

Enhanced passive surveillance to early detect African and classical swine fevers

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Summary

African swine fever (ASF) and classical swine fever (CSF) are transboundary animal diseases (TADs) of pigs. Much effort and resources are regularly put into preventing these diseases' introduction in free areas. Passive surveillance activities bring the highest chances for the early detection of TAD incursions because they are routinely

and widely conducted at the farm, and because these activities focus on the time between introduction and the time the first sample is sent for diagnostic testing. Here, we proposed the implementation of an enhanced passive surveillance (EPS) protocol based on collecting data through participatory surveillance actions using an objective and adaptable scoring system to aid the early detection of ASF or CSF at the farm level. The protocol was applied in two commercial pig farms for ten weeks in the Dominican Republic, which is a CSF- and ASF-infected country. This study was a proof of concept, based on the EPS protocol to aid detection of substantial variations in the risk score triggering testing. One of the followed farms had score variation, which triggered testing of the animals, although the test results were negative. The study help assess some of the weaknesses and learn lessons applicable to the problem. Results demonstrate the potential for overcoming some issues preventing the broad application of EPS protocols and suggest that standardised approaches may contribute to the early detection of CSF and ASF introductions.

Keywords

African swine fever – Classical swine fever – Early detection – Enhanced passive surveillance – Health indicators – Necropsy – Participatory surveillance – Proxy-risk – Syndromic surveillance.

Introduction

Transboundary animal diseases (TADs), such as African swine fever (ASF) and classical swine fever (CSF), are highly contagious and transmissible diseases with the potential for rapid spread across national borders, typically causing far-reaching losses to affected countries and regions [1]. For that reason, notification of ASF or CSF outbreaks to the World Organisation for Animal Health (WOAH, founded as OIE) is mandatory. Only swine (Suidae family) are affected by ASF and CSF and, collectively, ASF and CSF are sometimes referred to as foreign haemorrhagic fevers (FHF) of swine by disease-free countries. Although both diseases have similar names, and cause significant disruption to the pig industry, they are caused by unrelated pathogens.

CSF is caused by a small, enveloped RNA virus of the genus *Pestivirus*, which is a member of the Flaviviridae family, referred to as CSF virus (CSFV). Clinical signs of CSFV infection are related to the virulence of the strain, and in the most severe form, the mortality rate can be as high as 100%, mostly in naïve populations [2, 3]. Signs are most severe in young pigs, with mortality rates averaging 80%, whereas in adult pigs CSFV infection may be sub-clinical or with mild signs, which delay or prevent the diagnosis of the disease [4, 5].

ASF is caused by a double-stranded DNA, enveloped arbovirus, which is the sole member of the Asfarviridae family, and referred to as the ASF virus (ASFV). Although ASF is associated with high lethality in domestic pigs, it may not be as infectious as some other relevant TADs such as foot and mouth disease. ASF usually spreads slowly within the herd, and some animals may not be clinically affected especially wild pigs such as warthogs, bush pigs, and giant forest hogs [6, 7, 8].

Since the re-introduction of ASFV into Europe, through Georgia in 2007, no country has been able to eliminate the disease after it reached its domestic pig population. The sustained ASF spread through Asia and Europe highlights the lack of success of control programmes [9]. In 2021, ASFV was also detected in Central America (Dominican Republic and Haiti), and some have argued that ASF spread should be considered as a pandemic [10]. Similarly, CSF has recently re-emerged in Japan and other regions, many located near free areas with dense swine production such as in Brazil. Consequently, the swine industry is globally concerned about the increasing risk associated with FHF incursions and the associated impacts on animal health and economics.

Much work has been done to reduce the time to confirm an FHF incursion into a free area after a first suspect is identified. Outbreaks can be confirmed within hours or at most a few days of sample collection and submission of these samples to a laboratory with proper testing capabilities, depending on the country and region [11, 12]. However, the duration of time between virus introduction and identifying the first suspect of the disease in a free region triggering sample submission is quite uncertain and, in many cases, may be

extended for weeks or months, resulting in secondary disease spread. Figure 1 shows some examples of the estimated number of undetected outbreaks that occurred before the first detection (index case) in the high-risk period (HRP), which is the period of time between the initial infection and official diagnosis and notification of the disease for selected ASF and CSF epidemics [13, 14]. Delays in identification of FHF incursions is, in part, explained by the absence of pathognomonic clinical signs, resulting in relatively broad case-definitions for the diseases, wide range of presentations, and a relatively long period of undetected spread [3, 5, 15, 16, 17].

Consequently, there is a need for implementing actions for reducing the HRP as much as possible, which may be most effectively achieved by enhancing the industry capacity to early detect and report FHF incursions.

Early detection of a TAD incursion may be defined in terms of the temporal sensitivity of a surveillance system and its ability to accurately identify an agent at any given time in a population [23]. An effective early detection surveillance system is expected to detect a TAD incursion as soon as possible, preventing or mitigating its spread into other farms and regions [24]. Awareness and engagement among relevant stakeholders, including the industry, practitioners, and the regulatory sector, are important components of an effective early detection system. For example, official estimates suggesting that Vietnam discovered the first ASF case in 2019 within five–ten days of its first introduction may be explained by the alert issued in the country soon after the detection of the disease in the People’s Republic of China in 2018 [25, C. Vo, personal communication, 2022]. In many western countries, where primary veterinary assistance relies on the private sector, producer and veterinary practitioner awareness is a key component of early detection and industry-led passive surveillance efforts tend to be more effective in the spontaneous detection of outbreaks than active surveillance. For example, when ASF was introduced into Latvia in 2014, 32 outbreaks were recorded, 31 of which were identified by passive surveillance activities following the

initiation of awareness campaigns by the Official Veterinary Services (OVS) [26].

Passive surveillance refers to systems where information on disease events is brought to the attention of OVS without them actively seeking it [24]. Typically, passive surveillance methods rely on the ability and willingness of farmers, veterinarians, and animal health workers to identify sick animals, and subsequently communicate to the OVS what may be considered a reportable event. This type of surveillance is arguably the most important form of surveillance in any country because the coverage may achieve 100% of the herd under farmers supervisions [27, 28]. However, it is difficult to expect that farmers and health workers would spontaneously engage in passive surveillance activities for foreign animal diseases and, for that reason, there is a need to increase their engagement through the implementation of enhanced passive surveillance (EPS) systems.

EPS is an observer-initiated provision of animal health related data with active investigator involvement, e.g. by actively encouraging producers to report certain types of disease or by active follow-up of suspect disease reports [29]. The EPS concept includes technology development, which enhance the value of passively collected data by integration, analysis, and dissemination to capture health and syndromic information on animal population which requires the participation of producers, veterinarians, and health workers [30].

One may argue that, consequently, EPS actions through public-private partnerships (PPPs) is an effective strategy to support the goal of early detection of TAD incursions. However, implementing passive surveillance systems on a large scale is challenging due to a number of factors that, including, for example, the lack of standardised methods, definitions, and procedures.

The objective of the study here was to explore a proof of concept that may help countries address some of the weaknesses associated with the implementation of passive surveillance systems. Specifically, we demonstrated the development of an EPS protocol for FHF of swine to aid the early detection of ASF and CSF incursions into pig farms. The

work here is intended to motivate the use and application of an approach that is very much required, but that, unfortunately, is only marginally implemented by many countries. The protocol presented here represents the first known standardised attempt to combine systematic and routine collection of data with anomaly detection systems to inform a public–private action with the ultimate objective of shortening the high-risk period of undetected spread after disease introduction and mitigating the impact of ASF and CSF outbreaks in free farms or regions. The concepts presented here may be easily adapted for implementation by farms, countries, and regions to enhance actions for early detection of FHF in their free populations.

Materials and methods

General approach

An EPS protocol was developed to demonstrate how the approach may be implemented to characterise the risk for an FHF incursion into a farm. The system uses a scoring system that serves as a proxy for the risk to trigger sampling activities to confirm or rule out suspects. The EPS protocol was piloted in the Dominican Republic, an ASF- and CSF-infected country, where the protocol was used in two ASF- and CSF-free farms for ten consecutive weeks to evaluate the temporal variation in scores in a population potentially exposed to FHF. An anomaly detection algorithm was implemented to inform the decision to collect samples and support early detection of cases.

Enhanced passive surveillance protocol and scoring system

The EPS protocol was built considering three components, namely:

- a)* the biosecurity background of the farm;
- b)* the routine observation of clinical or syndromic data;
- c)* the result of necropsy findings (Table I).

Each of the three components included the assessment of presence or absence of certain factors, weighted by scores to model their relative importance. The final score was computed following an additive model, i.e., as the sum of the presence (1) or absence (0) of the factors and conditions, weighted by the relative importance of the factor. Both the selection of factors for each of the three components and the weights were estimated in consultation with experts that represented three ASF reference laboratories located in Madrid, Spain, in Plum Island Animal Disease Center, in the United States of America, and in Russia. Each of the experts identified the factors and weighed the factors independently. Factors and weights were compiled and shared again with the experts to reach final consensus on the values. The list of components and variables, along with the final weights and the references that support the inclusion of the variables is provided in Table I. Noteworthy, the weights used here are the reflection of consensus among the consulted experts and could be easily modified or adapted if deemed necessary.

A closed-question survey [46] was developed in an Microsoft Excel spreadsheet, and transferred to a Qualtrics software [47], which allowed a collection of data using a platform that could be used also offline. This allowed data collection in a paper-free format using cell phone devices or laptops decreasing possible errors in transcriptions and giving options of accessibility for producers collect data during inspection of their pigs.

Study populations

A survey based on a participatory surveillance approach, with the use of a scoring system, was developed [29], considering pig producers as the target audience of the protocol. In the context used here, we used the term participatory surveillance to refer to the use of ways for data collection, like scoring systems, to develop risk-based surveillance, with the use of semi-structured interviews with farmers, with answers of the weekly survey with questions regarding syndromic signs and necropsy findings. The approach is intended to take advantage of knowledge provided by farmers, practitioners, and farm workers about issues that are important to them, such as diseases affecting their

animals, to take advantage of that knowledge and the activities the routinely conduct in the farm by incorporating them into a formal surveillance system [29, 48].

The study was conducted in two ASF and CSF-free commercial pig farms in the Dominican Republic over a ten-week period, between 13 December 2021 and 20 February 2022, and anomaly detection algorithm was used to assess the temporal variation of the score and informing the decision to collect samples. Those two farms, referred to here as Farms A and B for confidentiality reasons, are located in the province of San Pedro de Macorís, a region that first reported ASF outbreaks in August 2021 [21]. Farm A is a finishing site with an average of 6,500 pigs, whereas Farm B is an independent farm, working in a farrow to finish system, with total average of 280 pigs. The biosecurity background of those two farms was assessed only at the first week of the study because practices remained stable for the entire period, in case of any alteration, a reassessment would be performed with adjustment of the score for the biosecurity component. For the second and third components, syndromic surveillance and necropsy findings, respectively, data were collected weekly using a generic electronic application. The questions in the survey guided the animal caretakers to see the presence or absence of the factor, and we used a lay language. A composite score was computed for each farm on a weekly basis.

Anomaly detection for targeted surveillance activities

An anomaly detection algorithm was used to detect periods of time in which variations in the score would result in the recommendation for active sampling of FHF. Specifically, a purely temporal scan statistic model was performed to identify clusters of weeks with highest chances of being associated with an FHF incursion, as indicated by the value of the scores. Briefly, the scan statistics in a temporal analysis may be interpreted as a scanning window that moves across time. The window represented the number of weeks considered as candidate high risk clusters [49]. A discrete Poisson purely temporal scan statistic model was performed for Farms A and B separately, under the null hypothesis

that the rate of observed-to-expected score was homogeneous through the study period, whereas the alternative hypothesis was that there were certain weeks in which the rate was significantly higher or lower than the expected under the null hypothesis. The ratio of observed-to-scores within each candidate cluster was computed and their significance was tested using a Monte Carlo simulation approach with 999 iterations [49, 50, 51]. The SaTScan, version 10.0, software was used to identify these temporal clusters of weekly scores [52]. The graphs were generated in Microsoft Excel.

Results

The mean scores over the ten-week period for Farms A and B in the Dominican Republic were 95.6 (standard deviation [SD] = 8.22) and 143.6 (SD = 1.78), respectively. The biosecurity background risk score remained constant through the study period and was 79 and 130 for Farms A and B, respectively. The weekly fluctuation during the study period, associated with variations in the values estimated for the second (clinical surveillance) and third (necropsy findings) components of the EPS is depicted in Figure 2.

Although the background risk (associated with biosecurity practices) was higher for Farm B, the highest weekly fluctuation was observed in Farm A due to the presence of clinical signs and necropsy findings compatible with ASF or CSF.

The results of the anomaly detection algorithm showed that there was a 6% increase over the expected scores between weeks five and nine for Farm A and a 1% decrease in Farm B (Figure 3). Although, those variations were not significant ($p > 0.05$), acknowledging that absence of significance may be due to insufficient data collected, ASF testing was recommended for Farm A at week six and whole blood was collected from randomly selected pigs. Polymerase chain reaction results were negative.

Discussion

Results of this proof of concept study presented here suggest that EPS protocols may help standardise participatory surveillance methods, in a format of scoring system based on risk factors, aiding swine producers to detect early evidence of FHF incursions thus reducing the time between disease introduction into a free country and first suspect and reporting. Because passive surveillance approaches are rarely implemented by the swine industry of many countries, the objective of the paper here was to promote its use by demonstrating a system that overcomes some of the issues preventing its application in the field.

Passive surveillance actions implemented at the farm level play a critical role in early detection of TAD incursions, and systems that can help identify early signs of infection are critically needed. Passive surveillance is highly dependent on the awareness and engagement of each individual producer. Consistency of passive surveillance systems increases when the industry follows the principles of a participatory process including systematic data analysis to trigger diagnostic testing. Results presented here show that the formal incorporation of an explicit scoring system to replace casual passive observations combined with data collection and analysis to identify a trigger for testing may help standardise actions implemented for early detecting FHF incursions.

Animal health organisations encourage the development of early disease detection systems using non-diagnostic information, often derived from electronic data [49]. One advantage of the EPS protocol here is that it quantifies what are typically qualitative observations related to biosecurity, morbidity and necropsy findings. This protocol not only standardises the data that were collected but it also allows a level of analysis not routinely performed on such observations. In disease surveillance, to guarantee an early detection of disease outbreaks computationally efficient methods must be designed [53]. As demonstrated in the study in Dominican Republic, the data collected with this protocol captured quickly and shared electronically using a generic data collection tool [47]. Incorporating such an algorithm into the information technology (IT) systems already used by companies to

collect health and production data is straightforward and would allow decisions to submit samples for testing to be made at the farm level. Additionally, if location of farms were incorporated into a regional database, it would be possible to explore the spatial relationship among results, in addition to their temporal scale [45, 46, 47]. This approach may be tested in other commercial pig farms systems to increase the number of data collection to aid a precise result interpretation, addressing different types and regions of pig production.

The statistical technique employed here was just one among many that could be considered and, regardless of the specific technique used, it highlights opportunities to further leverage data collected through this EPS protocol and inform early detection systems in a reliable and accurate way. Because the algorithm may be incorporated into the IT systems routinely used by swine companies to collect health and production data, the EPS may not necessarily increase the work already performed by farmers and farm workers. In addition to systematise the collection and interpretation of data, the approach proposed here may also help the design and implementation of risk-based testing to early detect FHF incursions, for example, through the use of point of care tests [54].

The ability to detect significant high-risk clusters is influenced by the number of observations assessed, which affects the power of the statistical test. Because the analysis here was purely temporal, the sample size is then determined by the number of units of times (weeks here) through which data were collected. The limited number of weeks for which data were available is a potential explanation for the absence of significance in the detection of clusters and should be considered when implementing the system at a large scale. It is possible that at least one year of routine data collection, to incorporate seasonal fluctuations and to increase the power of detection in variations of the score, may be needed before the EPS protocol could be implemented at a fully operational scale in a country or region. Similarly, the first component of the EPS, focused on the assessment of farm biosecurity, should be regularly updated to reflect changes in the farm practices and conditions.

Certain diseases show clinical signs similar to ASF or CSF and that are endemic or not reportable, such as porcine reproductive and respiratory syndrome, post-weaning multisystemic wasting syndrome, or certain forms of Salmonellosis. Presence of these diseases may delay the diagnosis of an FHF because the FHF will not be the first suspicion by producers and veterinary practitioners, which also seems to be the case for the ASF virus isolated in the Dominican Republic in 2021 [55].

Consequently, in addition to knowledge about the clinical signs of the disease, awareness of the increase in risk for the incursion of a new disease is an important factor influence rapid detection and response. Having a participatory surveillance system in place may help identify an outbreak of one of these endemic diseases more quickly and may eventually provide a profile for these diseases to help distinguish between more common disease and an FHF. Additionally, the EPS protocol may aid the design of targeted surveillance efforts. For example, in the study in the Dominican Republic, Farm A showed lower scores than Farm B, suggesting that the former was, *a priori*, less vulnerable to FHF introduction than the latter. However, the relatively high variation in the scores observed in Farm A were suggestive of an introduction of disease and triggered the recommendation for testing. This observation highlights the value of systematic, long term surveillance efforts to detect early signs of disease incursions.

There were some important lessons learned through the pilot of the proof of principle here that may help countries overcome some of the issues they face when attempting the large-scale application of passive surveillance approach. One of the most important perceived benefits was the standardisation of signs that may lead to the identification of a suspected foreign animal disease case. Another important benefit was the systematisation of longitudinal data analysis, which should increase the temporal sensitivity of the detection system. The testing also helped identifying opportunities for improving the system. For example, the detection of alarms may be linked to specific protocols for testing, using traditional methods, or point of care tests, which may help reduce the time to reporting of a foreign animal disease. WOAHA has recently published guidelines for the use of point of care tests in the detection of

FHF that may be relevant to this discussion [56]. We also learned that a reassessment of the biosecurity component after a certain period of time (for example, every three months, to adjust for seasonal changes) may have been desirable. The movement of animals, mostly if the farms received animals was another point that this EPS protocol did not account for, and that should be considered. Finally, we believe that the system may be valuable only for aiding early detection in commercial farms, particularly those that are relatively large, given that the benefit relates to the probability of identifying signs, which is not possible if there is not a sufficient number of animals to evaluate.

There is still work to be done in enhancing awareness and implementation of biosecurity in this swine densely populated and highly productive region. More activities in sanitary education, developed through PPPs, to increase the receptiveness of pig producers to actions related to surveillance and monitoring should be stimulated.

The outbreaks of ASF and CSF in Dominican Republic increase risk of wider spread in the western hemisphere. Strong PPPs are needed to support efforts for early detection of disease incursion in free areas. Both WOA and Food and Agriculture Organization for the United Nations (FAO) highlight need for PPPs to prevent and detect TADs including systems for early detection. The EPS protocol here promotes mechanisms that allows producers to perform surveillance, aiding the OVS contributing to the faster action in case of introduction of any TADs. For that reason, the protocol may be applied as a bridge between public and private sectors and facilitating the communication between those sectors necessary to coordinate rapid assessment of potential TAD incursions. Additionally, according to WOA, the establishment of PPPs contributes to a more efficient use of public and private sector resources, finding synergies through an active and structured collaboration to bring, among other things, a well-structured surveillance system with active and passive surveillances very efficient [57]. According to the Global Framework for Progressive Control of Transboundary Animal Diseases from WOA and FAO, a multi-sectoral approach, with the involvement of all actors at the national, regional and global levels are essential to the success of preventing,

detecting and responding to TADs [58]. This same document also mentioned the importance of developing tools that advocate to TADs, focusing on many aspects of control programmes, but also to warning systems for early detections of TADs.

Conclusions

Shortening the time between incursion and first detection is critical to limit the impact of ASF or CSF incursions in free areas. However, implementation of passive surveillance approaches has been impaired by a number of weaknesses and limitations. Results here offer a proof of principle to demonstrate the opportunity for standardising data collection processes through the use of EPS protocols and participatory surveillance methods. The results offer an opportunity to promote and motivate effective PPPs implemented with the objective of early detecting the incursion of FHF of swine and supporting the ultimate goal of reducing the time to first report of a suspect, and the impact of TAD epidemics in free countries and regions.

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Table I

Components and factors included in an enhanced passive surveillance protocol for scoring risk and supporting the early detection of African swine fever and classical swine fever in swine farms

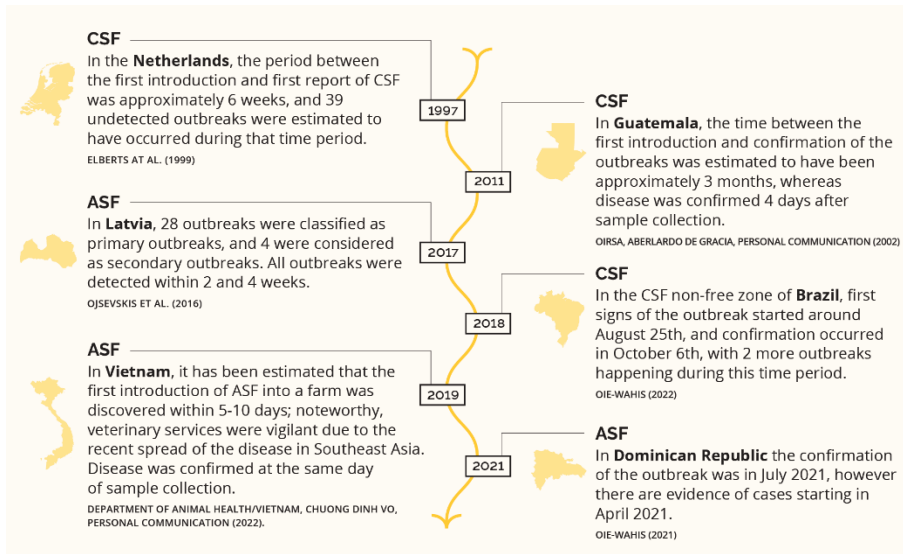
Score	0	1	2	3	4	5	6	7	8	9	10
Probability of finding the sign/factor (qualitative)	Negligible		Low			Medium			High		Very high
Probability of finding the sign/factor (quantitative)	< 0.1		0.1–0.4			0.4–0.7			0.7–0.9		> 0.9

Components	Factors	Increase in risk						Reference
		Area with feral pigs			Area without feral pigs			
		Commercial – sows	Commercial – finishers and nurseries	Small holders and outdoors	Commercial – sows	Commercial – finishers and nurseries	Small holders and outdoors	
Biosecurity background (farm-level risk factors)	Use of feed with ingredients of foreign origin	3	3	3	3	3	3	[31, 32, 33, 34]
	Swill-fed	5	5	5	1	1	1	[3, 34, 35, 36, 37, 38, 39]
	Absence of double fencing	7	7	8	4	4	4	[40]
	Presence of flies and ticks	7	7	8	7	7	7	[34, 35, 36, 37, 38, 39, 40, 41]

Presence of small and domestic mammals (rats, dogs, cats)	7	7	9	5	5	8	[6, 38]
Absence of a protocol for changing clothes, of separate entries and exits, of disinfection of objects, introduction of food allowed, and external individuals allowed in the farm	10	10	10	10	10	10	[6, 38]
Cars and trucks may enter premises	8	8	8	8	8	8	[6, 38]
Non-closed herd with recent introduction of new animals, but no quarantine station or location within 0.5–1 mile from premises, or sharing personnel	9	9	9	9	9	9	[6]
Dead animals disposed in a manner that does not prevent the attraction of wildlife, rodents, and scavengers	9	9	9	9	9	9	[6]
Personnel (including vets, inseminators, technicians) move between this farm and other farms with trusted biosecurity	6	6	6	6	6	6	[38]
Personnel (including vets, inseminators, technicians) move between this farm and other farms WITHOUT trusted biosecurity	9	9	9	9	9	9	[38]

Syndromic surveillance	Increase in mortality (sudden death)	4	[2, 4, 42, 43, 44, 45]
	Drop in feed consumption	1	[2, 4, 42, 43, 44, 45]
	Fever	2	[2, 4, 42, 43, 44, 45]
	Erythema	2	[2, 4, 42, 43, 44, 45]
	Cyanosis of ears and limbs	3	[2, 4, 42, 43, 44, 45]
	Abortion	1	[2, 4, 42, 43, 44, 45]
	Constipation followed by diarrhea	1	[2, 4, 42, 43, 44, 45]
	Haematochezia (diarrhea with frank blood)	6	[2, 4, 42, 43, 44, 45]
	Reduced motility/movements or abnormal recumbence	2	[2, 4, 42, 43, 44, 45]
	Vomiting	5	[2, 4, 42, 43, 44, 45]
	Haematuria	7	[2, 4, 42, 43, 44, 45]

	Hematemesis	7	[2, 4, 42, 43, 44, 45]
	Bleeding from nose	7	[2, 4, 42, 43, 44, 45]
Necropsy/ samples collected	Kidney haemorrhages	7	[2, 4, 42, 43, 44, 45]
	Lymphadenomegaly	7	[2, 4, 42, 43, 44, 45]
	Lymph node haemorrhage or necrosis	9	[2, 4, 42, 43, 44, 45]
	Splenomegaly	9	[2, 4, 42, 43, 44, 45]
	Hydropericardium	7	[2, 4, 42, 43, 44, 45]
	Hydrothorax	7	[2, 4, 42, 43, 44, 45]
	Shock lung/acute respiratory distress syndrome	7	[2, 4, 42, 43, 44, 45]
	Pneumonia	5	[2, 4, 42, 43, 44, 45]
	Haemorrhagic intestinal contents	8	[2, 4, 42, 43, 44, 45]



ASF: African swine fever
CSF: classical swine fever

Figure 1

Estimated duration of the time period between virus introduction and disease confirmation, and number of outbreaks that occurred over that period, for selected African swine fever and classical swine fever epidemics [18, 19, 20, 21, 22]

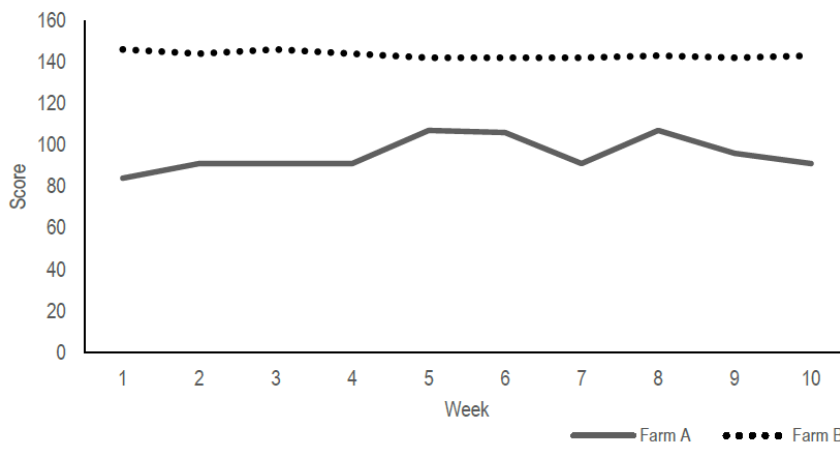


Figure 2

Weekly variation in the risk score for African and classical swine fevers estimated using an enhanced passive surveillance protocol in two pilot farms in the Dominican Republic over a ten-week period

Farm A in solid line, and Farm B in dotted line

Pre-print

Farm A



Farm B

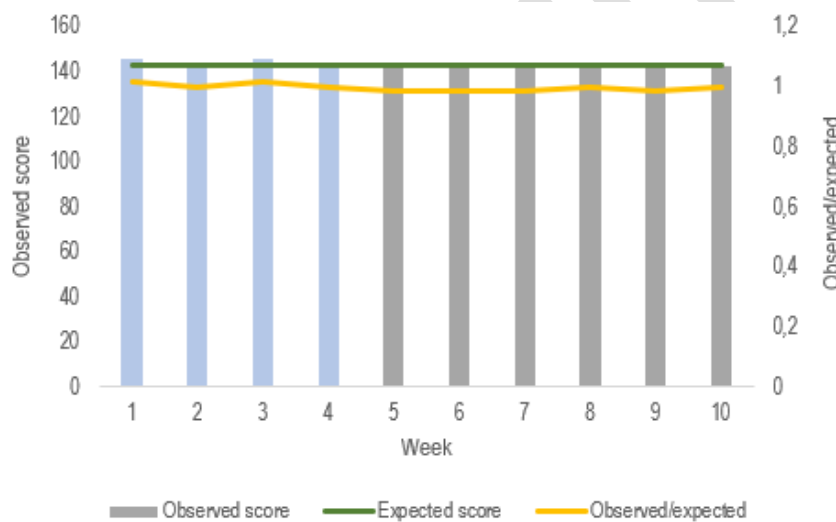


Figure 3

High-risk periods (light blue) detected using a temporal scan statistic model on two pig farms in the Dominican Republic denoted as Farm A (top) and Farm B (bottom) using data collected during ten weeks of application, and follow-up of an enhanced passive surveillance protocol