Final report to the AASV Foundation

Research Project Award:

Assessment of immediate production impact following attenuated PRRS virus vaccination in endemically infected breeding herds

Authors:

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Introduction

Porcine reproductive and respiratory syndrome virus (PRRSv) continues to significantly increase the cost of pig production due to reproduction losses and reduced growth performance (Holtkamp, Kliebenstein and Neumann 2013, Nieuwenhuis, Duinhof and van Nes 2012, Neumann et al. 2005). To reduce losses due to PRRSv infection, veterinarians have implemented practices to prevent virus introduction (i.e. biosecurity), as well as developed strategies to control, and/or eliminate the virus from individual pig herds and from regions (Perez et al. 2015, Corzo et al. 2010, Torremorell et al. 2008). Most PRRSv control/elimination efforts consist of decreasing (or eliminating) virus replication in the herd based on a combination of strategic PRRSv immunization and changes in pig flow. Immunization of US swine populations against PRRSv has been accomplished in large part with the use of modified-live (attenuated) virus vaccine (MLV) or field virus inoculation (FVI) (Arruda et al. 2016).

The American association of swine veterinarians proposed a standardized terminology for communicating the PRRSv status of breeding herds (Holtkamp et al., 2011). Briefly, upon infection herds are classified as “positive unstable”. When there is the failure of PRRSv RNA detection by RT-PCR in due-to-wean piglets for at least 90 consecutive days, the herd is classified as ‘positive stable’. Then, when there is no evidence of PRRSv circulation in the breeding herd, as demonstrated by lack of PRRS-associated clinical signs, and incoming gilts remaining serologically negative for PRRSv, the herd is defined as “provisional negative”. Finally, when there is no virus circulation, and no anti-PRRSv antibody circulation in the population, the herd is defined as PRRS-negative (or naïve).

Field studies have compared exposure programs to control PRRSv in sow herds, in terms of time to produce PRRSv-negative piglets at weaning, and/or production losses following the outbreak (Linhares et al. 2014, Linhares, Betlach and Morrison 2017). One important reported finding was that herds with recent history of PRRSv infection achieved stability (i.e. failure to detect PRRSv RNA in due to wean piglets consistently for 3 consecutive months testing 30 piglets by RT-PCR), and recovered productivity significantly sooner than herds without recent history of PRRSv infection. Another study approached the question of the economic benefit of practicing preventative vaccination using attenuated virus vaccine as an attempt to "build" anti-PRRSv immunity prior to outbreak with wild type strains (Linhares, Johnson and Morrison 2015). It was demonstrated that in the one hand vaccination increases herd immunity and reduces time-to-stability and impact on productivity when the herd becomes infected with wild type viruses. On the other hand, preventatively vaccinating a breeding herd also increases production costs (vaccine costs) and potentially attenuated PRRSv from vaccines has a negative impact on farm productivity (Bøtner et al. 1997, Dewey et al. 2004b, Dewey et al. 1999b, Nielsen et al. 2002). The study documented that it was economically beneficial to preventatively vaccinate breeding herds whenever the expected outbreak frequency was less than every 2.1 years. However, the "2.1 year" mark is highly sensitive to the attributed "negative impact" of MLV on PRRSv-negative or PRRSv-stable breeding herds. The authors of that study, due to the scarce availability to studies documenting safety of contemporary attenuated PRRSv vaccines, used a conservative approach assuming that preventative use of MLV vaccines resulted in decrease of 1 piglet per sow per year in the breeding herd productivity. Thus, there is the need to better define the production impact on PRRS-stable breeding herds adopting MLV.

The objective of this field study was to measure the immediate impact of MLV on key breeding herd performance parameters using natural experiments under field conditions. This information will provide information to best feed the existing economic models to assist swine veterinarians to take informed decisions regarding the use of PRRSv MLV vaccine as a preventive tool.

Materials and Methods

Study design. This was a retrospective field study to evaluate the immediate impact of PRRSv MLV vaccination on the breeding herd productivity. Eight PRRS-stable (Holtkamp, Polson and Torremorell 2011) sow farms adopting quarterly vaccinations using commercially available PRRS MLV vaccines were enrolled in the study. To assess immediate changes in productivity parameters associated with MLV vaccination, vaccination dates, and weekly production records were obtained from study farms. A statistical model was used to assess changes in production parameters on subsequent weeks following MLV PRRS vaccination events.

The analysis was conducted on the aggregated data from the 65 herd vaccinations. To assess the immediate impact of the vaccination on each productivity parameter, a 6 weeks period prior to each vaccination was established as baseline. The productivity of each of the following 6 weeks was compared to the baseline, for each production parameter (figure 1). For the purpose of the study, it was considered that MLV had a negative impact on a production parameter if there was a significant change in the respective production parameter within 6 weeks of vaccination, which is the expected viremic period following PRRSv infection of individual sows (Xiao et al. 2004).

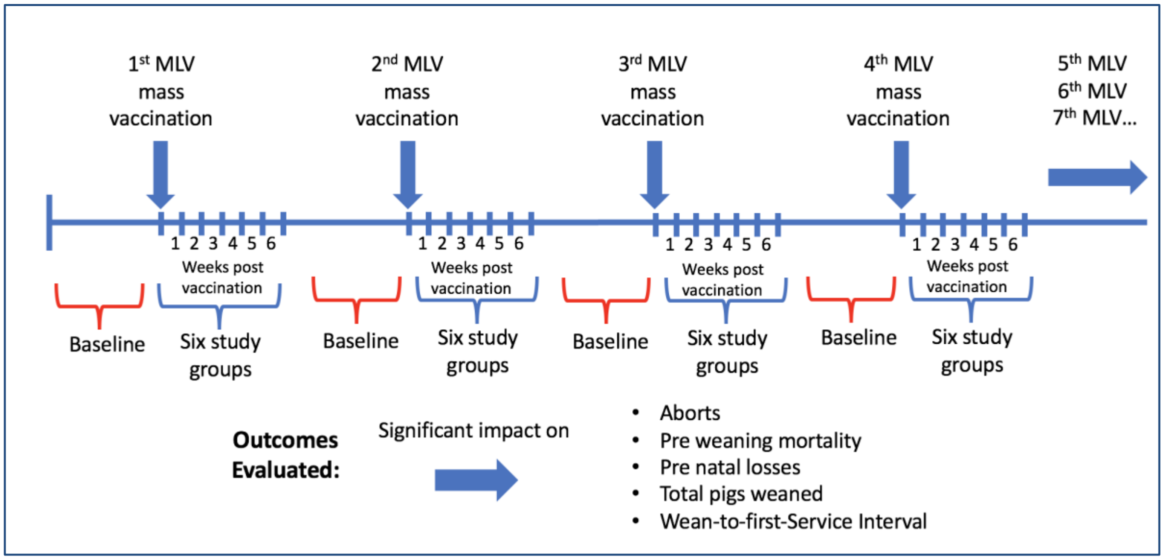

Figure 1: Study design: analysis with aggregated data from 65 herd-vaccinations with PRRSv MLV.

Production parameters, and vaccination dates. The following production parameters were recorded from the study herds, in a Microsoft Excel spreadsheet: number of aborts, defined as the counts of aborts per week; pre-weaning mortality, defined as the number of dead piglets on that week; prenatal losses, defined as the difference of total born and born alive means of the week; total pigs weaned, defined as the total number of pigs weaned per week; and wean-to-first-service interval, defined as the average number of days between weaning and first service. The vaccination dates for each study herd were also collected on a Microsoft Excel spreadsheet.

Herd enrollment eligibility criteria. Breeding sow farms were eligible for this study if they were a) PRRS stable according to the AASV guidelines, b) farms implementing routine vaccinations with a commercial PRRSv MLV vaccine (PRRS Ingelvac MLV, PRRS Ingelvac ATP, or Fostera PRRS), c) availability of vaccination dates, and weekly production records required for this study.

Statistical analysis. A PROC MACONTROL procedure of SAS 9.4 (SAS Institute, Inc., Cary, NC) was used to do a statistical process control (SPC) analysis of the data on the individual farm level to detect negative impact on productivity within 1-6 weeks after each MLV intervention. It was used the exponential weighted moving average, with 3 sigmas, and a lambda constant of 0.4, as the SPC method. We did not include changes in productivity followed by a PEDV outbreak. Negative impact (signal) was defined as a significant decrease in productivity followed by vaccination. More specifically, an increase of frequency of aborts, pre-weaning mortality, neonatal losses, or wean to first service interval; or a decrease in total pigs weaned. The frequency of significant changes in productivity following MLV vaccination, as well as the magnitude of these changes were reported.

Moreover, it was conducted analysis with the aggregated data from all 65 herd-vaccinations to assess the 'production system effect' of MLV vaccination on sow farm productivity. The PROC GLIMMIX procedure of SAS 9.4 (SAS Institute, Inc., Cary, NC) was used to build a mixed hierarchical regression model to assess change of each production parameter on up to 6 weeks following the reported PRRS MLV vaccination date, compared to a 6-week period immediately before vaccination. Poisson distribution was used for aborts, pre-weaning mortality and number of pigs weaned per week, since those responses were defined as counts. We used an offset variable to adjust the analysis for herd size, controlling aborts by the average sow inventory of the week, pre-weaning mortality by the total number of pigs born on the week, and total pigs weaned by the number of sows weaned on the week. For neonatal losses, we used a log-normal distribution, because it was the difference between two means. Exponential distribution was selected for the wean to first service interval, since it was a time to event response. Moreover, herd was used as random effect, and weeks after MLV vaccination was used as fixed effect for all the models. On the pre-weaning mortality and total pigs weaned analysis we also included PEDV status as a random effect. A level of significance of $P < 0.05$ was used for all analysis, with a one-sided p-value detecting only if the change in productivity represented a negative impact on performance, compared to the baseline.

Results:

There were 65 eligible herd-vaccinations, and 4 non-eligible herd-vaccinations. The reason for non-eligibility were: PRRS outbreak causing herd instability (n=4). The median number of vaccinations per herd was 8, with minimum of 5 and maximum of 11. The median period between vaccinations was 13 weeks, with the minimum value of 4 and maximum of 41. There were 780 production record weeks evaluated.

On the SPC analysis, which described the herd-level production losses following each of the 65 MLV vaccinations, there was a significant increase in aborts following 4 herd-vaccinations, a significant increase in prenatal losses after 7 herd-vaccinations, significant increase in pre-weaning mortality after 2 herd-vaccinations, and increase in wean-to-first-service interval after 2 herd-vaccinations. There was no significant change on total pigs weaned after MLV interventions (table 1).

Table 1: Negative impact on productivity following 65 herd vaccinations with PRRSV MLV.

Production parameter	**Frequency and percentage of negative production impact following MLV vaccination**	**Range of the production impact**
Aborts	4/65 (6.1%)	1.60 to 6.96 aborts/1000 sows
Prenatal losses	7/65 (10.8%)	0.03% to 0.66% of total born
Pre-weaning mortality	2/65 (3.1%)	0.09% to 0.20% of born alive
Total pigs weaned	0/65 (0.0%)	N/A
Wean to first service interval	2/65 (3.1%)	1.03 to 1.44 days

There was no negative effect of PRRS MLV vaccination on the aggregated data of all herd vaccinations, with the exception of an increase in pre-weaning mortality of 0.26 percentage points on the week 2 post vaccination (Table 2).

Table 2: Effect of PRRS MLV vaccination on productivity, on a system level.

Weeks	Abort rate (P>0.05)	Neonatal losses (P>0.05)	Pre-weaning mortality (P 0.0025)	Pigs weaned per sow (P>0.05)	Wean to first service interval (P>0.05)
Baseline	0.069% [a]	0.979 [a]	13.97% [a]	10.48 [a]	5.82 [a]
1	0.073% [a]	0.979 [a]	13.12% [a]	10.74 [a]	5.87 [a]
2	0.070% [a]	0.978 [a]	14.23% [b]	10.49 [a]	5.88 [a]
3	0.076% [a]	0.990 [a]	13.89% [a]	10.49 [a]	5.86 [a]
4	0.068% [a]	0.997 [a]	13.28% [a]	10.52 [a]	5.81 [a]
5	0.070% [a]	0.958 [a]	12.59% [a]	10.80 [a]	5.83 [a]
6	0.068% [a]	0.999 [a]	13.09% [a]	10.63 [a]	5.72 [a]

Different subscript letters mean significant worsening of production parameter as compared to the baseline.

There was no significant increase on the abort rate (figure 1), neonatal losses (figure 2), pigs weaned per sow (figure 3), or wean to first service interval (figure 4) in any of the 6 weeks post vaccination compared to the baseline period.

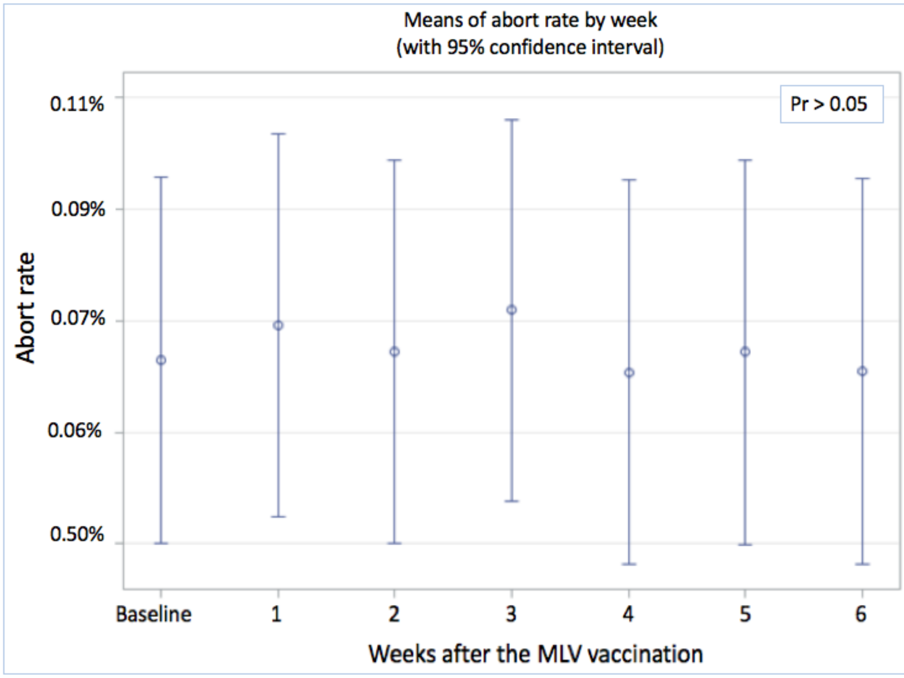

Figure 1: Means of abort rate over time, following 65 herd vaccinations.

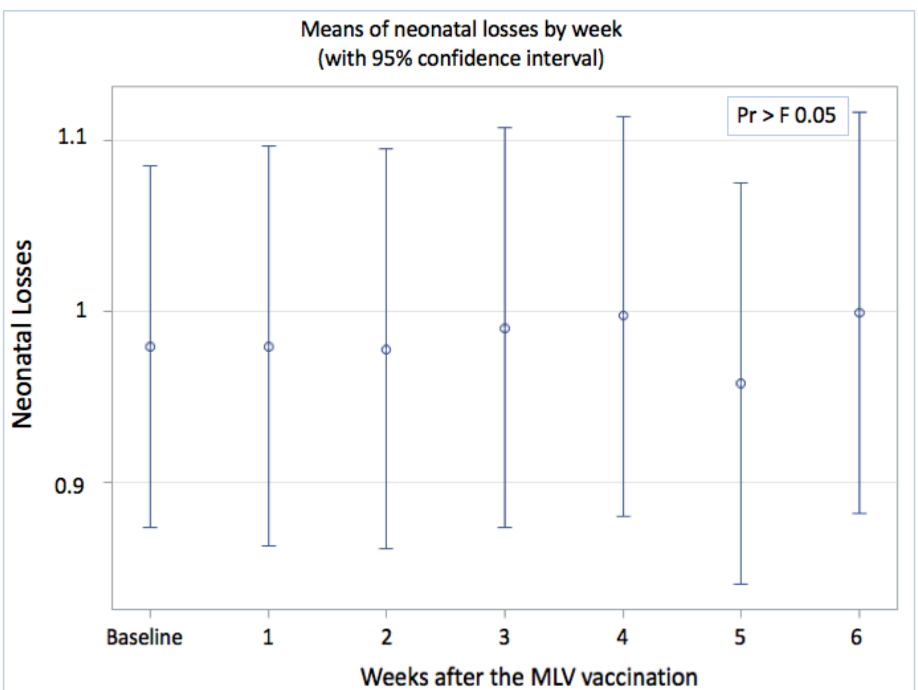

Figure 2: Means of neonatal losses over time, following 65 herd vaccinations.

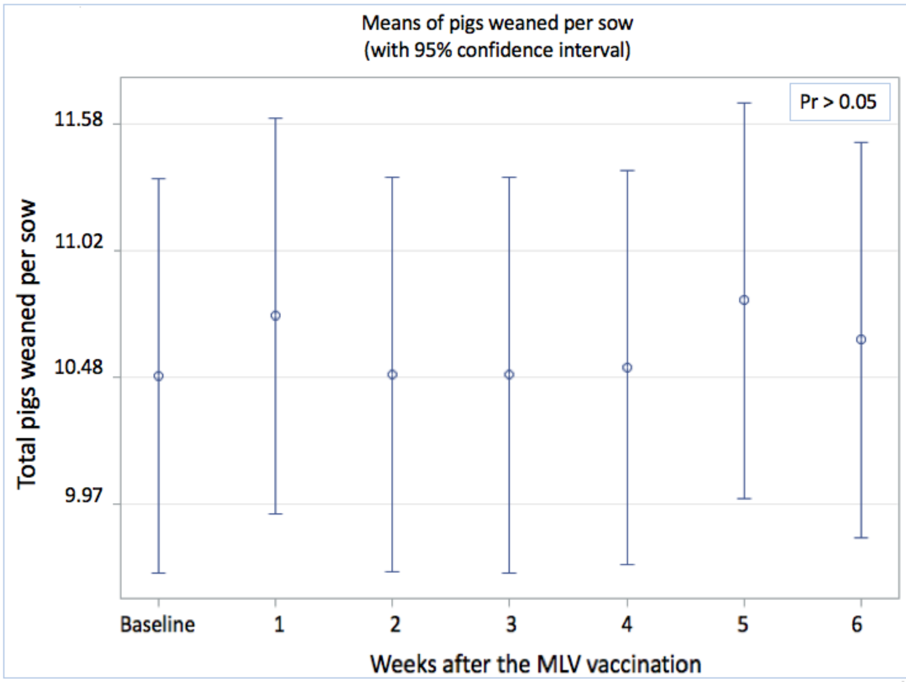

Figure 3: Means of pigs weaned per sow over time, following 65 herd vaccinations.

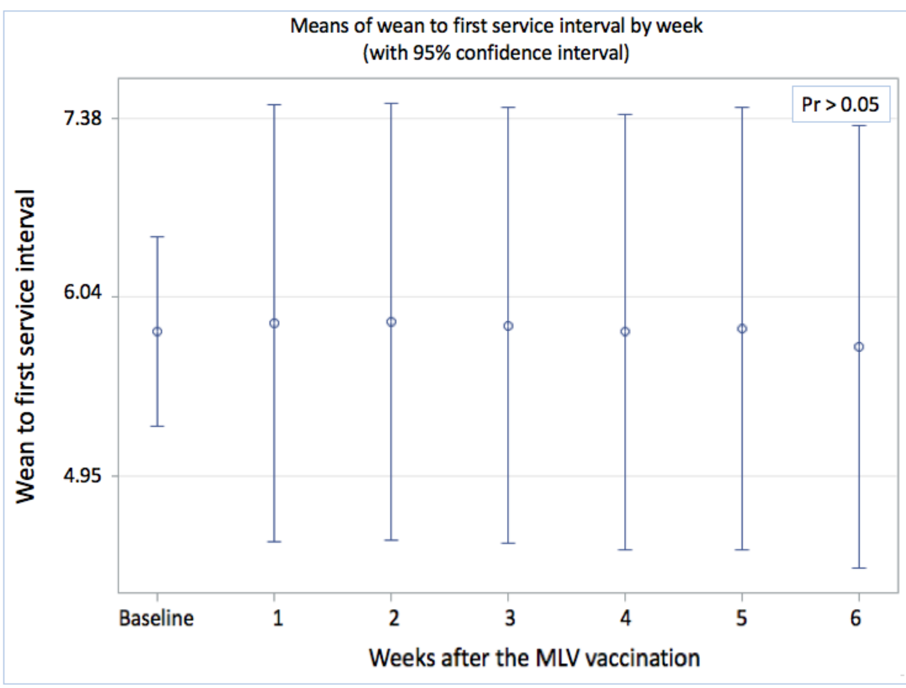

Figure 4: Means of wean to first service interval over time, following 65 herd vaccinations.

The only significant increase of pre-weaning mortality, compared to the baseline, was on the week 2 after the MLV intervention (P<0.0025) (figure 5).

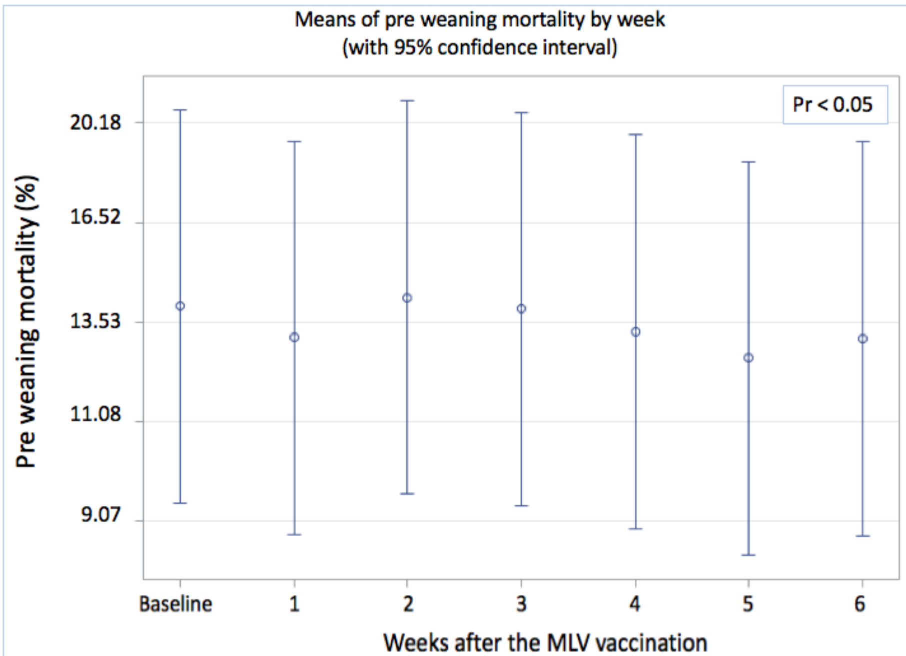

Figure 5: Means of pre-weaning mortality over time, following 65 herd vaccinations.

Discussion:

This study investigated the immediate effect of PRRS MLV vaccination on selected key production performance indicators. The 'immediate' effect was defined as having a significant change on production parameters within 6 weeks of vaccination, as compared to 6 weeks prior to vaccination. Six weeks was chosen to represent the expected duration of the viremic phase following infection of individuals sows. It was assumed that if MLV vaccination has a significant impact on the productivity parameters under field conditions, the change should happen within the viremic phase of infection.

Under the conditions of this study, vaccinating for PRRSv using MLV had no significant impact on the five production parameters observed (number of aborts, pre-wean mortality, prenatal losses, total pigs weaned, and wean to first service interval) with the exception of an increase in pre-weaning mortality of 0.26 percentage points on the week 2 post vaccination. Although not significant on a system level, individual farms might have some small changes in productivity following the MLV intervention. As previously mentioned, this data will provide information to best feed the existing economic models to assist swine veterinarians to take informed decisions regarding the use of PRRSv MLV vaccine as a preventive tool.

It is important to highlight that this study included only PRRS stable sow farms, and thus results may not be applicable to PRRS-naïve, and/or positive-unstable PRRS sow farms. The implementation of preventive vaccination of the breeding stock for PRRSv, with intent to minimize losses following wild-type virus introduction has been described (Arruda et al. 2017, Murtaugh and Genzow 2011). To the best of our knowledge, this is the first epidemiological study with multiple herd-vaccinations to document the effects of PRRS MLV vaccination on productivity parameters under field conditions.

Some negative effects of vaccinating pregnant sows for PRRS with a MLV vaccine have been reported and contrast the results of that this study (Bøtner et al. 1997). One study reported that the vaccination should be avoided on pregnant sows and implemented only on non-pregnant females, due to decreasing of the number of pigs born alive and weaned (Dewey et al. 2004a). On another study, the same author reported that vaccinating sows against PRRS caused production losses by increasing the number of stillbirths and mummified pigs (Dewey et al. 1999a). Similarly, intranasal immunization of sows, at late stage of gestation, for PRRS was associated with neonatal losses and pre-weaning mortality in a PRRSV-seronegative herd (Nielsen et al. 2002).

The variables defined as counts were adjusted by herd size by having log-herd size as an offset parameter in the model with a Poisson distribution. Likewise, other intrinsic factors from specific herds were also in part adjusted for, by having the variable ‘Farm’ as random effect in the regression models. For pre-weaning mortality and Pigs weaned per sow the PEDV status was also a random effect. Season has been reported as a risk factor for PRRS infection and related with changes in production parameters of breeding sows, such as aborts, prenatal losses, and pre-weaning mortality (Alkhamis et al. 2018, Tousignant et al. 2015, Holtkamp et al. 2010, Rangstrup-Christensen et al. 2017). Thus, to take seasonality into account, this study had a dynamic baseline parameter for herd vaccination. More specifically, the effect of MLV vaccination on each production parameter was compared to the average of 6 weeks prior to vaccination, making the assessment of the effect of vaccinations robust to seasonal effects.

It was a limitation of the study the fact that it was retrospective, which makes it naturally subjected to recall and information bias. Also, the analyses were not adjusted to other factors that had potential effect on the outcome variables.

In conclusion, although some farms had some changes in productivity, at the aggregated data analysis level there was no significant change in abort rate, neonatal losses, number of pigs weaned per sow, and wean to first service interval on PRRS-stable herds implementing PRRS MLV quarterly vaccinations. For pre-weaning mortality, there was an increase of 0.26% on the week 2 after vaccination compared to the baseline. All changes were compared to up to 6 weeks post vaccination, as compared to 6 weeks prior to vaccination. Results from this study support that adopting PRRS MLV quarterly vaccinations on PRRS-stable herds has little impact on breeding herd productivity parameters.

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