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Risk-based early detection system of African Swine Fever using mortality thresholds

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Abstract

African swine fever (ASF) is an infectious disease of swine causing major losses in the swine industry worldwide. Early detection of ASF is challenging because of the wide range of non-specific clinical signs produced and its relatively low contagiousness. Monitoring pig mortality is a promising approach for early detection of ASF, but such approach has been associated with delay in disease detection in large pig farms. The purpose of this study was to compare the effectiveness and suitability of early detection strategies for ASF in large commercial pig farms using mortality monitoring at the pen, room or barn level. The within-barn spread of the disease was modelled including the non-homogeneous probabilities of transmission within pens, between pens and between rooms. The performances of early detection surveillance based on mortality thresholds established for different epidemiological units were compared in terms of sensitivity, time to detection and number of false alarms per year. A barn with a capacity of 3,200 pigs divided into 8 rooms with 10 pens each containing 40 pigs per pen was used as an example. Our results show that using room- or pen-based mortality thresholds provided a time to detection of 8 days post-disease introduction. Similar detection performances could be achieved with barn-level mortality threshold but at the cost of an increased number of pigs to be tested each year. The different scenarios tested also show that barn characteristics such as baseline mortality rate and pen size had a limited impact on the pen-level mortality thresholds required for disease early detection. These results offer strong support for using mortality data for early detection of ASF not only in small pig herds but also in large commercial barns. Furthermore, the mortality thresholds defined in this study might be relevant to a wide range of pig production sites.

KEYWORDS
African swine fever, domestic pigs, early detection, modelling, mortality data, surveillance

1 | INTRODUCTION

African swine fever (ASF) is an infectious disease of swine, notifiable to the World Organisation for Animal Health (OIE) and responsible for causing major losses in the swine industry worldwide (Chenais

et al., 2019; Sánchez-Cordón, Montoya, Reis, & Dixon, 2018). Currently, no approved vaccine or treatment for ASF is available. Early disease detection through rapid investigation of field suspicions and timely laboratory diagnosis is essential to prevent further spread and to minimize direct and indirect losses associated with the disease,

such as high losses due to mortality and economic losses caused by control measures such as pig movement restrictions and culling.

Early detection of ASF is challenging because of the wide range of clinical presentations of the infection varying from peracute, acute to chronic disease and subclinical infections (OIE, 2019a). The more virulent strains produce haemorrhagic disease characterized by high fever, loss of appetite, haemorrhages in the skin and internal organs, and are associated with a case fatality rate near 100%. On the other hand, less virulent strains produce only mild non-specific clinical signs which can be easily mistaken for endemic diseases such as erysipelas or porcine reproductive and respiratory syndrome. In addition, the low contagiousness of ASF observed both in experimental conditions (Guinat, Gogin, et al., 2016; Guinat, Gubbins, et al., 2016; Pietschmann et al., 2015) and in the field (Lamberga, Seržants, & Oļševskis, 2018; Nurmoja et al., 2018; Oļševskis et al., 2016) complicate early disease detection and can delay it for several weeks.

OIE recommendations (OIE, 2019b) have highlighted clinical surveillance as the most effective tool for early detection of ASF. It is recommended that all cases of clinical signs or lesions suggestive of ASF accompanied by high mortality should be investigated. In terms of clinical surveillance, Guinat et al. (2017) ranked monitoring pig mortality alone (as opposed to other methods or combined detection approaches) as the best option for early detection of ASF in domestic pig farms. At the time of writing, the value of monitoring pig mortality for ASF early detection has only been assessed for barn-level mortality thresholds (Andraud, Halasa, Boklund, & Rose, 2019; Guinat et al., 2018; Halasa et al., 2016b; Nurmoja et al., 2018). While this approach seems well-adapted to small herds, it has been associated with delays in ASF detection in large production systems (Chenais et al., 2019; Guinat et al., 2018; Lamberga et al., 2018; Nurmoja et al., 2018). For example, (Nurmoja et al., 2018) reported that mortality rates strongly depend on the herd size, being lowest in the largest herd size category (0.7% in herds >1,000 pigs) and highest in the smallest herds (29.7% in herds <1,000 pigs). Such findings indicate that the monitoring of barn-level mortality will be less effective for early detection of ASF in larger herds. The delays observed when using barn-level mortality thresholds in large herds can be explained by the low contagiousness of ASF combined with

the internal physical layout of the barn in these large production units. Pigs raised in large herds (>1,000 pigs) are generally divided into pens, sometimes grouped within rooms, which significantly reduces the probability of disease transmission within a given barn, as shown for example by Guinat, Gogin, et al. (2016) and Nielsen, Larsen, Halasa, and Christiansen (2017).

The purpose of this study was to compare the effectiveness and suitability of early detection strategies for ASF in large commercial pig farms using mortality monitoring at the pen, room or barn level. Our study focuses on the detection of the first infected farm in a previously ASF-free area. The within-barn spread of the disease was modelled including the non-homogeneous probabilities of transmission of ASF within pens, between pens and between rooms. The performance of early detection surveillance based on mortality thresholds established for different epidemiological units (pen, room, barn) were compared in terms of sensitivity, time to detection and expected number of false alarms per year.

2 | MATERIAL AND METHODS

2.1 | ASF within-barn spread model

A stochastic Monte Carlo simulation model using daily discrete time steps was developed in order to simulate the spread of ASF within a domestic pig unit comprising several rooms, each divided into multiple pens. For simplicity, we considered only one finisher barn type, housing pigs in 8 rooms, each divided into 10 pens holding an equal number of pigs at the start of the outbreak (see Figure 1). The presence of hallways between pens or rooms was not considered in the model. The animals were assumed to mix randomly within pens, that is to have equal opportunity for contact with each other. The number of new infections per unit of time was assumed to be proportional to the product of the proportion (or frequency) of infectious animals and the number of susceptible animals (Vynnycky & White, 2010).

A susceptible–exposed–infectious–removed (SEIR) model was used, with state-transition probabilities based on the findings of Guinat, Gogin, et al. (2016)), and considering the baseline pig mortality in the
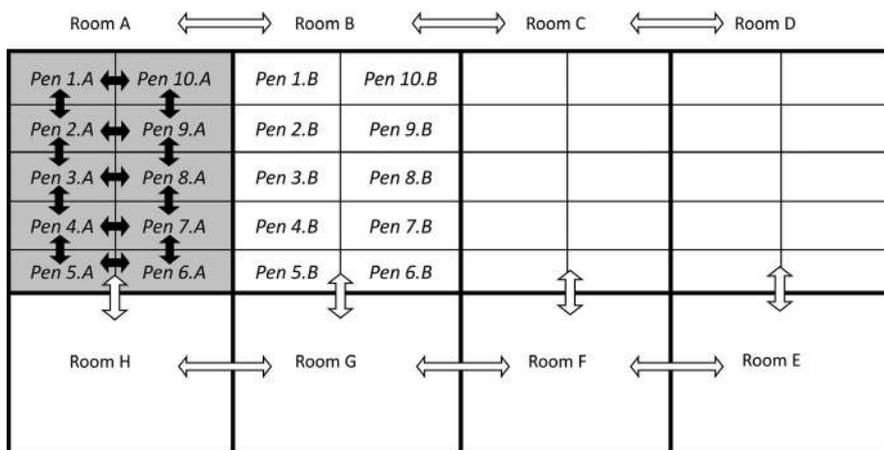

FIGURE 1 Schematic representation of the barn made of 8 rooms with 10 pens each (grey area = room A). No hallway between pens or room was included. Black arrows = between-pen transmission, white arrow = between-room transmission

absence of ASF as well as between-room disease transmission (see Figure 2). Pigs leave the susceptible compartment ($S_{i,A,t}$) and die of causes other than ASF ($R_{i,A,t}$) or become infected with ASF ($E_{i,A,t}$), with respectively a probability of μ and $P_{i,A,t}$. Then, the pigs leave the exposed compartment and become infectious ($I_{i,A,t}$) after L days. Finally, they leave the infectious compartment and enter the 'removed' compartment ($R_{i,A,t}$) after T days. The 'removed' compartment includes dead animals and animals that had recovered and became immune. In the model, the latent period was considered equal to the incubation period (from infection to clinical signs). The contamination of the environment by dead pigs before they are removed from the pen was not considered.

The probability $P_{i,A,t}$ depends on the number of infectious pigs in pen i of room A, and in neighbouring pens and rooms, the total population size in the different pens ($N_{i,j,t}$), and how frequently the pigs make effective direct or indirect contact with each other within and between pens (β_w and β_b) and between rooms (β_r). In the model, a given pen or room can only infect its direct neighbours (see Figure 1). For example, pigs in pen 1.A can only infect (and be infected by) pigs located in pens 2.A and 10.A. On the other hand, pigs in pen 2.A can infect (and be infected by) pigs located in pens 1.A, 3.A and 10.A. Similarly, for simplicity, pigs in room A can only infect (and be infected by) pigs in rooms B or H.

Considering a pen i with only two neighbouring pens ($i + 1$ and $i - 1$) located in a room A, and two neighbouring rooms B and H, $P_{i,A,t}$ follows the equation:

$$P_{i,A,t} = 1 - e_0^{-\left(\beta_w \times \frac{I_{i,A,t}}{N_{i,A,t}} + \beta_b \times \frac{I_{(i-1),A,t}}{N_{(i-1),A,t} + N_{i,A,t}} + \beta_b \times \frac{I_{(i+1),A,t}}{N_{(i+1),A,t} + N_{i,A,t}} + \beta_T \times \frac{I_{B,t}}{N_{A,t} + N_{B,t}} + \beta_r \times \frac{I_{H,t}}{N_{A,t} + N_{H,t}} \right)}$$
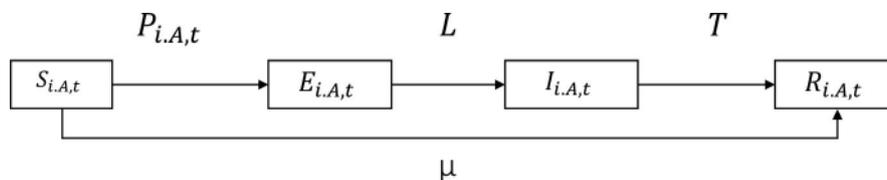
where $N_{B,t}$ and $N_{H,t}$ are the total population size in rooms B and H, respectively. The equation can be then extended to a third neighbouring pen x and room Y by adding $\beta_b \times \frac{I_{x,A,t}}{N_{x,A,t} + N_{i,A,t}}$ and $\beta_T \times \frac{I_{Y,t}}{N_{A,t} + N_{Y,t}}$, respectively, in the exponential term.

The model was developed using R version 3.1.3 (R Development Core Team, 2019).

2.2 | Disease transmission parameters

The model was built and parameterized to represent a specific ASF strain, the highly virulent Georgian strain that is causing most of the current outbreaks worldwide and for which the transmission parameters have been best documented (Davies et al., 2017; Gallardo et al., 2017; Guinat, Gogin, et al., 2016; Guinat, Gubbins, et al., 2016; Guinat et al., 2014). We simulated 5,000 independent outbreaks initiated by the introduction of a single infectious pig in a single pen at time $t = 0$. The infectious pig was introduced in pen 1.A.

For each simulation, parameters were sampled from distributions presented in Table 1 and see Appendix A for Figure A1 under the assumption that these parameters are independently distributed. Prediction intervals were estimated based on the 5th and 95th percentiles of the outcome distribution. No published data were available for the between-room transmission rate. The value of the daily between-room transmission rate was chosen in order to reach 2.55% cumulative mortality at the barn level 21 days after disease

FIGURE 2 schematic representation of the SEIR model for estimating the African swine fever virus transmission considering a pen i in room A at time t. Pigs leave the susceptible compartment ($S_{i,A,t}$) and died of causes other than ASF ($R_{i,A,t}$) or become infected ($E_{i,A,t}$) with respectively a probability of μ and $P_{i,A,t}$. Then, they leave the infected compartment and become infectious ($I_{i,A,t}$) after L days. Finally, they leave the infectious compartment and die ($R_{i,A,t}$) after T days

TABLE 1 Distributions used for ASF transmission parameters

Parameter	Probability distribution	Distribution parameters	Source
L = Length of the incubation period (days)	Gamma Distribution	shape = 13.299, scale = 0.3384482	Guinat, Gogin, et al. (2016), Guinat, Gubbins, et al. (2016) de Carvalho Ferreira et al. (2012, 2013)
T = Length of the infectious period (days)	Uniform Distribution	min = 3, max = 5.5	Guinat, Gogin, et al. (2016), Guinat, Gubbins, et al. (2016)
β_w = Within-pen transmission rate/ day	Truncated normal distribution	Mean 0.6, Sd = 0.4 Min = 0, Max = 14.3	Guinat, Gogin, et al. (2016), Guinat, Gubbins, et al. (2016) de Carvalho Ferreira et al. (2013)
β_p = Between-pen transmission rate/ day	Truncated normal distribution	Mean = 0.3, Sd = 0.2 Min = 0, Max = 14.3	Guinat, Gogin, et al. (2016), Guinat, Gubbins, et al. (2016) de Carvalho Ferreira et al. (2013)
β_r = Between-room transmission rate/ day	Truncated normal distribution	Mean = 0.01, Sd = 0.05 Min = 0, Max = 0.1	Hypothesis

introduction. This threshold is similar to the one used in previous studies (Halasa et al., 2016a, 2016b; Nielsen et al., 2017).

2.3 | Disease spread and early detection performance

For simplicity, disease spread parameters and early detection performances were only computed for a reference scenario: baseline daily pen-mortality rate of 0.038% and 40 pigs per pen. The values of baseline mortality rate and number of pigs per pen were chosen based on the characteristics of a commercial pig production system in Canada. Baseline mortality included all pigs dying of unknown causes excluding non-infectious events such as accident or euthanasia of lame pigs. The cumulative mortality rate was calculated using the number of pigs alive in each epidemiological unit at the beginning of the outbreak as the denominator.

Three surveillance strategies were compared based on mortality thresholds defined either at the pen, room, or barn level. Mortality thresholds were defined as a given number of pigs dying within 7 days using a rolling observation window. Different mortality thresholds were tested. The lowest mortality thresholds were set above the average number of dead pigs expected per week and per epidemiological unit in the absence of ASF (i.e. >1 dead pig per pen, >2 dead pigs per room and >8 dead pigs in the barn). The highest mortality thresholds tested were those that resulted in a median of zero false alarms per year.

We used the time to detection and the expected number of false alarms per year as outcome measurements to compare the three strategies and to evaluate the effect of different parameter values. Activity Monitoring Operating Characteristic (AMOC) curves (Fawcett & Provost, 1999) were used to measure the performance of each early detection strategy evaluating the trade-off between timeliness of detection and the false alarms rate, and between timeliness of detection and number of dead pigs to be tested to ensure the detection of at least one ASF-infected dead pig. We estimated the number of dead pigs to be tested assuming that we will sample the pig triggering the alarm and all the pigs dying within the next 3 days in the epidemiological unit where the alarm was raised (i.e. pen, room or barn). We assumed a test specificity and sensitivity equal to 100%. The 3-day period was chosen based on the model outcome in order to capture at least one ASF-infected dead pig after an alarm has been raised.

The number of false alarms associated with each mortality threshold was estimated by simulating a random distribution of the baseline mortality across pens over a one-year period over 1,000 iterations. As with the ASF spread model, we assumed no clustering of the baseline mortality.

2.4 | Sensitivity analysis

The influence of pen size and baseline mortality rate on the model outcomes was assessed by simulating six different scenarios and

comparing them to the reference scenario named scenario 1 (i.e. baseline daily mortality rate of 0.038% and 40 pigs per pen). In all scenarios, the baseline mortality was assumed to be randomly distributed across the barn. Scenarios 2–4 used a baseline barn-mortality rate equal to the mortality rate of the reference scenario (i.e. 0.038% per day) but differed in terms of pen size: scenarios 2–4 modelled 20, 60 and 80 pigs per pen, respectively. In scenarios 5, 6 and 7, the number of pigs per pen was the same as in the reference scenario (i.e. 40 pigs) but the baseline daily mortality rate was halved (0.018%), doubled (0.076%) or multiplied by four (0.154%), respectively.

3 | RESULTS

3.1 | Within-barn ASF spread

Considering the reference scenario (i.e. scenario 1), the median within-barn prevalence of ASF reached 5% 21 days after introduction of a single infectious pig. At day 21, the median room-level prevalence ranged from 0% to 29% depending on the room considered, while the median pen-level prevalence ranged from 3% to 75% in room A (see Figure 3 and Figure A2). Fourteen days post-disease introduction (dpi), the median within-room prevalence was above 8% in the first infected room while remaining below 2% in the rest of the rooms. Similarly, the within-pen prevalence was above 30% in the first infected pen at 14 dpi but below 5% in half of the pens located in the same room.

In the first infected pen, the median cumulative mortality rate reached 2.5% (i.e. 1 dead pig) at 5 dpi (see Figure 4). In the first infected room, the median mortality rate reached 2.5% at 13 dpi. At the barn level, the cumulative median mortality rate remained below 2.5% until 21 dpi. Differences were also found within the first infected room. For example, the median number of dead pigs in the first infected pen was 7 at 15 dpi, while in the direct neighbouring pen fewer than 3 dead pigs were observed.

3.2 | Early detection performance

Using a mortality threshold of 4 dead pigs per room (400-head room) within a 7-day rolling observation window, the time to detection was 8 days post-disease introduction for a median number of 9 false alarms per year (Figure 5). Using a pen-mortality threshold of 2 dead pigs per pen (40-head pen) within a 7-day rolling observation window provided the same time to detection and number of pigs tested per year, while raising 24 false alarms per year. Using a barn-mortality threshold achieved the same time to detection and number of false alarms per year but led to a higher number of dead pigs to be tested per year (Figure 5). For example, using a mortality threshold of 11 dead pigs in the barn (3,200-head barn) within a 7-day rolling observation window, 72 dead pigs should be tested per year per barn. On the other hand, only 45 or 48 dead pigs are tested per year while using mortality thresholds of 4 dead pigs in a room or 2 dead pigs in a pen, respectively.
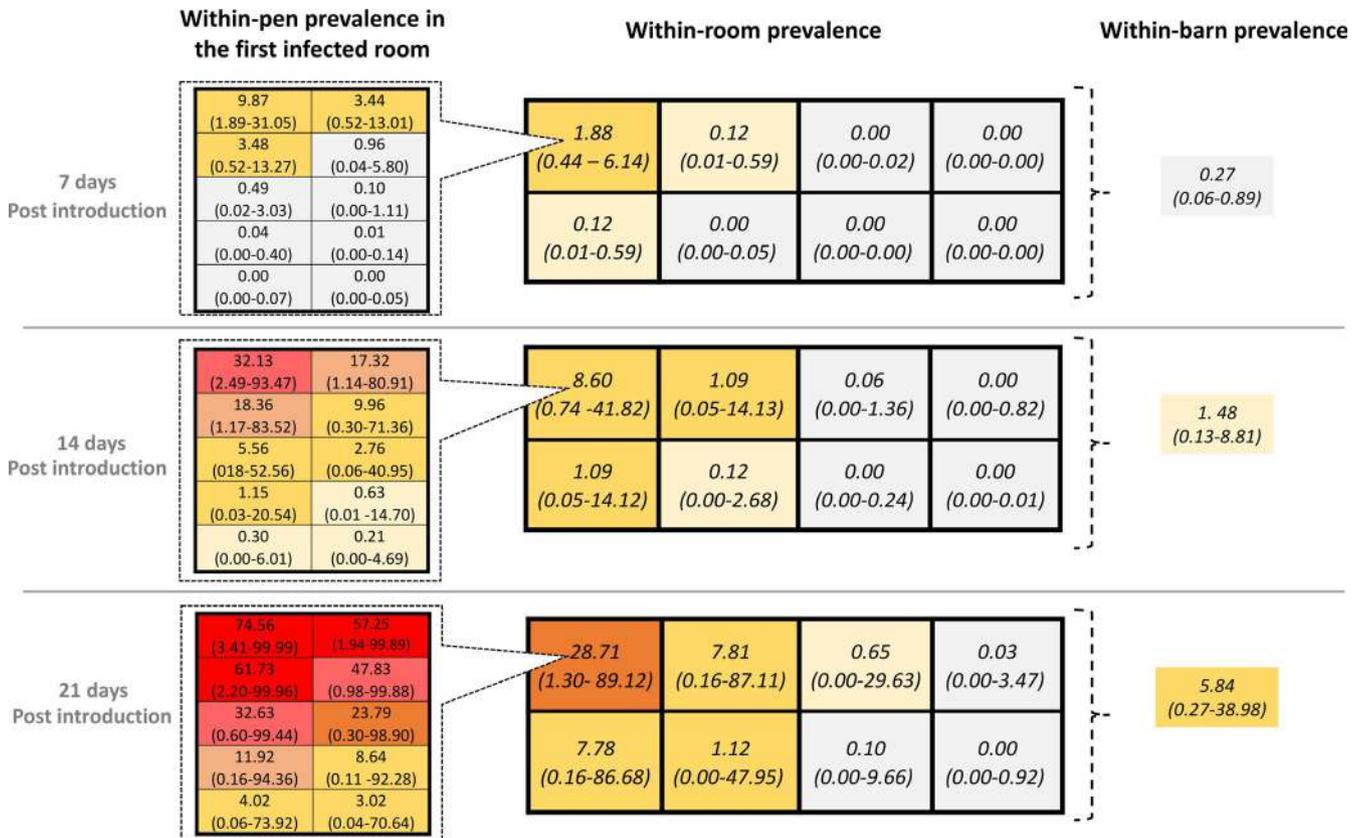
FIGURE 3 Median prevalence (%) in different epidemiological units (pen, room, barn) and associated 5th and 95th percentiles of the 5,000 simulations at days 7, 15 and 21 post-introduction of a single infectious pig for scenario 1. A single infectious pig was introduced at day 0 in pen 1.A (see Figure 1). Grey = prevalence <0.1%, Light yellow = prevalence between 0.1% and 1%, Dark yellow = prevalence between 1% and 10%, Light orange = prevalence between 10% and 20%, Dark orange = prevalence between 20% and 30%, Light Red = prevalence between 30% and 50%, Dark Red = prevalence above 50%

FIGURE 4 Cumulative mortality rate in the first infected pen, in the first infected room and in the barn during the first 21 days post-introduction of a single infectious pig at time 0 (scenario 1)
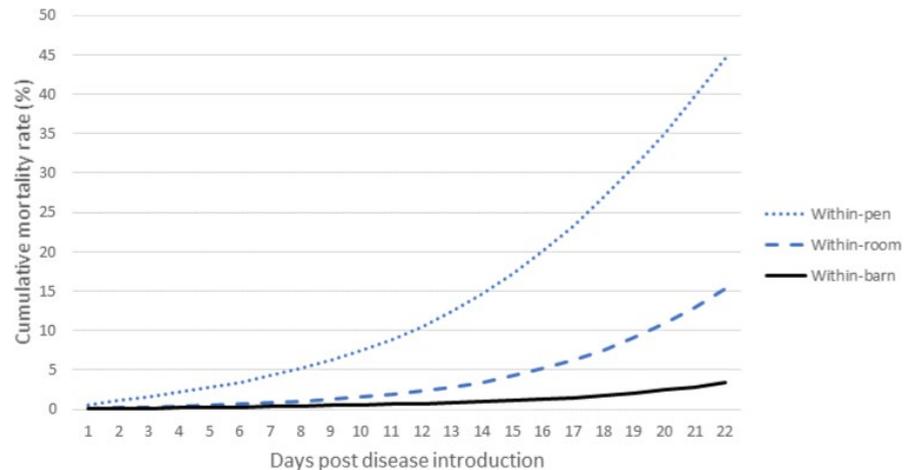
Defining mortality thresholds at the room level provided the optimal balance between rapid detection and lowest rate of false alarms although the time to detection was similar.

Using lower mortality thresholds at any level decreased the time to ASF detection but was associated with an increased number of false alarms. For example, using a mortality threshold of 3, instead of 4, dead pigs per room within a 7-day rolling observation window shortened the time to detection by one day, while leading to a 450%

increase of false alarms per year (i.e. from 8 to 44 false alarms per year).

3.3 | Sensitivity analysis

The results of the sensitivity analysis to assess the impact of assumptions relating to baseline (non-ASF) mortality rate and the
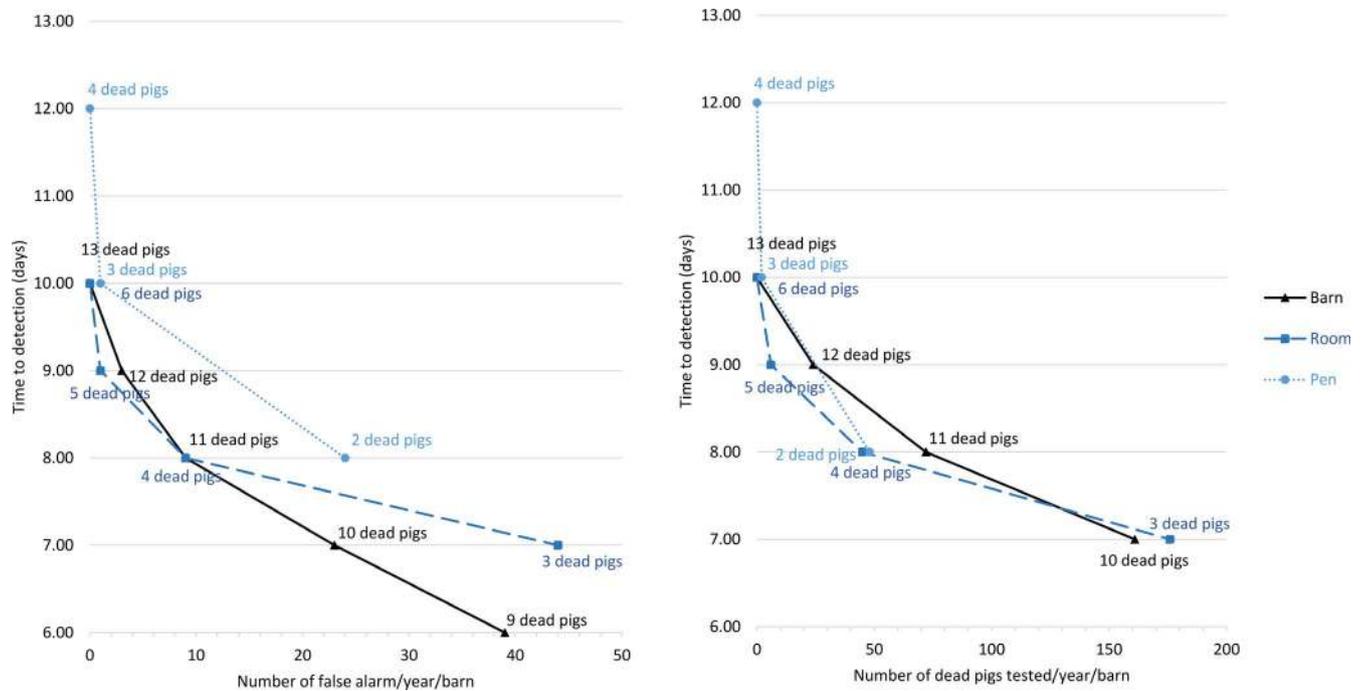
FIGURE 5 Activity Monitoring Operating Characteristics (AMOC) curves based on the number of false alarms per year per barn (left graph) or number of tests performed per year per barn (right graph). The numbers indicated on the curves represent the different mortality thresholds considered in the study. For example, '3 dead pigs' means that the alarm threshold was defined as follow '3 dead pigs per epidemiological unit within a 7-day rolling observation window'

TABLE 2 Scenario tested

Scenario			Median cumulative number of dead pigs in the first infected pen (5th and 95th percentiles)		
ID	Baseline daily mortality rate (%)	Pen size (number of pigs)	7 dpi	14 dpi	21 dpi
1 Reference scenario	0.038	40	1.7 (1.0–3.1)	5.8 (1.8–16.6)	15.9 (2.8–32.2)
2	0.038	20	1.6 (1.0–2.9)	5.1 (1.6–11.3)	11.3 (2.5–17.5)
3	0.038	60	1.7 (1.1–3.4)	6.30 (1.9–21.6)	18.8 (2.9–46.3)
4	0.038	80	1.8 (1.1–3.5)	6.5 (2.0–27.7)	20.6 (3.0–59.1)
5	0.038/2 = 0.019	40	1.6 (1.0–3.2)	6.06 (1.7–17.7)	16.6 (2.6–32.6)
6	0.038*2 = 0.076	40	1.7 (1.1–3.3)	6.0 (2.0–17.6)	16.3 (3.0–32.7)
7	0.038*4 = 0.154	40	2.0 (1.3–3.5)	6.67 (2.4–18.0)	17.2 (3.7–32.7)

dpi = days post-introduction of a single infectious pig.

number of pigs per pen are shown in Table 2. Changing the baseline mortality rate (i.e. scenarios 1, 5, 6 and 7) had a limited impact on the model outcome: the median number of dead pigs and 5th and 95th percentiles remained very similar across the study period.

Increasing the number of pigs per pen (i.e. scenarios 1 to 4) had a limited impact on the model outcome at 7 and 14 dpi. The expected number of dead pigs ranged from 1.6 to 1.8 at 7 dpi and from 5.1 to 6.5 at 14 dpi. However, substantial differences were observed at 21 dpi: the expected number of dead pigs increased from 11.3 to 20.7 when pen size increased from 20 to 80 animals.

Changing the baseline mortality rate and pen size influenced the expected number of false alarms per year. The lower the mortality threshold, the higher the impact of these parameters on the expected number of false alarms (see Figure 6).

4 | DISCUSSION

In our study, we have simulated a risk-based approach to early detection of ASF in a 3,200-head indoor commercial finisher pig barn. Our proposed approach focused on the epidemiological units, that is pens
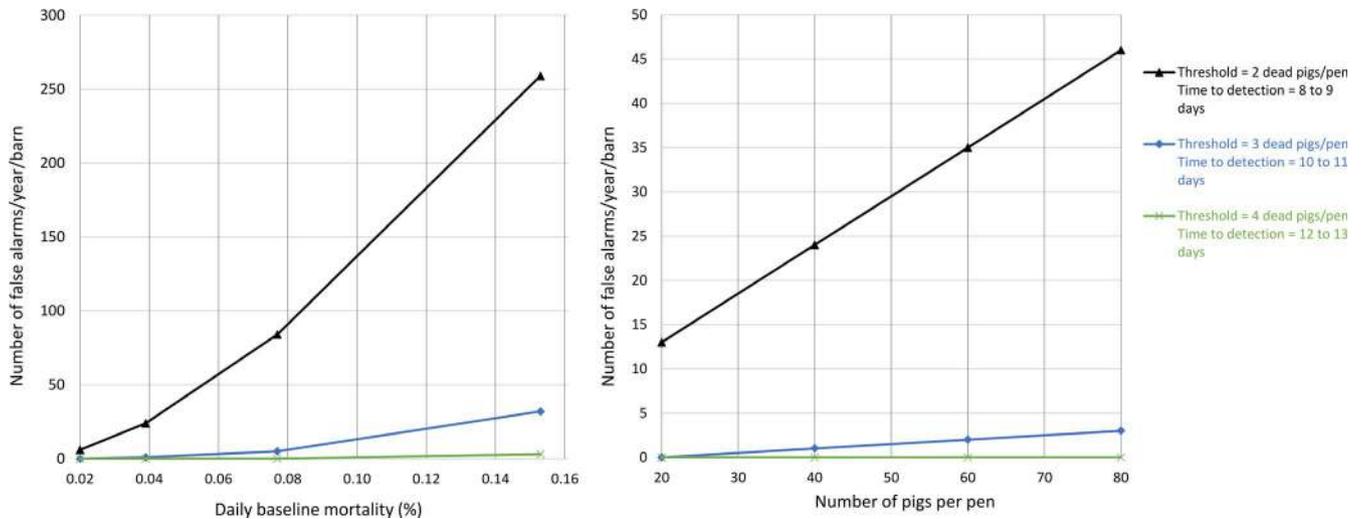
FIGURE 6 Expected number of false alarms for each mortality threshold and time to detection depending on daily mortality rate (left graph) and number of pigs per pen (right graph). For the graph on the left, the number of pigs per pen was set at 40. For the graph on the right, the baseline daily mortality rate was set at 0.038%

or rooms, with the higher initial risk of disease transmission and thus the higher likelihood of pig mortality. With this approach, a threshold of 4 dead pigs per room (400-head room) within a 7-day rolling observation window provided a time to detection of 8 days post-introduction. Similar detection performances could be achieved using a barn-mortality threshold of 11 dead pigs or a pen-mortality threshold of 2 dead pigs. However, when using a barn-mortality threshold, the number of pigs to be tested per year was much higher. The risk-based approach is an effective strategy to shorten the time to detection and optimize the cost-effectiveness of surveillance (Cameron, Njeumi, Chibeu, & Martin, 2014; Stärk et al., 2006). Our results show that it can be effectively used to improve early detection and cost-effectiveness of surveillance of ASF in large pig commercial farms when using mortality events occurring in subpopulations (rooms or pens) at higher risk of being infected. These results offer strong support for using mortality data for early detection of ASF not only in small pig herds but also in large commercial barns.

Our results show that the barn layout influences the within-barn ASF spread, due to the low contagiousness of ASF and the probability of disease transmission via different routes: the probability of transmission by direct contact between pigs is higher than the probability of transmission via indirect contact (e.g. between pens ; ; Guinat, Gogin, et al., 2016; Guinat, Gubbins, et al., 2016; Olesen et al., 2017), or via the environment (Olesen et al., 2018). Barn layouts which allow for more contact, or decreased levels of internal biosecurity between pens and/or rooms, are expected to increase disease spread within the barn. For example, for simplicity in our study, we only consider ASF transmission between neighbouring rooms, but in practice between-room transmission might mainly occur because of workers' footwear and one infected room might have an equal probability of infecting any other rooms of the barn. However, our assumptions in terms of the probability of transmission between epidemiological units do not affect the results obtained

in the first infected pen. They only have an impact on the number of pigs expected to be infected and dead at different time steps in the other epidemiological units (room or barn). Similarly, our results show that baseline mortality rate and pen size had a limited impact on the median number of dead pigs in the first infected pen, and thus on the selection of pen-based mortality thresholds used for disease early detection. These results can be explained by the relatively low baseline mortality rates used in the study. Even in the scenarios with the two highest mortality rates (i.e. 0.076% and 0.1544% daily), only one pig out of a 40-pig pen is expected to die of non-ASF causes every 33 days and 16 days, respectively. Pen-mortality thresholds defined in this study might be thus relevant to a wide range of pig production sites. However, in barns with very large pen sizes and/or significantly higher baseline mortality rates, adjusted mortality thresholds may be required. Pen-based mortality thresholds should be thus reassessed for different types of housing systems and different performances in terms of baseline mortality.

Under our assumptions, the use of a room-based mortality threshold was the most cost-efficient strategy; however, changing the baseline mortality significantly changed the expected number of dead pigs, from non-ASF causes, in the first infected room, having a large influence on the selection of room-based mortality thresholds (see Figure A3). As a result, the room-based mortality thresholds are expected to vary a lot depending on baseline mortality rates and room size. Such an early detection system might be complicated to set up and maintain in production systems where barn performances and layouts are expected to be diverse. A within-barn surveillance system based on pen-level mortality would allow the definition of standard mortality thresholds applicable to different types of barns and may thus be the optimal strategy to support ASF early detection in large commercial pig farms. However, these results are based on expected spread of ASF in a typical finisher barn where pigs are housed in groups. For pigs not

housed in groups, other surveillance designs for early detection of ASF may be more appropriate.

Using a lower mortality threshold is expected to decrease the time to ASF detection but at the cost of a significantly increased number of false alarms per year. The cost–benefit of decreasing the time to detection should be thus carefully assessed as a higher number of false alarms might become quickly challenging to manage in large production systems made of multiple barns. In addition, results obtained and more specifically the expected number of false alarms per year were based on the assumption that baseline mortality was randomly distributed within the barn. It is difficult to assess the validity of this assumption as, at the time of writing, no information was available on the level of clustering of baseline mortality in post-weaning pig farms. Occurrence of within-barn clusters of mortality might either increase or decrease the expected number of false alarms per year, making the assessment of the impact of this assumption on our results even more difficult. This lack of information is critical to compare our results obtained at the barn-level with existing literature. For example, our results showed that, when using a barn-mortality threshold of 11 pigs (0.4% mortality), it was possible to detect ASF in 8 days in a large commercial barn of 3,200 pigs. This time to detection is substantially lower than the one reported in the literature. For example, Halasa et al. (2016b) estimated a time to detection of 21 days when using as threshold a barn mortality of 2.55%. However, in this study the time to detection varied greatly (extreme values of 12 and 50 days) because it has been estimated for both small and large herds together impairing more detailed comparison with the results of our study. In our study, we were able to detect such a small increase in mortality because of our low baseline mortality. However, based on the results observed in field conditions (Chenais et al., 2019; Guinat et al., 2018; Lamberga et al., 2018; Nielsen et al., 2017; Nurmoja et al., 2018), detecting such small increases in the number of dead pigs at the barn level might be challenging for most of large commercial barns. Future work should focus on incorporating a more detailed understanding of the distribution of post-weaning mortality occurring in large commercial pig farms in order to obtain a more accurate estimate of the number of false alarms raised by our proposed early detection system in the absence of ASF outbreak. This information would also help better assess the value of mortality data for disease surveillance in large commercial pig farms such as the resources needed to implement and maintain such surveillance system.

Other surveillance approaches based on systematic testing have been proposed to improve ASF early detection. For example, in the United States, tissues submitted to diagnostic laboratories originating from clinically ill pigs where ASF should be considered as part of the differential diagnosis list are systematically tested for ASF (USDA, 2019). The time to detection of ASF and the costs associated with this approach are currently unknown. The European Commission recommends testing the first 2 dead pigs occurring in each production unit every week (EC, 2018). Although the early detection performance of this approach is currently unknown, it

has only been recommended for high-risk farms (e.g. swill feeding, infected area) (Lamberga et al., 2018). Using our approach and a room mortality threshold of 4 dead pigs within 7 days, we can estimate performing 45 tests per year per barn (see Figure 5), which is below the number of tests performed following the recommendations of the European Commission (104 tests per year). However, our approach implies that sampling of dead pigs cannot be planned in advance, which might be more complicated to implement for large commercial farms compared to weekly testing. Future studies should focus on cost–benefit analysis of different ASF early detection strategies.

Our results were based on several assumptions. First, we only considered the introduction always in the same pen of a single infectious pig. Such event might occur if a single pig of the barn had contact with infected animals (e.g. wild boar, boar semen), contaminated feed (e.g. contaminated pork meat or pork meat products), contaminated fomites (e.g. bedding materials, vehicle, farm material) or persons carrying the virus on their skin, hair, clothing, footwear or personal items (; ; Guinat, Gogin, et al., 2016; Guinat, Gubbins, et al., 2016). The likelihood of occurrence of such event is probably low as multiple pigs might be infected at the same time by, for example infected materials or feed. Our model assumption can be however considered as the worst-case scenario for early detection as the introduction of multiple infectious pigs would lead to an increased number of dead pigs in the first few weeks of the outbreak. Disease introduction should be thus detected earlier than with the worst-case scenario while using the same alarm thresholds. In addition, the effect of the location of the first infectious pig is expected to have very limited impact on our results as shown by Nielsen et al. (2017). Second, our model parameters were defined for a highly virulent strain (Davies et al., 2017; Gallardo et al., 2017; ; ; Guinat, Gogin, et al., 2016; Guinat, Gubbins, et al., 2016; Guinat et al., 2014). An outbreak due to a strain with lower virulence is expected to lead to a delayed detection. Early detection of low virulent strains would require using lower alarm thresholds, which would lead to significantly increased number of tests associated with higher surveillance costs. For future studies, it would be interesting to compare the cost–benefit of our approach under different disease transmission assumptions.

Early detection of ASF in large commercial barn is challenging because mortality due to ASF might easily be masked by baseline mortality at the beginning of an outbreak. The approach presented in this paper allows to improve the time to detection and the cost-effectiveness of surveillance by focusing on the epidemiological units with the highest risk of disease incidence (i.e. the pen or room). Pen-based surveillance offered the most promising perspective for developing standardized early detection surveillance plans as the same mortality thresholds could be used for barns with different baseline mortality and pen size.

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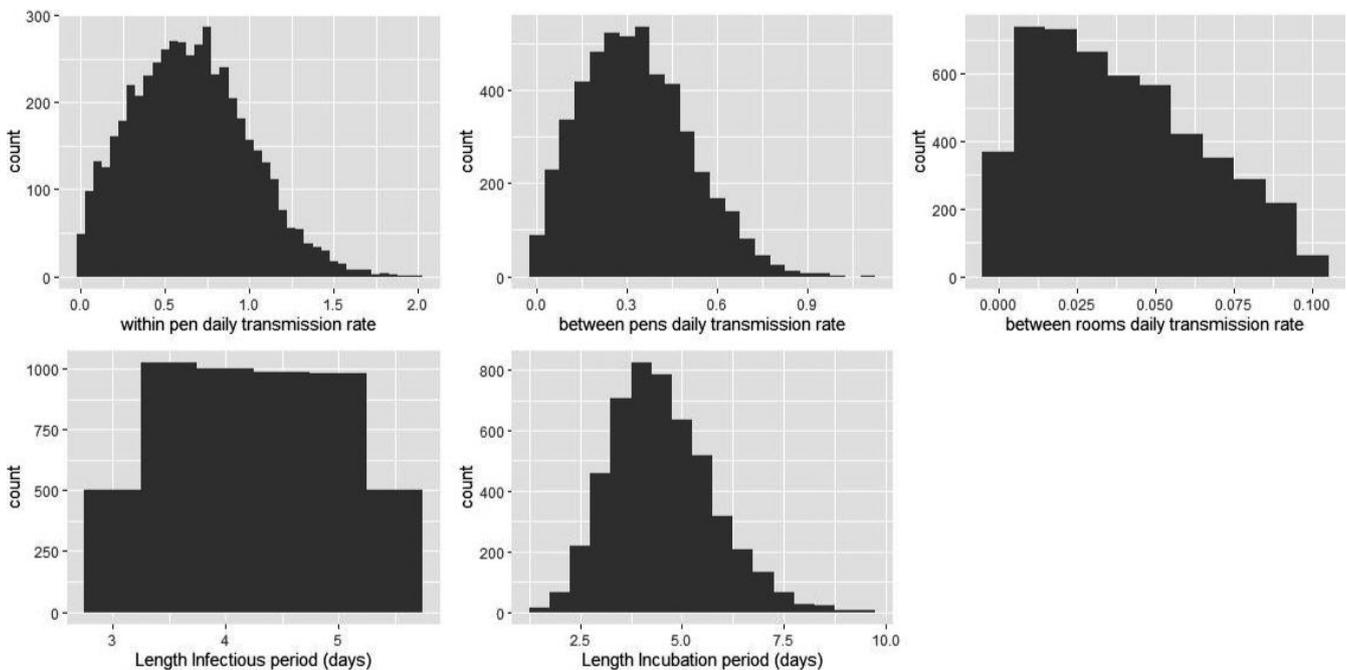
APPENDIX A

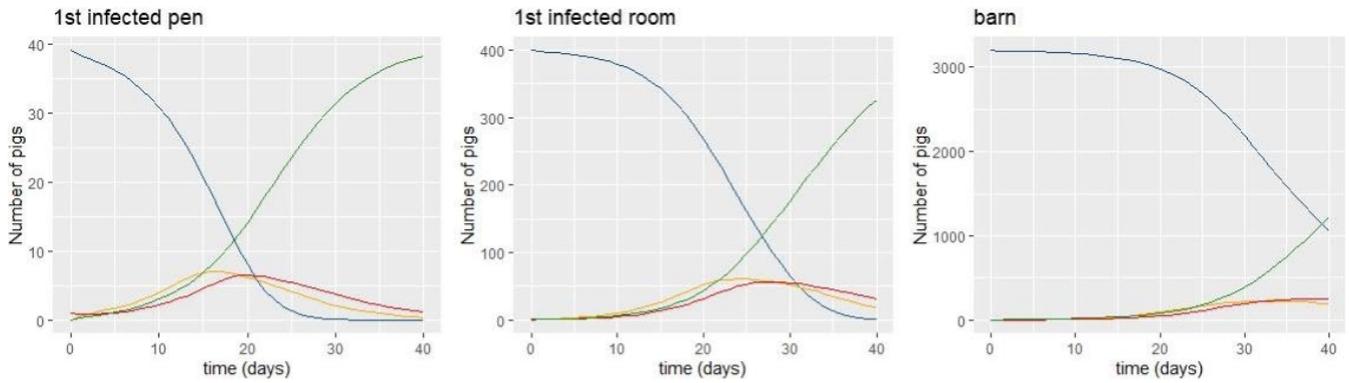**FIGURE A1** Parameter probability distributions

FIGURE A2 Overview of the ASF spread at different spatial scale (i.e., pen, room and barn) after introduction of a single infectious pig at time 0. The lines represent the median number of susceptible (blue), exposed (orange), infected (red) and removed/dead (green) pigs.

FIGURE A3 Expected number of false alarms depending on daily mortality rate, room-mortality threshold and associated time to detection