\text{P} \rightarrow \text{RegionalMaxInfectDist} - 1)$$

If negative exponential:

$$\text{eq.2b } \text{Distance} = \text{negexp}(\text{P} \rightarrow \text{RegionalMeanInfectDist}); \text{ on } 1 \leq \text{Dist.} \leq \text{RegionalMaxInfectDist}$$

With the resulting distance a geographic position of a recipient herd is searched that is closest by the randomly drawn distance. If necessary, the recipient is randomly selected out of multiple, evenly matching candidates.

If the recipient herd is not susceptible, or was already destroyed or protected by vaccination, the contact does not occur. If the recipient herd is susceptible the model randomly determines

whether an infectious contact happens based on the regional transmission probability [**Par**: RegionalInfectProb]. Then the recipient status becomes infected.

Successful transmission events are recorded and can be identified later during tracing investigations. The number of animals in a movement is not considered (Harvey et al., 2007).

Detection

Infected herds are detected by routine check for clinical suspicion, routine testing according to surveillance schemes, or targeted testing after successful establishment of a contact by tracing investigations or diagnostic protocols.

There are no false-positive detections in model.

The order of potential detection in the model is:

D1) Tracing related tests (diagnostic test; census or sample)

D2) Visit according to surveillance scheme (vet)

D3) Otherwise routine daily check (farmer)

Only infectious herds are detected by D2 and D3. D1 can detect even earlier according to the assumed diagnostic test characteristics. After detection the herd is designated as detected and measures that are dependent on detection are initiated subsequently, e.g. tracing of backward and forward contacts will be schedule for the next day.

Basic detection

If a herd gets infected a regular day of its detection is fixed. The value is randomly drawn of the interval [**Par**: MinFarmerDetectTime; **Par**: MaxFarmerDetectTime].

$$\text{DayOfFarmerDetection} = \text{today} + \text{MinFarmerDetectTime} \\ + \text{integer}[\text{uniform}[0,1] * (\text{MaxFarmerDetectTime} - \text{MinFarmerDetectTime})];$$

The standard interval is parameterized according to Dutch outbreak data (Klinkenberg et al., 2005) and covers MaxFarmerDetectTime = 21 and MinFarmerDetectTime = 55 days post infection. The resulting distribution reread from the model generally mimics the data while particularities might change with outbreak realisation.

Any process that is supposed to alter detection modulates the regular detection date per herd. For example, as long as the first notification is missing the respective detection date per herd is shifted later by 14 days [**Par**: FirstDetectDelay] (Stegeman et al., 1999b). Thus, during the high risk period the detection happens between day 35 and 69 (i.e. 5th to 10th week post infection; see Fritzemeier et al., 2000)

Farmer

Every day the model tests if a herd has reached the detection date. These notifications relate to the successful confirmation of the disease after farmers suspicion.

Veterinary Service

After outbreak notification inside of designated surveillance zones once a week a targeted visit by an expert is assumed that shortens time till detection by a number of days [**Par**: SurveillanceDetectReduction].

Tracing

If an infected herd was detected, next day tracing happens along the recorded transmission history. Tracing might establish the source contact (one step back; tracing backward) or any herd infected by the detected one (multiple one step forward; tracing forward). The actual identification of these links during tracing investigations is reflected by a probability value i.e. the tracing efficiency [**Par**: Forward/BackwardTracingEfficiency]. For example, assuming

100% tracing efficiency will guarantee the stepwise but full reconstruction of all regional transmission events. Traced herds are marked for diagnostic testing. Herds could be involved in multiple tracing investigations. Tracing only works if animals are present. If the herd traced next is already culled the tracing is terminated on that branch.

Diagnostic Testing

Diagnostic testing is simulated whenever the strategy requires diagnostic tests as basis for decisions on a herd status. Possible examples are: infected herds designated for testing from a traced link, herds designated for slaughter or pre-emptive destruction, companion test during vaccine administration, or final screening before the lift-up of restrictions. The diagnostic failures in confirmatory tests, e.g. after farmer suspicion, are not modelled explicitly but covered by the basic detection period. The model supposes different diagnostic test systems to consider basically different strategy concepts simultaneously.

The test system comprises of the following features:

Test target: virus or antibody positive test units [**Par**: TestSystem],

Test sensitivity: the usual probability to detect a truly positive test unit [**Par**: TestSensitivity]

Test operability: the time period necessary after infection until the test will notice CSF infections [**Par**: TestDaysTillDetect]

Test sample: The sampling in a tested herd either covers all animals (census) or a randomly selected part according to a specified sampling scheme e.g. accounting for herd size [**Par**: TestSample]

Selling

For all herds that are not yet detected as infected and are not emptied, the time since simulated last restocking is checked against the maximum fattening age [**Par**: DaysNeededTillSell]. If maximum fattening age was reached the slaughter and immediate restocking is simulated by resetting of disease state and age. If the CSF outbreak in the simulation area was already detected, then in accordance with the simulated strategy concept selling might be preceded by a mandatory diagnostic test with false negative tests being recorded, or selling might be completely excluded due to movement restrictions. In the latter the aging herd finally will be destroyed for welfare reasons. Sold herds produce zero loss record.

Intervention measures

Intervention measures refer to the establishment of surveillance and standstill zones. Before first notification none of these measures is activated in the model.

Surveillance zone

The circular area [**Par**: SurveillanceRadius] established around infected herds yet detected. Following detection of the centre herd the zone remains activated at least as long as strategy concept foresees [**Par**: SurveillanceDuration]. Subsequent detections during simulation might cause prolonged effective duration.

The intervention measure causes increased awareness e.g. by regular veterinary inspection. Thus likely more timely detection of an infected herd is based on an additional stochastic test once per week against a reduced basic detection time [**Par**: SurveillanceDetectReduction] (see chapter Detection).

Standstill zone

The circular area [**Par**: StandstillRadius] established around infected herds yet detected. The zone is activated after time necessary for legislative process [**Par**: StandstillDelay]. Following

detection of the centre herd the zone remains activated at least as long as strategy concept foresees [**Par**: StandstillDuration]. Subsequent detections during simulation might cause prolonged effective duration. This happens if any herd already in standstill zone A, became contained in a further newly established standstill zone B. In consequence, the standstill time [**Par**: StandstillDuration] is restarted also for the complete previous standstill zone A.

The intervention measure aims at halting of all animal movements. Thus, regional (or distances independent) transmission events initiated by the transmission process are suppressed with certain efficiency [**Par**: StandstillEfficiency] for contacts originating from or connect into active standstill zones. Any herd that becomes emptied by control measures will not be restocked as long it is assigned to a standstill zone. Standstill is assumed not to influence the local neighbourhood of the centre herd which is intended to result in less favourable outcome for any strategy that does not apply control measures to the core neighbourhood of an outbreak herd. The basic motivation was inconsistent knowledge. Certain contact in the close vicinity of an outbreak, however, should also be excluded by movement ban in practice.

After lift-up of standstill restriction in an area all empty herds are assumed to be restocked immediately (Mangen et al., 2002).

Control measures

Control measures simulated by CSFMM are stamping-out, pre-emptive culling, and emergency vaccination. Before first notification none of these measures is activated in the model.

Destruction

Immediately with the infected herd that is detected first, the destruction program starts. There are three cases where herds are destroyed in the model: stamping out of infected herds after detection, pre-emptive culling in a circular neighbourhood of detections (i.e. ring destruction), and welfare slaughter inside of standstill zones.

There is a limit to the number of animals that can be destroyed per day. This is referred to as the culling capacity [**Par**: CullCapacityPerDay]. Herds designated for destruction queue by priority (see list below). Every day queuing herds are culled upon saturation of the daily capacity. Queuing herds are not quarantined.

Stamping-out:

In the model all detections of infected herds are destroyed after a number of days reserved for preparation [**Par**: CullDelay]. Herds designated for stamping-out are assigned with the highest priority for destruction. Hence, they instantaneously will be destroyed. Therefore, if on one day the capacity limit is already reached by necessary stamping-out, it is assumed that ad hoc destruction capacity will become available to allow instantaneous destruction of all detected infected herds.

Pre-emptive culling:

Subsequent to stamping-out all herds in a circular area around the detected herd may be designated for pre-emptive culling in accordance with the simulated strategic concept. The size of the control area is defined by a radius [**Par**: CullRadius]. The culling zone is cleared by concentric distances from the centre either from inner to outer herds or vice versa. Herds designated for pre-emptive culling measures have second highest priority in the waiting list.

Welfare slaughter:

Finisher herds in standstill zone that reach fattening age remain in the model for an additional number of days [**Par**: SellDayExtension]. If then the standstill has still not been lifted these herds are destroyed and not restocked. Welfare slaughter designation results in the lowest priority for culling or might be performed instantaneously.

Vaccination

Not applicable.

Initialisation

On the squared simulation area [**Par**: AreaSize] herds are distributed randomly (or by given geographic attribute) according to herd density parameterization [**Par**: HerdDensity]. Herds are populated according to mean herd size parameter [**Par**: PigsDensity] randomly drawn between 26%-175% the parameter value. Each herd is randomly assigned with a fattening age up to a maximum [**Par**: DaysNeededTillSell]. The herd closest to the geometric centre is seeded as infected.

Costs

Estimates of costs and losses are accumulated in the model to compare the economic consequence of different strategic options. All monetary parameters (see Table CostParameters) are given in Euro and relate to the individual animal unit. For destruction measures bio-safety is assumed to increase the cost per animal unit (stamping-out and pre-emptive culling) compared to the welfare slaughter of over-fattened animals. All cost estimates for control application cover human resources and technical stuff (e.g. vaccine, killing facilities)

Costs for diagnostic testing are based on pooled samples of 40 units.

For herds that are not restocked due to restriction, opportunity costs are considered as losses per day and animal unit, targeting the market value of a finisher pig.

Table Cost parameters

If one animal is...	Unit cost in Euro	Unit
Destroyed (stamping-out + pre-emptive culling)	200	Per animal
Welfare slaughtered	150	Per animal
Vaccinated	6	Per animal
Not restocked (Opportunity cost)	0.5	Per day
Tested by RTPCR (pooled at 40)	3	Per animal

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