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Quantification of early detection surveillance in PRRS-free regions

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ABSTRACT

In May 2022, a national control program targeting porcine reproductive and respiratory syndrome virus was launched in Denmark, and the first regions are approaching a PRRS-free status. Hence, the question now arises as to how the surveillance should be performed to identify new incursions of the PRRS virus in PRRS-free regions as early as possible. The aim of the present study was to quantify the early detection sensitivity of the current and alternative PRRS surveillance systems in Denmark at a regional level. The current PRRS surveillance system is composed of a notifiable surveillance component and an active serological surveillance component, consisting of monthly sampling (breeding and multiplier farms) or yearly sampling (production farms). The results from the present study estimated that the current surveillance system would have a 21.5 % [16.0 %;32.4 %]$_{min;max}$ probability of detecting an incursion of PRRS into a PRRS-free region. If monthly serum samples were taken on all farms, the probability would be increased to 87.7 % [87.4 %;88.6 %]$_{min;max}$. Adding a syndromic surveillance component to the existing surveillance system resulted in an early detection sensitivity of 23.9 % [17.6 %;34.6 %]$_{min;max}$, while targeted risk-based sampling resulted in probabilities of 27.8 % [17.9 %;33.8 %]$_{min;max}$ and 62.6 % [17.9 %;79.5 %]$_{min;max}$ for quarterly or monthly sampling frequencies, respectively. Results from the present study indicate a relatively low chance of detecting newly infected farms within the first month in a PRRS-free region with the current surveillance system. The probability of early detection of PRRS can be increased either by increasing the sampling frequency on all farms or by using targeted risk-based sampling.

1. Introduction

A national control program for porcine reproductive and respiratory syndrome (PRRS) was launched in Denmark in May 2022. Its objective was to increase the number of PRRS antibody-negative sow farms and finishers (Anonymous, 2022a), and it has been accompanied by legislative changes in the surveillance system (Anonymous, 2023).

Although the spread of PRRS virus is mainly driven by the introduction of newly purchased pigs, air and local transmission also seem to account for a number of infections (Cho and Dee, 2006; Galvis et al., 2021). Therefore, PRRS control areas have been set up in Denmark. As the PRRS control program progresses, the first regions are expected to be declared free from PRRS in the near future. The reintroduction of the PRRS virus into a negative area could have considerable economic consequences, which is why early detection of PRRS is crucial.

The current PRRS surveillance system consists of two components: an active surveillance and a notifiable (passive) surveillance. The active surveillance is driven by the PRRS legislation implemented in 2023, which requires all pig farms with more than ten sows or 100 pigs in total to have a PRRS-antibody status assigned yearly (Anonymous, 2023). In addition to this, breeding and multiplier farms[1] conduct monthly testing of PRRS antibodies due to their enrollment in the voluntary industry-driven Specific Pathogen Free system (SPF-Sund, 2024). In all cases, serological testing is performed by ELISA testing of serum samples from 20 pigs. Additionally, PRRS is a notifiable disease, which means that, if there are clinical symptoms, the veterinarian is obliged to submit samples for virus testing by PCR (Anonymous, 2023). Another potential surveillance system for PRRS is syndromic surveillance. Productivity data including preweaning mortality rates and neonatal losses have been suggested, but not yet implemented, for surveillance (Pedro Mil-Homens

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[1] Breeding/multiplier farms supply production farms with breeding animals.

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et al., 2024).

Recently, a method to quantify the sensitivity of early detection surveillance (EDSSe) was proposed by Cameron et al., (2020). The chain of events for early detection is as follows: (1) the first infected farm must be included in the surveillance, (2) the farm must be tested within the defined time frame, and (3) the test must identify infected farms as being positive (Cameron et al., 2020).

The objective of the present study was to quantify the early detection sensitivity of the current PRRS surveillance system in Denmark at a regional level and explore alternative surveillance systems.

2. Materials and methods

2.1. Data

Data on farm demographics, movement of pigs, PRRS antibody status and farm type (production/breeding/multiplier farms) were extracted from the Central Husbandry Register (CHR) (Anonymous, 2022b) and the Specific Pathogen Free register (SPF) (SPF-Sund, 2024) on 10 April 2024. Geographical information on the current PRRS regions was made available by the Danish Food and Agriculture Council in December 2023.

All farms enrolled in the national Danish PRRS control program were identified, including farms with more than ten sows or 100 pigs in total. Furthermore, farms with hazardous movements were defined as farms with incoming movement of non-breeding pigs from a PRRS antibody-positive region during 2023, not counting the movement of pigs from the same region as the farm itself.

2.2. Surveillance systems for evaluation

Three surveillance components were assumed to be of relevance: a notifiable surveillance component, a (currently hypothetical) syndromic surveillance component, and an active surveillance component based on serum samples submitted with varying frequencies. A combination of the presented surveillance components and frequencies resulted in the following surveillance systems being evaluated:

- **Current surveillance** (*EDSSe*): a notifiable surveillance and the active surveillance including serum samples taken yearly (production farms) or monthly (breeding/multiplier farms).
- **Current surveillance with increased frequency** (*EDSSe (all monthly)*): as the current surveillance, but with monthly serum samples taken on all farms, irrespective of the farm type.
- **Risk-based surveillance** (*EDSSe +risk move (quarterly)* and *EDSS +risk move (monthly)*): the current surveillance, but with more frequent surveillance (either quarterly or monthly serum samples) on farms with hazardous inward movements of non-breeding pigs from PRRS-positive regions.
- **Current surveillance + syndromic surveillance on farms with sows** (*EDSSe +syndromic*)**:** as the current surveillance, added a potential syndromic surveillance component based on productivity data on all farms with sows.

2.3. Early detection estimation

For the EDSSe estimation, the unit was defined as the farm, and the time frame for detection was set at one month. Thus, EDSSe is an estimate of the probability of detecting PRRS within the first month of a PRRS incursion having occurred on a single farm in an otherwise PRRS-free region.

For each farm, the herd sensitivity (SeH) was estimated for each of the three surveillance components: $SeH_{notifiable}$ (historical information), $SeH_{syndromic}$ (estimated information), and SeH_{serum} (number of individual samples investigated). Input values for $SeH_{notifiable}$ were based on unpublished historical data identifying the number of PRRS positive farms diagnosed by clinical suspicion or PCR, while $SeH_{syndromic}$ was based on a conservative approximation (Table 1). SeH_{serum} indicates the probability of finding at least one positive sample out of the 20 samples investigated, given that 10 % of the pigs on the farm have antibodies. In previous studies, the design prevalence (P^*_{animal}) has been set at 47.5 % (28.3 % - 67.5 %) (Suess et al., 2002), whereas, in this case, we chose a more conservative approximation of 10 % (Table 1). For the risk-based sampling, we assumed farms purchasing weaner pigs from another non-free region to have five times higher risk of becoming PRRS positive, compared to farms which do not purchase (Table 1). This relative risk is a conservative estimate, as it was not possible to quantify the risk of purchase until free regions are available.

The EDSSes were calculated for each of the three surveillance components ($EDSSe_{notifiable}$, $EDSSe_{syndromic}$, $EDSSe_{serum}$), as suggested by (Cameron et al., 2020):

$$EDSSe = Cp * Ct * SeH * RR_i$$

where *Cp* is the population coverage, *Ct* is the temporal coverage, *SeH* is the herd sensitivity, and RR_i is the proportional relative risk. The population coverage was set at 100 %, since all farms in the PRRS control program were included in the surveillance. The temporal coverage varied between monthly (1), quarterly (1/4) and yearly (1/12) sampling frequencies depending on the surveillance system being evaluated. The risk was accounted for by transforming the relative risk of hazardous incoming movements into a stratum-specific proportional relative risk (RR_i) (Table 1).

Finally, the EDSSes of the independent surveillance components were combined into EDSSes for the surveillance systems of interest (*EDSSe (all monthly)*, *EDSSe +risk move (monthly* or *quarterly)*, and *EDSSe +syndromic*), accounting for overlap between the components:

$$EDSSe_{combined} = EDSSe_{notifiable} + EDSSe_{serum} + EDSSe_{syndromic} - (EDSSe_{notifiable} * EDSSe_{serum}) - (EDSSe_{notifiable} * EDSSe_{syndromic}) - (EDSSe_{serum} * EDSSe_{syndromic}) - (EDSSe_{notifiable} * EDSSe_{serum} * EDSSe_{syndromic})$$

The regional mean and 95 % confidence intervals for each surveillance system evaluated were estimated based on 1000 simulations for the parameters assigned a distribution (Table 1).

The methodology assumes 100 % specificity, meaning that all farms declared PRRS-negative are assumed to have been declared correctly, thereby resulting in no false positives.

All data were managed and analyzed in R version 4.3.0 (R Core Team, 2023) using the packages Sf (Pebesma et al., 2024), Tidyverse (Wickham et al., 2019) and ggplot2 (Wickham et al., 2024).

3. Results

The initial dataset included 4393 farms enrolled in the PRRS control program. Farms without an assigned PRRS region were deleted (n = 25), resulting in a final dataset of 4368 active pig farms, distributed into 43 regions of where 16 regions were officially declared as regions of PRRS reduction (Suppl). The farms were made up of 4.4 % (193/4368) breeding/multiplier farms and 95.6 % (4175/4368) production farms.

Three islands, Zealand (R2), Funen (R3) and Bornholm (R5) were approaching PRRS-free status in 2024. In April 2024, these regions included 2.5 % (10/395), 6.3 % (30/476) and 18.8 % (19/101) PRRS antibody-positive farms, respectively. In addition, the same three regions had the smallest percentage of farms with hazardous incoming movements, namely 6.6 % (26/395), 8.2 % (39/476) and 0 % (0/101). For comparison, the remaining regions included an average of 87 farms, ranging from 24 to 228 farms per region: 31.0 % $[5.7\ \%;61.8\ \%]_{min;max}$ PRRS antibody-positive farms, and a mean of 31.0 % $[7.5\ \%;54.7\ \%]_{min;}$

Table 1
Input values for the estimation of early detection sensitivity (EDSSe) of PRRS in PRRS-free regions. Estimation of herd sensitivities from each of the three surveillance components: active surveillance (SeH_{serum}), passive surveillance ($SeH_{notifible}$), and syndromic surveillance ($SeH_{syndromic}$) are presented, along the relative risk (RR) for the risk-based surveillance.

	Parameter	Source of information	Category	Input value
Active surveillance	P^*_{animal}	Literature	Input values for SeH_{serum}	0.1
	Se_{elisa}	Estimated		(0.95, 1.00)[a]
	$n_{animals}$	20 serum samples from individual pigs per sampling		20
	$N_{animals}$	CHR register		Total number of registered pigs on the farm.
	SeH_{serum}	Hypergeometric approximation	All farms	$1-\left(1-Se_{elisa}*\frac{n_{animals}}{N_{animals}}\right)^{P*_{animal}*N_{animals}}$
Passive surveillance	$SeH_{notifiable}$	Historical data	Farms with weaners and/or finishers	(0.02, 0.05, 0.09)[b]
			Sow and integrated farms	(0.24, 0.29, 0.34)[b]
Syndromic surveillance	$SeH_{syndromic}$	Estimated	Farms with weaners and/or finishers	0
			Sow and integrated farms	(0.08, 0.10, 0.12)[b]
Risk-based surveillance	RR	Estimated	Farms purchasing non-breeding pigs from PRRS-positive regions[c]	5

[a] Estimated by the laboratory performing the analysis. Input values described as a uniform distribution (minimum, maximum), 1000 simulations.
[b] Input value described as a Beta Pert distribution (minimum, mode, maximum), 1000 simulations.
[c] Compared to farms that only purchased pigs from own region or other PRRS-negative regions.

$_{max}$ farms with hazardous movements.

The estimated EDSSes of the four surveillance systems under evaluation are presented in Fig. 1. The mean EDSSe for the current surveillance across all regions was 21.5 % [16.0 %;32.4 %]$_{min;max}$, with the variation mainly driven by the proportion of breeding/multiplier farms in the given region. The average EDSSe was 85.9 % [85.2 %;88.3 %]$_{min;max}$ and 7.2 % [7.1 %;8.3 %]$_{min;max}$ for breeding/multiplier farms and production farms, respectively. This difference can be explained by the variation in sampling frequency from monthly (breeding/multiplier farms) to yearly (production farms). Thirteen regions did not include any breeding/multiplier farms, and these were also the regions with the smallest EDSSe.

When the hypothetical syndromic surveillance component was added to the current surveillance, the EDSSe increased to a mean of 23.9 % [17.6 %;34.6 %]$_{min;max}$ across regions. The variation was dependent on the proportion of farms with sows in the region, since only farms with sows were included in the syndromic surveillance component. Similarly, when the frequency of surveillance was intensified on farms with hazardous movements, the EDSSe increased to a mean of 27.8 % [17.9 %;33.8 %]$_{min;max}$ and 62.6 % [17.9 %;79.5 %]$_{min;max}$ for quarterly and monthly sampling, respectively.

Monthly serum sampling on all farms in a PRRS-free region resulted in an average EDSSe of 87.7 % [87.4 %;88.6 %]$_{min;max}$.

4. Discussion

Early detection surveillance sensitivity is a measure of the effectiveness of the surveillance system to detect every disease incursion within a defined timeframe. Hence, it is a more stringent target compared to other types of surveillance evaluation systems, e.g. surveillance for demonstrating freedom from disease, where the goal is to find at least one case.

The results from the present study indicate the current surveillance to have a relatively low chance of detecting newly PRRS incursions in a

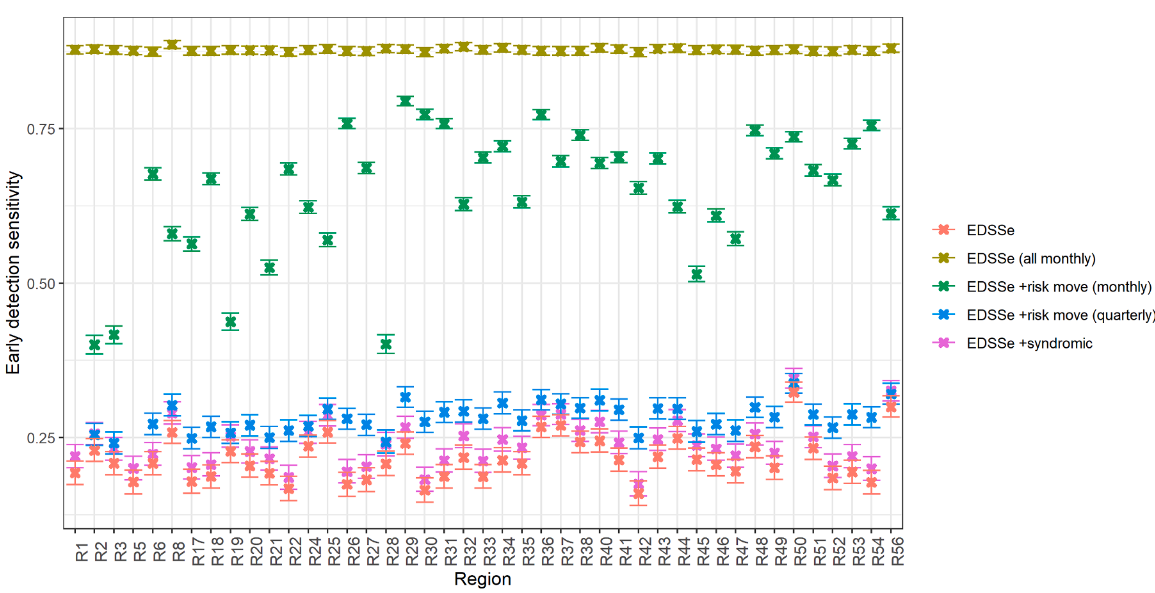

Fig. 1. Early detection system sensitivity (EDSSe). Four potential PRRS surveillance systems under evaluation for the early detection of PRRS in 43 regions in Denmark, April 2024. The surveillance systems evaluated include the current surveillance system (*EDSSe*), a surveillance system with increased frequency of antibody serum sampling on all farms enrolled (*EDSSe (all monthly)*), a surveillance system with increased sampling (either monthly or quarterly) on farms with hazardous incoming movement of non-breeding pigs (*EDSSe +risk move (monthly)* and *EDSSe +risk move (quarterly)*), and a surveillance system in which the current system is supplemented with a syndromic surveillance component on farms with sows (*EDSSe +syndromic*).

PRRS-free region within the first month. This low probability was mainly due to the rare frequency of serum sampling of production farms, which constitute 95.6 % of the population. The results from the present study estimated that the current Danish PRRS surveillance system has a mean probability of detecting an incursion of PRRS into a PRRS-free region within the first month of 21.5 % for the 43 regions presented (assuming they have all achieved PRRS-free status). Hence, it is more likely that an outbreak will remain undetected using the current surveillance system. An increase in the temporal coverage to 100 %, with 20 monthly serum samples taken on all farms resulted in an increase in the EDSSe to a mean of 87.7 %. However, this test setup would be associated with high costs. Therefore, targeted risk-based sampling could be considered to increase the sensitivity with a smaller increase in the number of samples. Quarterly or monthly serum samples taken on farms with a high risk of PRRS introduction due to hazardous movement of non-breeding pigs resulted in an EDSSe of 27.8 % and 62.6 %, respectively. However, the effort of setting up a risk-based surveillance may exceed the gain in EDSSe from quarterly sampling. This is why a monthly risk-based sampling strategy may be favored if this approach is chosen.

Although not yet implemented, syndromic surveillance would have the advantage of being relatively inexpensive and easy to set up, as productivity data are already collected continuously for a number of sow farms. A relatively conservative estimate of the syndromic surveillance was assigned in the current study compared with previous publications (Pedro Mil-Homens et al., 2024), which may explain the small gain in sensitivity obtained from adding a syndromic surveillance system (23.9 %). The conservative estimate was chosen due to the variation in data availability, clinical symptoms of PRRS, and the definition of a 'PRRS case' between countries. As the syndromic surveillance and relative risk parameters were estimated by the authors in the absence of existing data, this may imply a certain degree of uncertainty of the final results. A sensitivity analysis of the results was not performed due to the resource reasons.

In the current study, we included the risk of incoming movements from PRRS-positive regions as the main risk to be considered. The risk from airborne spread is an ongoing subject of discussion (Cho and Dee, 2006; Desrosiers, 2023). Nevertheless, the risk from airborne spread will be affected by the number of neighboring farms which actively excrete the PRRS virus, and which are therefore categorized as PRRS-unstable (Holtkamp et al., 2021). As the PRRS control program progresses, the number of PRRS-unstable farms is expected to fall to a minimum, and therefore the amount of virus particles in the air is expected to decrease accordingly. In addition, the three initial regions that are approaching PRRS-free status are islands, thereby increasing the distance to potential PRRS-excreting farms even further. Because of this, we found it acceptable to limit a potential risk-based surveillance system to the effect of hazardous movements only.

To our knowledge, this is the first example of an applied use of the EDSSe methodology. The PRRS control program requires early detection of PRRS in PRRS-free regions to mitigate the risk of further transmission. The results from the present study indicate that the chance of detecting newly infected farms within the first month in a PRRS-free region with the current surveillance system is relatively low. While increased frequency of testing on all farms or on high-risk farms would improve the EDSSe, it raises further economic considerations.

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CRediT authorship contribution statement

FERTNER METTE: Writing – original draft, Investigation, Funding acquisition, Conceptualization. **Cameron Angus:** Writing – review & editing, Supervision, Methodology. **Boldsen Søren Kjærgaard:** Writing – review & editing, Software, Investigation, Data curation. **Willkan Mira:** Writing – original draft, Visualization, Validation, Methodology. **Chapot Lorraine:** Writing – review & editing, Supervision, Methodology.

Declaration of Competing Interest

None.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prevetmed.2025.106461.

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