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Genetic analysis of reproductive performance in sows during porcine reproductive and respiratory syndrome (PRRS) and porcine epidemic diarrhea (PED) outbreaks

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Genetic analysis of reproductive performance in sows during porcine reproductive and respiratory syndrome (PRRS) and porcine epidemic diarrhea (PED) outbreaks

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NOMENCLATURE

AB	Abortion
AIC	Akaike information criteria
EBV	Estimated breeding value
ELISA	Enzyme-linked immunosorbent assay
HYW	Herd-year-week
ID	Identification
MUM	Number of piglets mummified
NBA	Number of piglets born alive
NBD	Number of piglets born dead
NW	Number of piglets weaned
PED	Porcine epidemic diarrhea
PEDV	Porcine epidemic diarrhea virus
PROP	Proportion of piglets born dead
PRRS	Porcine reproductive and respiratory syndrome
PRRSV	Porcine reproductive and respiratory virus
qPCR	Quantitative polymerase chain reaction
RA	Rolling average
SB	Number of piglets stillborn
SD	Standard deviation
TB	Total number of piglets born

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ABSTRACT

Porcine reproductive and respiratory syndrome (PRRS) and porcine epidemic diarrhea (PED) are diseases that have been plaguing the swine industry for years and strategies to prevent and control them have shown limited success. Studies have suggested that selection for improved performance during PRRS infection is possible. In this thesis, we analyzed the effects of PRRS and PED on reproductive performance in commercial sows. The first chapter of this thesis is a review of the current literature related to the impact, causes, clinical signs, and methods of control for both PRRS and PED. This chapter also encompasses the genetic response to disease and methods to select for improved performance. The second chapter presents results of a genetic analysis for reproductive traits in commercial sows infected or not with PRRS or PED viruses. Results show that disease (PRRS or PED) was significant ($P < 0.05$) for all reproductive traits, except for total piglets born. Performance during PED and Clean was similar for all traits, with the exception of number of piglets weaned and abortion, which were lower for PED than for Clean. Heritability estimates were generally low, but these increased during for PED and PRRS compared to Clean. Genetic correlations within trait, between disease statuses, estimates ranged from -0.17 (number weaned between PRRS and PED) to 0.99 (abortion between Clean and PRRS). Overall, genetic correlations were positive between disease statuses, indicating that relationships between clean and disease are favorable for selection. Overall, these results indicate that selection for improved performance during PRRS and PED in commercial sows is possible and would not negatively impact performance in clean environments.

CHAPTER 1: LITERATURE REVIEW

Introduction

In the late 1980's [1], a new disease broke out in the United States, now known as porcine reproductive and respiratory syndrome (PRRS). Since this outbreak, PRRS has spread throughout the United States and the world, costing the swine industry an estimated $664 million each year in the United States alone [2]. Since PRRS affects both respiration and reproduction, it affects pigs at all levels of production [3].

Porcine reproductive and respiratory syndrome virus (PRRSV) is a positive-stranded RNA virus, which belongs to the family *Arteriviridae*, of the order *Nidovirales* [4]. The virus has two genotypes, Type 1, the European strain and Type 2, the North American strain, which are 67% homologous at the nucleotide level [5,6]. The virus is transmitted via nose to nose contact, contact with urine or feces, via infected semen, and aerial transmission [7,8]. PRRSV can persist within infected pigs for long periods of time and is rapidly mutating within the herd, which enables it to persist and spread easily [9–11].

Clinical signs of infection with PRRSV are respiratory infection and impaired performance, slower growth in growing pigs and reproductive failure in sows [12]. With PRRSV infection, there is an increase in mortality of young pigs and also an increase in secondary infections which can also lead to death [3,13].

Methods of control for PRRSV include biosecurity, which helps to prevent infection and limit the spread of disease once the farm is infected. Vaccination is also a method to help prevent and control severity of disease, although currently no vaccine is able to completely prevent the disease due to high rates of mutation of the virus [14–16]. Other strategies are used to remove the

virus from the farm after infection including, de-population and re-population and herd closure [17,18]. Due to the ineffectiveness of these strategies at adequately controlling PRRSV and alternative strategy has been proposed to select for more tolerant animals. The most successful strategy would include a combination of current strategies, including vaccination, farm management, increase in biosecurity, and improved resistance using genetic selection.

Another disease that has been devastating to the swine industry is porcine epidemic diarrhea (PED). PED is a gastric disease that was first observed in 1971 in England and soon spread throughout Europe and into Asia [19,20]. In 2013, porcine epidemic diarrhea virus (PEDV) spread to the United States and then to both Canada and Mexico and based on homology, it is believed to have come from the more severe Chinese strain of the virus [21,22]. The United States lost approximately 10% of its swine population within the first year of infection [23]. This, plus costs associated with attempts to control the spread of PEDV had a very large economic impact on the U.S. swine industry [24].

PED is caused by a single stranded RNA virus in the *Coronavirdae* family in the order *Nidovirales* [25]. PEDV is transmitted via fecal and oral transmission with infected animals, surfaces, or feed [26–28]. Clinical signs include diarrhea, vomiting, and dehydration followed by anorexia and depression [23]. In suckling piglets, mortality is around 95% for piglets under 2 weeks of age and drops to 40% for piglets between 2 and 4 weeks of age [21].

Methods of control for PEDV is similar to that of PRRS, using biosecurity and vaccination to attempt to prevent and control the spread of the disease [24]. Under experimental conditions, vaccination is effective, but vaccines seem to be strain specific and thus not very effective in the field [29–32]. An alternative to these methods is the use of feedback to intentionally infect pregnant sows to stimulate rapid immunity and shorten the outbreak on the

farm [24]. It is possible that other infections like PRRSV can be spread through this method or that sow will not reach an adequate level of immunity to protect offspring, but will instead facilitate further disease spread [24,33,34].

Porcine Reproductive and Respiratory Syndrome (PRRS)

Impact

The first outbreak of porcine reproductive and respiratory syndrome (PRRS) in the United States was described in the late 1980's [1]. It has since spread across the world causing both economic and welfare concerns. It is estimated that PRRS costs $664 million in the United States alone in productivity losses for breeding and growing pig herds combined [2]. There is also an additional cost of $477.8 million in health, biosecurity, and other outbreak related costs per year [2]. In the United States, it is estimated that 40% to 60% of herds are or have been infected, with variation from 0% to 80% in different states [35,36]. Since PRRS is both a respiratory and reproductive disease, it affects pigs at all levels. At the reproductive level, there is an increase in piglet mortality and in growing pigs, there is a decrease in growth and an increase in mortality, especially with an increased risk of co-infection [3,37].

Cause

The cause of PRRS is a positive-stranded RNA virus, which belongs to the family *Arteriviridae*, of the order *Nidovirales* [4]. Porcine reproductive and respiratory virus (PRRSV) is similar to the equine arteritis cirus, mouse lactate dehydrogenase-elevating virus, and simian hemorrhagic fever virus which are in the same family [38]. There are two stains of the PRRSV, type 1 (Eurpopean strain) and type 2 (American strain) [5]. The two types of the virus are 67%

homologous at the nucleotide level [6]. Domestic pigs and wild boars are the only known animals to become naturally infected with PRRSV [8]. Route of transmission is through nose to nose contact, contact with urine or feces, via infected semen, and aerial transmission up to 20 km [7,8]. Many excretions of the infected animals have been shown to contain PRRSV, which increases the spread [3]. The spread of PRRS is enhanced in the winter, when temperature, wind speed and exposure to ultra violet light are low and humidity is high [12]. PRRSV can persist for long periods of time in pigs that are infected, which enables it to persist in the herd [9]. Since PRRSV is a rapidly mutating virus, multiple strains of the virus can infect the herd at the same time [10,11]. Due to these possible transmission routes and persistence of PRRSV, risk factors for PRRSV infection seem to be: large herd size, lack of quarantine upon entrance to the farm, and a large number of animal introductions within a farm. Once pigs become infected ~95% of the herd will become positive within 2 to 3 months [39] and infection can persist for more than 3 months following initial infection [13].

Clinical signs

Animals infected with PRRSV show respiratory symptoms and impaired performance, such as slower growth rates in newborn and growing pigs and reproductive failure in pregnant sows [12]. Reproductive failure includes abortion storms, increase in number of piglets born dead and decrease of number of piglets born alive. Piglets that are born alive are often born weak and fail to thrive [40]. The virus can transmit across the placenta and infect piglets while still in utero [41]. Other symptoms includes sneezing, coughing, fever, blue coloration of the ears, and decreased growth rate [42–44]. Infection with PRRSV causes and increase in mortality and

morbidity in young pigs and increases the chance of secondary infections [3]. Secondary infections can include *Eshichia coli, Streptococcus suis,*and *Salmonella choleraesuis* [13].

Methods of control

Methods of PRRS control has been largely ineffective. Low pig densities and limitation of pig movement can help to decrease spread, but in areas with higher pig populations, this is impossible. One method to help prevent diseases and decrease the spread if the farm breaks is biosecurity. Things to consider regarding biosecurity is pig contact, herd location, vehicles, visitors and staff, feed and water, and wildlife and vermin [45]. Pig to pig contact is the biggest risk for new infections, even pigs that show now physical symptoms may be carriers [45]. The movement of pigs facilitates the spread, so closing the herd can help to limit spreading the disease [18]. Once a herd breaks with PRRS, the herd can be closed and no replacements are allowed to enter the farm for a minimum of six months. A negative to this method of herd closure is that genetically superior females are unable to be brought into the farm, so genetic progress may suffer due to an outbreak. Another biosecurity method that attempt to prevent infection is in the farm itself. The farm should be in a remote location with only a single approach road, controlled access to the farm, defined farm boundary with wildlife proof fence, separate clean and dirty areas with showers and changing rooms, dedicated clothing and boots, and separate isolation units for new pigs [45].

Another method of control for PRRS is vaccination. There is a high amount of genetic diversity between and within the European and American strains of the virus [46–49]. Due to the high amount of genetic diversity with and between the strains, it has been difficult to produce a vaccine that is both effective and cross-protective for the different strains. Some studies [50]

suggest that vaccines developed from the American strain of PRRS are more effective on the American strain, but also show some degree of efficacy for the European strain as well. There are two types of vaccines: killed and modified live (MLV), with modified live being more effective against PRRS [15,17,51]. A problem with MLV is that, although clinical signs are reduced, the vaccine does not prevent infection, so naïve pigs could be infected with the vaccine [11]. Adding to the difficulty is the high rate of mutation of the virus, which causes more variants developed, decreasing the effectiveness of the vaccine [48,51,52]. Currently, there is no vaccine that fully protects against strains of PRRSV [14–16]. It is difficult to develop a vaccine that is effects even for only one farm because multiple PRRSV variants can exists within one farm, even within one animal during an infection [52]. In order to create a vaccine that could eradicate PRRS, it would need to be universal, effective, safe, and able to differentiate between pigs that have been vaccinated and those that are infected [53].

A different method of vaccination is to use a “load-close-expose” approach, which attempts to increase immunity to PRRS within the herd by exposing them to replicating PRRSV, since studies show that previously exposed herds recover faster than naïve herds when re-exposed [54]. Although the herd became PRRS negative faster with this approach, there were more production losses when compared to the use of normal vaccination [54].

Another strategy of PRRS control is the de-population and re-population of a farm that has a PRRS outbreak. After an outbreak, all animals are removed from the farm, the facilities are cleaned thoroughly, and then new PRRS-free animals are brought in to re-populate the farm. This method, while effective, is also very expensive [17]. The cost incurred are due the euthanasia of the pigs, the loss of production during disinfection, and the cost of the replacement

animals. This method seems to be more effective for farms that are isolated rather than in an area that is more densely populated with pigs.

An alternative strategy that deals with pig flow through a farm is an all-in all-out strategy. This is a more costly approach than closing the herd [18]. Pigs are grouped together in separate rooms by age that keep older possibly infected pigs from coming into contact with new pigs entering the farm in order to control horizontal transmission [55].

Due to insufficiencies in other attempts at controlling the spread of PRRS, producing more tolerant animals to PRRSV has been seen as an alternate or additional method. There has also been pressure from consumers to increase animal welfare, which has shifted the breeding goal of producers to creating a more disease resistant pig [56]. For PRRS, several studies have indicated that there is a genetic component to disease resilience [43,56–58].

The most successful PRRS control strategy would probably need to include a combination of the current strategies. There would need to be good farm management, an increase in both farm and transportation biosecurity, vaccination, and improved resistance by genetic selection.

Porcine Epidemic Diarrhea (PED)

Impact

Porcine epidemic diarrhea (PED) is a gastric disease that was first observed in 1971in England [20]. Initially, PEDV presented like a similar disease, porcine transmissible gastroenteritis virus (TGEV), but when PEDV re-emerged after five years, it began effecting pigs of all ages, including newborn piglets, so the initial outbreak was then classified as type 1 and the later outbreak as type 2 [20,59]. In 1978, the causative pathogen of PED was identified,

CV777, which was found to be distinct from other known coronaviruses [20,60]. Like PRRS, outbreaks are more frequent during the winter months. In the 1980's and 1990's, PED spread throughout Europe [19] and into Asia soon after. Outbreaks of porcine epidemic diarrhea virus (PEDV) in Asia were oftentimes more severe than the outbreaks that occurred in Europe [19]. In 2013, PEDV spread to the United States and spread rapidly through the U.S. and to both Canada and Mexico [21]. It is believed that the initial outbreak in the United States is from China due to 99% homology of the strains [21,22]. Due to the increase in mortality in piglets and costs associated with vaccination and attempts to control the spread of infection, the economic impact of PEDV is very high, with U.S. losing almost 10% of its pig population within the first year of infection, which was approximately 7 million piglets [23]. After the outbreak in North America, PEDV has since re-emerged in Asia and has made itself one of the most devastating swine viral diseases in the world with significant concerns for the swine industry globally [24].

Cause

PED is caused by a single stranded RNA virus in the *Coronavirdae* family in the order *Nidovirales* [25]. It was grouped based on similarities in replication and genome organization. Like other viruses, PEDV may disrupt signaling pathways or other factors within the host, to enable it to spread and multiply [24]. Unlike PRRS, piglets are not infected in utero during a PEDV outbreak, piglets are born healthy and subsequently infected after birth. PEDV is transmitted through fecal to oral route through contact with infected animals, surfaces, or feed [26–28]. After infection, PEDV spreads through diarrhea and then collects in the tissues and small intestine [60].

Clinical signs

PED causes malabsorptive watery diarrhea, vomiting, dehydration, and blood electrolyte imbalances followed by anorexia and depression [24]. There is approximately a 2 day incubation period, there are 3-4 weeks between when symptoms start and cease, and the virus is shed in the feces for up to 4 weeks [32,61,62]. In piglets less than 2 weeks of age, mortality is around 90-95%, but drops to 40% for piglets between 2 and 4 weeks of age. [21]. During necropsies on piglets that died from PEDV, lesions were found in the small intestine, which was also filled with yellow fluid and villi on the walls of the small intestine were atrophied [19]. Severity of disease and mortality are inversely related to age of the pig, with young pigs having the most severe infection and highest mortality, growing pigs tend to have decreased growth performance due to diarrhea, and sows have the fewest symptoms, but often exhibit depression and anorexia [32]. Due to its similarity to another virus, transmissible gastroenteritis virus (TGEV), it is difficult to diagnose PEDV without laboratory testing [19].

Methods of control

Many control methods of PED are similar to that of PRRS. Biosecurity is of utmost importance to try to prevent diseases. Like for PRRS, farms should be isolated with limited access, with separate isolation barns for new animals, shower-in/out facilities, dedicated work clothes and boots, and means of disinfecting [45]. Many commercially available viral disinfectants seem to inactive PEDV, but other disinfectants may be less effective, especially in the winter months when PEDV seems to spread the most [24,63]. Recommended disinfection protocol includes: cleaning with a high pressure washer using warm water, disinfection with an appropriate disinfectant, and overnight drying [24].

Another method of control for PED is vaccination. Outbreaks in Europe were not severe enough to warrant vaccine development, but economic loses in Asian were much more severe and several vaccines were developed to help combat PED [24]. An attenuated vaccine was created using the CV777 strain in China, the 83P-5 strain in Japan, and the SM98-1 and DR-13 strains in South Korea [64–66]. Live vaccines have also been created using Japanese and South Korean virulent strains [24]. Under experimental conditions, the attenuated vaccines have been shown to be effective, but field effectiveness is still debated [24]. In South Korea, the vaccination program administers 3 or 4 vaccine doses as 2 to 3 week intervals before farrowing to maintain antibodies in pregnant gilts and sows, so piglets are protected by maternal antibodies via colostrum [67]. Current commercially available vaccines are shown to be low to moderately effective due to differences in vaccine and field strains of the virus [29–32]. In order to create a more effective vaccine, the next generation of vaccines need to be created using the current field strains of PEDV [31]. An inactivated vaccine was created and is commercially available in the United States using PEDV strains from recent outbreaks [68,69].

There are alternative strategies that are also used to try to control PED. The use of feedback to intentionally expose pregnant sows to the virus during an acute infection stimulates rapid immunity and shortens the outbreak on the farm [24]. Although it may help to shorten the outbreak on the farm, there are several potential negative consequences to this approach. Using feedback may also expose the herd to other pathogens, like PRRSV, that can then spread throughout the farm [33,34]. It is also possible that sows will not reach an immunity level that would be sufficient to protect offspring, but instead will further spread the disease through fecal shedding [24].

REFERENCES

1. Keffaber KK. Reproductive failure of unknown etiology. Am Assoc Swine Pr Newsl. 1989;
2. Holtkamp DJ, Kliebenstein JB, Neumann EJ, Zimmerman JJ, Rotto HF, Yoder TK, et al. Assessment of the economic impact of porcine reproductive and respiratory syndrome virus on United States pork producers. J Swine Heal Prod [Internet]. 2013;21(2):72–84. Available from: http://www.aasv.org/shap/issues/v21n2/v21n2p72.html
3. Zimmerman JJ, Yoon KJ, Wills RW, Swenson SL. General overview of PRRSV: A perspective from the United States. In: Veterinary Microbiology. 1997.
4. Cavanagh D, Cavanaugh D. Nidovirales: a new order comprising Coronaviridae and Arteriviridae. Arch Virol. 1997;
5. Rowland RRR, Lunney J, Dekkers J. Control of porcine reproductive and respiratory syndrome (PRRS) through genetic improvements in disease resistance and tolerance. Frontiers in Genetics. 2012.
6. Rowland RRR, Morrison RB. Challenges and Opportunities for the Control and Elimination of Porcine Reproductive and Respiratory Syndrome Virus. Transboundary and Emerging Diseases. 2012.
7. Yaeger MJ, Prieve T, Collins J, Christopher-Hennings J, Nelson N, Benfield D. Evidence for the transmission of porcine reproductive and respiratory syndrome (PRRS) virus in boar semen. Swine Heal Prod. 1993;
8. Albina E. Epidemiology of porcine reproductive and respiratory syndrome (PRRS): An overview. In: Veterinary Microbiology. 1997. p. 309–16.
9. Wills RW, Doster AR, Galeota JA, Sur JH, Osorio FA. Duration of infection and

proportion of pigs persistently infected with porcine reproductive and respiratory syndrome virus. J Clin Microbiol. 2003;

10. Fang Y, Schneider P, Zhang WP, Faaberg KS, Nelson EA, Rowland RRR. Diversity and evolution of a newly emerged North American Type 1 porcine arterivirus: Analysis of isolates collected between 1999 and 2004. Arch Virol. 2007;
11. Kimman TG, Cornelissen L a, Moormann RJ, Rebel JMJ, Stockhofe-Zurwieden N. Challenges for porcine reproductive and respiratory syndrome virus (PRRSV) vaccinology. Vaccine. 2009;
12. Lunney JK, Steibel JP, Reecy JM, Fritz E, Rothschild MF, Kerrigan M, et al. Probing genetic control of swine responses to PRRSV infection: Current progress of the PRRS host genetics consortium. In: BMC Proceedings. 2011.
13. Chung W Bin, Lin MW, Chang WF, Hsu M, Yang PC. Persistence of Porcine Reproductive and Respiratory Syndrome Virus in Intensive Farrow-to-Finish Pig Herds. Can J Vet Res. 1997;
14. Diaz I, Darwich L, Pappaterra G, Pujols J, Mateu E. Immune responses of pigs after experimental infection with a European strain of Porcine reproductive and respiratory syndrome virus. J Gen Virol [Internet]. 2005;86(7):1943–51. Available from: http://jgv.microbiologyresearch.org/content/journal/jgv/10.1099/vir.0.80959-0
15. Charerntantanakul W. Porcine reproductive and respiratory syndrome virus vaccines: Immunogenicity, efficacy and safety aspects. World J Virol. 2012;
16. Li X, Galliher-Beckley A, Pappan L, Trible B, Kerrigan M, Beck A, et al. Comparison of host immune responses to homologous and heterologous type II porcine reproductive and respiratory syndrome virus (PRRSV) challenge in vaccinated and unvaccinated pigs.

Biomed Res Int. 2014;

17. Corzo CA, Mondaca E, Wayne S, Torremorell M, Dee S, Davies P, et al. Control and elimination of porcine reproductive and respiratory syndrome virus. Virus Research. 2010.
18. Schaefer N, Morrison R. Effect on total pigs weaned of herd closure for elimination of porcine reproductive and respiratory syndrome virus. J Swine Heal Prod. 2007;
19. Song D, Park B. Porcine epidemic diarrhoea virus: a comprehensive review of molecular epidemiology, diagnosis, and vaccines. Virus Genes. 2012;44(2):167–75.
20. Wood EN. An apparently new syndrome of porcine epidemic diarrhoea. Vet Rec. 1977;
21. Stevenson GW, Hoang H, Schwartz KJ, Burrough ER, Sun D, Madson D, et al. Emergence of Porcine epidemic diarrhea virus in the United States: clinical signs, lesions, and viral genomic sequences. J Vet Diagn Invest [Internet]. 2013;25(5):649–54. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23963154
22. Huang YW, Dickerman a W, Pineyro P, Li L, Fang L, Kiehne R, et al. Origin, evolution, and genotyping of emergent porcine epidemic diarrhea virus strains in the United States. MBio. 2013;4(5):e00737-13.
23. Jung K, Saif LJ. Porcine epidemic diarrhea virus infection: Etiology, epidemiology, pathogenesis and immunoprophylaxis. Vol. 204, Veterinary Journal. 2015. p. 134–43.
24. Lee C. Porcine epidemic diarrhea virus: An emerging and re-emerging epizootic swine virus. Virology Journal. 2015.
25. Weiss SR, Navas-Martin S. Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. Microbiol Mol Biol Rev. 2005;
26. Alonso C, Goede DP, Morrison RB, Davies PR, Rovira A, Marthaler DG, et al. Evidence of infectivity of airborne porcine epidemic diarrhea virus and detection of airborne viral

RNA at long distances from infected herds. Vet Res. 2014;

27. Dee S, Clement T, Schelkopf A, Nerem J, Knudsen D, Christopher-Hennings J, et al. An evaluation of contaminated complete feed as a vehicle for porcine epidemic diarrhea virus infection of nai¨ve pigs following consumption via natural feeding behavior: Proof of concept. BMC Vet Res. 2014;
28. Lowe J, Gauger P, Harmon K, Zhang J, Connor J, Yeske P, et al. Role of transportation in spread of porcine epidemic diarrhea virus infection, United States. Emerg Infect Dis. 2014;
29. Lee S, Lee C. Outbreak-related porcine epidemic diarrhea virus strains similar to US strains, South Korea, 2013. Emerg Infect Dis. 2014;
30. Lee DK, Park CK, Kim SH, Lee C. Heterogeneity in spike protein genes of porcine epidemic diarrhea viruses isolated in Korea. Virus Res. 2010;
31. Oh J, Lee KW, Choi HW, Lee C. Immunogenicity and protective efficacy of recombinant S1 domain of the porcine epidemic diarrhea virus spike protein. Arch Virol. 2014;
32. Lee S, Kim Y, Lee C. Isolation and characterization of a Korean porcine epidemic diarrhea virus strain KNU-141112. Virus Res. 2015;
33. Jung K, Ha Y, Ha SK, Kim J, Choi C, Park HK, et al. Identification of porcine circovirus type 2 in retrospective cases of pigs naturally infected with porcine epidemic diarrhoea virus. Vet J. 2006;
34. Park JS, Ha Y, Kwon B, Cho KD, Lee BH, Chae C. Detection of Porcine Circovirus 2 in Mammary and Other Tissues from Experimentally Infected Sows. J Comp Pathol. 2009;
35. Cho SH, Freese WR, Yoon IJ, Trigo A V, Joo HS. Seroprevalence of indirect fluorescent antibody to porcine reproductive and respiratory syndrome virus in selected swine herds. J

Vet Diagn Invest. 1993;

36. Bautista EM, Morrison RB, Goyal SM, Collins JE, Annelli JF. Seroprevalence of PRRS virus in the United States. Swine Heal Prod. 1993;

37. Christianson WT, Joo HS. Porcine reproductive and respiratory syndrome: a review. Swine Heal Prod. 1994;

38. Lunney JK, Fang Y, Ladinig A, Chen N, Li Y, Rowland B, et al. Porcine Reproductive and Respiratory Syndrome Virus (PRRSV): Pathogenesis and Interaction with the Immune System. Annu Rev Anim Biosci [Internet]. 2016;4(1):129–54. Available from: http://www.annualreviews.org/doi/10.1146/annurev-animal-022114-111025

39. Terpstra C, Wensvoort G, van Leengoed L. Persistence of Lelystad virus in herds affected by porcine epidemic abortion and respiratory syndrome. Proc 12th Congr IPVS, Hague, Netherlands. 1992;

40. Wensvoort G, Terpstra C, Pol JM, ter Laak EA, Bloemraad M, de Kluyver EP, et al. Mystery swine disease in The Netherlands: the isolation of Lelystad virus. Vet Q. 1991;

41. Christianson WT, Choi CS, Collins JE, Molitor TW, Morrison RB, Joo HS. Pathogenesis of porcine reproductive and respiratory syndrome virus infection in mid-gestation sows and fetuses. Can J Vet Res [Internet]. 1993;57(4):262–8. Available from: http://www.hubmed.org/display.cgi?uids=8269364

42. Doeschl-Wilson AB, Kyriazakis I, Vincent A, Rothschild MF, Thacker E, Galina-Pantoja L. Clinical and pathological responses of pigs from two genetically diverse commercial lines to porcine reproductive and respiratory syndrome virus infection. J Anim Sci. 2009;

43. Boddicker N, Waide EH, Rowland RRR, Lunney JK, Garrick DJ, Reecy JM, et al. Evidence for a major QTL associated with host response to porcine reproductive and

respiratory syndrome virus challenge. J Anim Sci. 2012;

44. Rossow KD. Porcine Reproductive and Respiratory Syndrome. Veterinary Pathology. 1998.

45. Pritchard G, Dennis I, Waddilove J. Biosecurity: Reducing disease risks to pig breeding herds. In Pract. 2005;

46. Forsberg R, Storgaard T, Nielsen HS, Oleksiewicz MB, Cordioli P, Sala G, et al. The genetic diversity of European type PRRSV is similar to that of the North American type but is geographically skewed within Europe. Virology. 2002;

47. Lunney JK, Benfield DA, Rowland RRR. Porcine reproductive and respiratory syndrome virus: An update on an emerging and re-emerging viral disease of swine. Virus Research. 2010;

48. Nelsen CJ, Murtaugh MP, Faaberg KS. Porcine reproductive and respiratory syndrome virus comparison: Divergent evolution on two continents. J Virol. 1999;

49. Zimmerman J, Benfield D, Christopher-Hennings J, Dee S, Stevenson G. Swine Diseases: Porcine Reproductive and Respiratory Syndrome (PRRS). Agricultural Disaster Preparedness and Recovery, Hogs, Pigs, and Pork. 2012.

50. Lager KM, Mengeling WL, Brockmeier SL. Evaluation of protective immunity in gilts inoculated with the NADC-8 isolate of porcine reproductive and respiratory syndrome virus (PRRSV) and challenge-exposed with an antigenically distinct PRRSV isolate. Am J Vet Res. 1999;

51. Meng X. Heterogeneity of porcine reproductive and respiratory syndrome virus: implications for current vaccine efficacy and future vaccine development. Vet Microbiol. 2000;

52. Goldberg TL, Lowe JF, Milburn SM, Firkins LD. Quasispecies variation of porcine reproductive and respiratory syndrome virus during natural infection. Virology. 2003;317(2):197–207.

53. Mateu E, Diaz I. The challenge of PRRS immunology. Vol. 177, Veterinary Journal. 2008. p. 345–51.

54. Linhares DCL, Johnson C, Morrison RB. Economic analysis of vaccination strategies for PRRS control. PLoS One. 2015;

55. Scheidt AB, Cline TR, Clark LK, Mayrose VB, Alstine WG Van, Diekman M a, et al. The effect of all-in-all-out growing- finishing on the health of pigs. Swine Heal Prod. 1995;

56. Lewis CRG, Ait-Ali T, Clapperton M, Archibald AL, Bishop S. Genetic Perspectives on Host Responses to Porcine Reproductive and Respiratory Syndrome (PRRS). Viral Immunol [Internet]. 2007;20(3):343–58. Available from: http://www.liebertonline.com/doi/abs/10.1089/vim.2007.0024

57. Lewis CRG, Torremorell M, Galina-Pantoja L, Bishop SC. Genetic parameters for performance traits in commercial sows estimated before and after an outbreak of porcine reproductive and respiratory syndrome. J Anim Sci. 2009;87(3):876–84.

58. Serão NVL, Matika O, Kemp RA, Harding JCS, Bishop SC, Plastow GS, et al. Genetic analysis of reproductive traits and antibody response in a PRRS outbreak herd. J Anim Sci. 2014;92(7):2905–21.

59. Chasey D, Cartwright SF. Virus-like particles associated with porcine epidemic diarrhoea. Res Vet Sci. 1978;

60. Debouck P, Pensaert M. Experimental infection of pigs with a new porcine enteric coronavirus, CV 777. Am J Vet Res. 1980;

61. Pensaert MB, de Bouck P. A new coronavirus-like particle associated with diarrhea in swine. Arch Virol. 1978;

62. Wang X meng, Niu B bei, Yan H, Gao D sheng, Yang X, Chen L, et al. Genetic properties of endemic Chinese porcine epidemic diarrhea virus strains isolated since 2010. Arch Virol. 2013;

63. Bowman AS, Nolting JM, Nelson SW, Bliss N, Stull JW, Wang Q, et al. Effects of disinfection on the molecular detection of porcine epidemic diarrhea virus. Vet Microbiol. 2015;

64. Sato T, Takeyama N, Katsumata A, Tuchiya K, Kodama T, Kusanagi KI. Mutations in the spike gene of porcine epidemic diarrhea virus associated with growth adaptation in vitro and attenuation of virulence in vivo. Virus Genes. 2011;

65. Kweon CH, Kwon BJ, Lee JG, Kwon GO, Kang YB. Derivation of attenuated porcine epidemic diarrhea virus (PEDV) as vaccine candidate. Vaccine. 1999;

66. Song DS, Oh JS, Kang BK, Yang JS, Moon HJ, Yoo HS, et al. Oral efficacy of Vero cell attenuated porcine epidemic diarrhea virus DR13 strain. Res Vet Sci. 2007;

67. Park CK, Lee CH. Clinical examination and control measures in a commercial pig farm persistently infected with porcine epidemic diarrhea(PED) virus. J Vet Clin. 2009;

68. Chen Q, Li G, Stasko J, Thomas JT, Stensland WR, Pillatzki AE, et al. Isolation and characterization of porcine epidemic diarrhea viruses associated with the 2013 disease outbreak among swine in the united states. J Clin Microbiol. 2014;

69. Oka T, Saif LJ, Marthaler D, Esseili MA, Meulia T, Lin CM, et al. Cell culture isolation and sequence analysis of genetically diverse US porcine epidemic diarrhea virus strains including a novel strain with a large deletion in the spike gene. Vet Microbiol. 2014;

70. Bishop SC. Disease Resistance: Genetics. In: Encyclopedia of Animal Science, Second Edition. 2016.

71. Warner CM, Meeker DL, Rothschild MF. Genetic control of immune responsiveness: a review of its use as a tool for selection for disease resistance. Journal of animal science. 1987.

72. Mallard BA, Wilkie BN, Kennedy BW, Gibson JP, Quinton M. Immune responsiveness in swine: eight generations of selection for high and low immune response in Yorkshire pigs. In: Proceedings of the 6th World Congress on Genetics Applied to Livestock Production, Armidale, Australia, January 11-16, 1998 Volume 27: Reproduction; fish breeding; genetics and the environment; genetics in agricultural systems; disease resistance; animal. 1998.

73. Clapperton M, Bishop SC, Glass EJ. Selection for lean growth and food intake leads to correlated changes in innate immune traits in Large White pigs. Anim Sci. 2006;

74. Herrero-Medrano JM, Mathur PK, ten Napel J, Rashidi H, Alexandri P, Knol EF, et al. Estimation of genetic parameters and breeding values across challenged environments to select for robust pigs. J Anim Sci. 2015;93(4):1494–502.

75. Bishop SC, Woolliams JA. On the genetic interpretation of disease data. PLoS One. 2010;

76. Rashidi H, Mulder HA, Mathur P, Van Arendonk JAM, Knol EF. Variation among sows in response to porcine reproductive and respiratory syndrome. J Anim Sci. 2014;92(1):95–105.

CHAPTER 2: GENETIC ANALYSIS OF IN SOWS DURING REPRODUCTIVE AND RESPIRATORY SYNDROME (PRRS) AND PORCINE EPIDEMIC DIARRHEA (PED) OUTBREAKS

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Authors' contributions

CLS performed data editing and analyses, interpreted results, and drafted manuscript. AMP provided help and guidance for statistical analyses. KAG provided the data and interpreted results. NVLS assisted with data analysis and interpretation of results, and drafted manuscript. All authors read and approved the final version of the manuscript.

Abstract

Background

Porcine reproductive and respiratory syndrome (PRRS) is one of the most infectious swine diseases in the world, resulting in over $600 million dollars of economic loss in the U.S. alone. More recently, the U.S. swine industry has been having additional major economic losses due to the spread of porcine epidemic diarrhea (PED). However, information regarding the amount of genetic variation for response to diseases in reproductive sows is still very limited. The objectives of this study were to identify periods of infection with of PRRS virus (PRRSV) and/or PED virus (PEDV), and to estimate the impact their impact on the phenotypic and genetic reproductive performance of commercial sows.

Results

Disease (PRRS or PED) was significant ($P < 0.05$) for all traits analyzed except for total piglets born. Heritability estimates for traits during Clean (without any disease), PRRS, and PED ranged from 0.01 (number of mummies; Clean and PED) to 0.41 (abortion; PED). Genetic correlations between traits within disease statuses ranged from -0.99 (proportion born dead with number weaned; PRRS) to 0.99 (number born dead with born alive; Clean). Within trait, between disease statuses, estimates ranged from -0.17 (number weaned between PRRS and PED) to 0.99 (abortion between Clean and PRRS).

Conclusion

Results indicate that selection for improved performance during PRRS and PED in commercial sows is possible and would not negatively impact performance in Clean environments.

Key words: Genetic Evaluation, Porcine Epidemic Diarrhea, Porcine Reproductive and Respiratory Syndrome, Reproductive Performance, Swine

Introduction

Porcine reproductive and respiratory syndrome (PRRS) is one of the most infectious swine diseases in the world. Animals infected with the PRRS virus (PRRSV) show respiratory symptoms and impaired performance, such as slower growth rates in newborn and growing pigs and reproductive failure in pregnant sows [1]. This major disease results in $664 million dollars of economic loss per year to the US swine industry [2].

More recently, another disease that has been causing severe economic impacts in the US swine industry is porcine epidemic diarrhea (PED). Pigs of all ages infected with the PED virus (PEDV) show diarrhea and vomiting, with affected piglets experiencing nearly 100% mortality within two to three days of birth [3,4].

Vaccination and biosecurity have been the main prevention strategies to control PRRS. Although these strategies have shown to limit the impact of this disease at some degree, additional strategies should be evaluated to help further decrease the impact of PRRS. Recent studies have suggested that selection for improved performance in PRRSV-infected sows is possible [5–8]. These authors reported moderate to low heritability estimates for reproductive performance in infected sows. For PED, there is even less information in the literature, with only one genomic study to date, in which they identified regions associated with piglet recovery and death during PEDV infection, but no genetic parameters were estimated [9].

The objectives of this study were: (1) to identify periods of infection of PRRSV and/or PEDV, (2) to estimate the impact of diseases (PRRS and/or PED) on reproductive performance

of commercial sows, and (3) to estimate genetic parameters within and between challenged and non-challenged environments.

Materials and methods

Data

Performance data and a five-generation pedigree were available from 10 commercial farms in North Carolina, USA. Data included 21,160 farrowing records from 5,352 Large White x Landrace crossbred multiparous sows farrowing from April 2013 to January 2016. All sows used in this study were first parity gilts when collection started, and no new animals were added to the dataset. At the start of data collection, all the sows used were PRRS- and PED-negative for these viruses. The sows used were fully pedigreed and were progeny of 100 sires and 1,595 dams. Progeny of sires were well distributed across farms, with only 8 sires present in 3 or fewer farms. On average, sires had 5.96 progeny sows per farm. Traits analyzed included abortion (AB; a binary trait with either 0 [nonevent] or 1 [event]), total number of piglets born (TB, pigs/litter; calculated as sum of NBA, SB, and MUM), number of piglets born alive (NBA, pigs/litter), number of stillborn piglets (SB, pigs/litter), number of mummified piglets (MUM, pigs/litter), number of piglets born dead (NBD, pigs/litter; calculated as the sum of SB and MUM), proportion of piglets born dead (PROP, pigs/litter; calculated as NBD/TB), and number weaned (NW, pigs/litter). Traits with a large number of zeros (SB, MUM, and NBD) were analyzed as the natural log of the phenotype + 1 in order to create a more normal and narrow distribution for those traits [8,10]. Sows with duplicated identification (ID) numbers (i.e. wrong duplicated IDs) were removed as well as those with TB greater than 25 or less than 3. After data editing, 20,796 farrow events from 5,314 sows were used for analyses. The number of parities ranged from 1 to

8 with an average parity of 3.0 (SD = 1.7). The average number of animals and farrowing records per farm was 541.2 (SD = 186.0) and 2,195.6 (SD = 741.9), respectively. Table 2.1 shows summary statistics of the traits analyzed.

Identification of PRRS and PED Outbreaks

Data was split into PRRS and/or PED affected, or Clean status at each farm based on unique herd-year-week (HYW) estimates, as proposed by Rashidi et al. [7]. To obtain HYW estimates for each trait separately, the whole data was analyzed using the following model:

$$Y_{ijklm} = \mu + PAR_i + YR_j + FARM_k + hyw_l + sow_m + e_{ijklm} \quad \text{[Eq. 1]}$$

where Y_{ijklm} is the phenotypic value of a trait; μ is the mean; PAR_i is the fixed effect of the i^{th} parity; YR_j is the fixed effect of the j^{th} year; $FARM_k$ was the fixed effect of the k^{th} farm; hyw_l is the random effect of the l^{th} herd-year-week, assuming $hyw \sim N\left(0, \boldsymbol{I}\sigma^2_{hyw}\right)$, where $\boldsymbol{I}$ is the identity matrix; sow_m is the random effect of the m^{th} sow, assuming $sow \sim N(0, \boldsymbol{I}\sigma^2_{sow})$; and e_{ijklm} is the random residual associated with Y_{ijklm}, assuming $e \sim N(0, \boldsymbol{I}\sigma^2_e)$. All traits were analyzed with a linear mixed model, with the exception of AB, in which a logit mixed model was used. A total of 1,332 HYW levels were generated, ranging from 5 to 75 farrowing records per HYW level, with an average of 17.2 (SD =9.13). Because of removal of animals due to standard production procedures, such as lameness, poor insemination rates, and more, there were more data at the beginning of the study, and these decreased as time went on and animals were culled.

Outbreaks of PRRS were identified using only the traits AB, NBA, and NBD, whereas NW was used to identify PED outbreaks. These traits were chosen because an increase in AB

and NBD and a decrease in NBA are indicative of a PRRS outbreak [1], and a decrease in NW is indicative of a PED outbreak [4]. HYW estimates were standardized and considered extreme when greater or lower than 1.96 and -1.96, respectively. These values were chosen as they represent the limits for 95% of the data; since specific directions are expected (e.g. decrease in NBA for PRRS outbreaks), a one-tail limit was used. A window of time was deemed as a PRRS outbreak when simultaneous increases in AB and NBD occurred along with a decrease in NBA for a period of two or more consecutive weeks. A decrease in NW for a period of two or more weeks was used to identify PED outbreaks. This strategy to identify PRRS outbreaks was used and shown to be effective by Lewis et al. and Rashidi et al. [7,10]. Weeks where these traits did not show extreme standardized HYW estimates were considered to be disease free (i.e. Clean). All outbreaks were confirmed with results from periodic serological tests that each farm performed, following their standard operation procedures, in which PRRS and PED outbreaks were confirmed via ELISA and qPCR, respectively.

Figure 2.1 shows predicted disease windows for a single farm atop the rolling averages (RA) for AB, NBA, NBD, and NW. A 30-d RA was used for NBA, NBD and NW, and a 30-d RA of the proportion of abortions was used to depict AB. For AB, the proportion of abortions was defined as the RA of the ratio of the RA of number of abortions events to total events (sum of RA of abortions and RA of farrowing events per day). There were two instances in this data where there was an overlap in the predicted PRRS and PED windows. The overlaps were in total three weeks long and contained only 61 records. Preliminary analysis indicated that the mean performance of animals within the overlaps was different than both PRRS and PED, but because of this single event and small sample size, these data were excluded from the analysis.

Further Refining Disease Statuses

Initial analyses identified 8 and 15 periods of PRRS and PED outbreaks, respectively. The average length (in weeks) of the Clean, PRRS, and PED time windows were 44.1 (SD = 34.3), 5.4 (SD = 3.3), and 5.8 (SD = 2.3), respectively, with an average of 637.4 (SD = 652.4), 104.4 (SD = 56.2), and 111.1 (SD = 95.6) farrowing records per time window. However, preliminary analysis (genetic parameters) of the data indicated that the low number of observations per period, particularly for PRRS, resulted in problems with convergence of the model.

In order to fit the PRRS data better, weeks were either added or subtracted from the beginning and the end of the initially predicted time windows. The creation of these new time windows involved systematically adding or subtracting all possible combinations of weeks from -2 (i.e. removing 2 weeks) to 6 (i.e. adding 6 weeks) on both the beginning of the predicted window and also at the end of the predicted windows. These different combinations were tested for each of the traits to determine which window fit the data best. In addition to potentially increasing the number of records defined as PRRS status, this strategy allowed traits to have different periods of time for PRRS. In other words, PRRS windows were allowed to encompass different time points, depending on the trait, which is biologically reasonable since PRRS will have different effects on a trait depending on the stage of pregnancy at infection, with, for example, SB being expressed before MUM, as the former is due to infection at later stages of gestations, whereas the former at earlier stages [8]. Selection of the new time windows of PRRS (and thus Clean status) was based on several criteria. First, we selected time windows in which the additive genetic variance during the disease was greater than for the Clean status [6]. Akaike information criterion (AIC) was adjusted for the number of data points included in the windows

[11] and this was used to choose the final window of time for each trait and disease status, which were then used for all the remaining statistical analyses. The summary for the final time windows is shown in Table 2.2.

Impact of Disease on Reproductive Performance

The impact of the disease statuses (Clean, PRRS, or PED) on reproductive performance was assessed using a two-step approach because of confounding of disease status with other fixed effects in the model. First, reproductive performance data was analyzed with the following model:

$$Y_{ijklm} = \mu + PAR_i + YR_j + FARM_k + u_m + pe_m + e_{ijklm} \quad \text{[Eq. 2]}$$

where *Y, μ, PAR, YR,* and *FARM* are as defined previously; u_m is the additive genetic effect of the m^{th} animal, assuming $u \sim N(0, \boldsymbol{A}\sigma_u^2)$; where $\boldsymbol{A}$ is the additive relationship matrix; and pe_m is the random effect of the permanent environment on sow *m*, assuming $pe \sim N(0, \boldsymbol{I}\sigma_{pe}^2)$. The $\boldsymbol{A}$ matrix was estimated using a pedigree of 10,985 animals. Second, phenotypes were pre-adjusted (*Y**) for the fixed effects of parity, year, and farm, and then the impact of disease status was evaluated using the following model:

$$Y_{ij}^* = \mu + STAT_i + u_j + pe_j + e_{ij} \quad \text{[Eq. 3]}$$

where *μ, u, and pe* are as defined previously; Y_{ij}^* is the adjusted phenotypic value of a trait; $STAT_i$ is the fixed effect of the i^{th} disease status. Least-squares means of STAT were estimated and then

reconstructed based on the estimates of fixed effects from Eq. 2, according to the proportion of each respective level of *STAT*.

Additionally, the effect of season was also explored in initial analyses. Season was explored as a fixed effect in a number of ways, by month, by time of year (i.e. spring, summer, etc.), and as a seasonality covariate [7]. The effect of season was confounded with disease status as PRRS tends to break during the winter months [12] and was found to be not significant ($P > 0.1$) for this dataset.

Genetic Parameters of Reproductive Performance During Clean and Diseased Statuses

Genetic parameters (heritability and correlations) were estimated considering each trait defined within disease status (e.g. NBA during PRRS) as a separate trait. The univariate animal model below was used to estimate heritabilities:

$$Y_{ijklm} = \mu + PAR_i + YR_j + FARM_k + RA_l + u_m + e_{ijklm} \quad \text{[Eq. 4]}$$

where *Y*, μ, *PAR*, *YR*, *FARM*, and *u* are as defined previously; and RA_l is the fixed effect covariate of the RA of the traits analyzed. The effect of RA was fitted in order to account for the average productivity of the farm at a given time, intended to capture the epidemic severity and dynamics of the diseases [8,11]. For analysis of traits in the Clean status, a random permanent environment (pe) effect was added to the model, assuming $pe \sim N(0, \boldsymbol{I}\sigma^2_{pe})$, in order to account for repeated records (parities) in the same animal. A permanent environmental effect was not fit for PRRS or PED because there were no sows with repeated records for these diseases.

Genetic and phenotypic correlations were estimated using the same models describe above, but in a bivariate fashion. For AB, heritability was estimated using a logit function, but due to convergence problems, genetic correlations were estimated fitting AB as a quantitative variable in a linear mixed model. . When analyzing the same traits between disease statuses, it was assumed that there was no residual covariance between them. Similarly, animals that aborted did not have information for other reproductive traits, and the residual (and therefore phenotypic) covariances were not estimable. All statistical analyses were performed in ASReml4 [13].

Results

Reproductive Performance Between Diseased Statuses

The effect of disease status on reproductive performance can be found in Table 2.3. Disease status was found to be statistically significant ($P < 0.05$) for all traits, except TB (P = 0.68), as expected. In general, Clean and PED had similar reproductive performance, and PRRS had lower performance than both. All levels of status (Clean, PED, and PRRS) significantly ($P < 0.01$) affected outcomes for AB, with 2.9 ± 0.2, 38.8 ± 0.9, and 1.6 ± 0.5% incidence of AB in Clean, PRRS, and PED statuses, respectively. Clean and PED were found to be significantly different ($P < 0.05$) than PRRS for NBD, with 0.81 ± 0.01, 1.32 ± 0.03, and 0.82 ± 0.02 piglets for Clean, PRRS, and PED, respectively. Clean and PED were significantly different ($P < 0.01$) from PRRS for MUM, with 0.20 ± 0.01 and 0.22 ± 0.01 piglets for Clean and PED, respectively, and 0.46 ± 0.02 piglets for PRRS. For MUM, Clean and PED were not found to be significantly different ($P = 0.24$). Clean and PRRS were significantly different ($P < 0.01$) for PROP, with estimates of 0.08 ± 0.01 and 0.13 ± 0.01 piglets, respectively, but there was no difference ($P = 0.23$) between Clean and PED, with PED having an estimate of 0.09 ± 0.01 piglets. All statuses

were also found to be significantly different ($P < 0.01$) from each other for NW, with 9.51 ± 0.05 (Clean), 8.34 ± 0.13 (PRRS), and 5.58 ± 0.10 (PED) piglets. There was a significant effect of disease status ($P = 0.03$) for NBA, with lower NBA during PRRS (11.53± 0.10), compared to both Clean (12.65± 0.06) and PED (12.71± 0.10), which were statistically similar ($P = 0.48$). This same pattern was found ($P < 0.01$) for SB, in which PRRS (0.84 ± 0.02) had poorer performance ($P < 0.01$) than both Clean and PED statuses (0.60 ± 0.01 and 0.59 ± 0.02, respectively), while these were statistically the same ($P = 0.38$).

Genetic Parameters within Disease Status

Genetic parameters for sow performance traits during the Clean, PRRS, and PED statuses are shown in Tables 2.4, 2.5, and 2.6, respectively. Variance components for Clean, PRRS, and PED statuses are shown in Table 2.7. In general, traits had low heritability across all disease statuses. During the Clean status, TB showed the highest heritability and MUM had the lowest heritability with estimates of 0.11 ± 0.02 and 0.01 ± 0.01, respectively. Genetic correlations ranged from -0.83 ± 0.35 (between AB and NBA) to 0.99 ± 0.01 (between NBD with SB). Phenotypic correlations for the Clean status ranged from -0.38 ± 0.01 (between PROP and NBA) and 0.88 ± 0.01 (between PROP and NBD).

For PRRS, the highest and lowest heritability estimates were found for NBD and MUM with 0.18 ± 0.12 and 0.03 ± 0.05, respectively. Genetic correlations ranged from -0.99 ± 0.36 (between PROP and NW) to 0.94 ± 0.22 (between SB and NBD). The phenotypic correlations for the PRRS status ranged from -0.63 ± 0.02 (between NBA and PROP) to 0.85 ± 0.01 (between NBD and PROP). Additive genetic and residual variances numerically increased from Clean to

PRRS for all traits except MUM, where only the residual variance increased and the additive genetic variances from both statuses were very low.

The highest and lowest heritability estimates during PED were found for AB and MUM with 0.41 ± 0.06 and 0.01 ± 0.03, respectively. Genetic correlations ranged from -0.58 ± 0.81 (between NBD and NW) to 0.95 ± 0.05 (between TB and NBA). There were high genetic correlations between SB with NBD (0.87 ± 0.36) and PROP (0.85 ± 0.33) and between NBD and PROP (0.90 ± 0.16). The phenotypic correlations during the PED status ranged from -0.38 ± 0.02 (between PROP and NBA) to 0.88 ± 0.01 (between PROP and NBD). From Clean to PED, there was a numerical increase in additive genetic variance for AB, TB, and NW, and in residual variance for NBA, SB, MUM, NBD, PROP, and NW.

Genetic Parameters between Disease Status

The within trait estimates of genetic correlations between disease statuses for AB, TB, NBA, SB, NBD, and NW are depicted in Table 2.8. Estimates of genetic correlations between Clean and PED ranged from 0.10 ± 0.56 (NBD) to 0.99 ± 0.36 (AB). The genetic correlation estimates between Clean and PED for TB, NBA and SB were high, with 0.78 ± 0.09, 0.79 ± 0.14, and 0.96 ± 0.25, respectively. The genetic correlation estimate for NW between Clean and PED was moderate, with a correlation of 0.67 ± 0.12.

Genetic correlation estimates between Clean and PRRS were moderate to high, ranging from 0.54 ± 0.29 (NBD) to 0.99 ± 0.73 (AB). For TB and NBA, the estimates between Clean and PRRS were high, with correlations of 0.88 ± 0.08 and 0.82 ± 0.13, respectively. For SB and NW, the estimates were moderate, with correlations of 0.60 ± 0.15 and 0.62 ± 0.20, respectively.

Genetic correlation estimates between PED and PRRS ranged from -0.22 ± 0.26 (NW) to 0.92 ± 0.35 (NBA). The genetic correlation estimate for AB was low (0.38 ± 0.14), whereas for TB, SB and NBD, these were higher, with estimates of 0.63 ± 0.18, 0.68 ± 0.40, and 0.62 ± 0.68, respectively.

Discussion

Detecting PRRS and PED Outbreaks

There was a clear decrease in performance on every farm that had PRRS and/or PED outbreaks. These deviations from the normal production in each farm is what allowed us to detect the point at which a farm began to show the impact of the diseases. The reproductive losses, including increases in NBD and AB, and decreases in NBA are indicators for PRRS [1], which is why these were the traits used in detecting PRRS outbreaks. The indicator trait used in detecting PED was NW, because high piglet mortality rate is seen during PEDV infection, although piglets are born uninfected [4]. All but one of the 23 identified PRRS and PED outbreaks were confirmed via periodical serological tests performed at each farm. Although this PRRS outbreak was not confirmed serologically, it was retained since the other identified breaks were confirmed and other studies have shown the validity of this method in the identification of disease [10]. Lewis et al. [10] found that using a threshold method to partition animals into healthy and disease statuses has an advantage over partitioning based on serological results because it is stricter and thus, fewer healthy animals would be included in an outbreak window. However, one PRRS outbreak (based on serological results) was not captured using this method. This could be due to lack of severity of infection, so we were unable to capture it, or a false positive from the serological testing. Despite this, the disease windows that were predicted based

on the threshold reproductive data are a better representation of the course of the disease because, due to the stringency in predicting windows, the windows are shorter, representing only the time when reproductive performance was actually impaired and thus, only including animals that farrowed during this impaired performance time.

Reproductive Performance Between Diseased Statuses

In our study, we observed an impact of PRRS on all traits, except TB. A previous study by Lewis et al. [10] also found no significant ($P = 0.06$) difference for TB between PRRS and Clean. Differences in TB were not expected because infection prior to implantation of embryos results in resorption of embryos and the sow returns to estrus, but infection after implantation leads to an increase in MUM for infected fetuses [14], which is included in the calculation of TB. Previous studies showed significant decreases ($P < 0.01$) in NBA from 11.1 to 9.7 [10] and 12.8 to 11.6 [5] between Clean and PRRS statuses, respectively, which is in agreement with what was found in the current study, with a decrease from 12.7 (Clean) to 11.5 (PRRS). These studies also found significant decreases in NW between Clean and PRRS that are in agreement with our study. Lewis et al. [10] found a decrease in NW from 10.10 to 8.83 piglets for Clean and PRRS, respectively and Herrero-Medrano et al. [5] found a decrease from 11.00 to 9.35 piglets ($P < 0.01$), ours also showed a similar decrease from 9.5 to 8.3 piglets for Clean and PRRS, respectively. The significant differences between disease statuses for SB and MUM in the current study, with increases from Clean to PRRS, were in agreement with the results reported by Lewis et al. [10], whom found differences for SB (0.62 to 0.84 for Clean and PRRS, respectively) and MUM (-0.25 to 0.75 for Clean and PRRS, respectively). For PROP, Serão et al. [8] reported an increase from 0.10 to 0.18, between Clean and PRRS, respectively, which was

greater but in line with what was found in this study. A significant increase in AB was also found in the current study from 2.9% in Clean to 38.8% in PRRS. No other reports were found for comparison with these results, but the increase in AB is a well-known indicator of PRRS [1].

For PED, there is little information, with only one study to date that compares reproductive performance between Clean and PEDV infection. Since piglets are not infected when the sow is pregnant like they are during PRRSV infection, it is expected that AB, TB, NBA, SB, MUM, NBD, and PROP would be the same between PED and Clean statuses, but that there would be a significant difference for NW between the two. The NW result from the current study was as expected, with a significant decrease in NW from Clean to PED, from 9.5 to 5.6 piglets. Dastiherdi et al. [15] reported an increase in AB in early gestation after a PED outbreak and the raw data for our study indicate the same, with a higher percentage of AB during PED than in Clean (6.6% and 3.1%, respectively). However, once the data was analyzed, we observed a significant difference between Clean and PED in the opposite direction than expected, with a higher AB found during Clean than PED. There were no significant differences found in the current study for TB, NBA, SB, and NBD between Clean and PED, but differences were significant for NW. Using sow performance data in animals that broke with PED at different stages of gestation, [16] reported contrasting results for AB with an increase in AB from 2.0% in Clean to 2.7% in PED ($P = 0.05$). In agreement with our study, these authors found no difference for NBA between Clean and PED with estimates of 11.3 and 11.2 ($P = 0.38$). These authors also found that both SB and MUM increased ($P < 0.05$) from Clean to PED when sows are infected in early gestation. For later gestational infection, no significant difference between Clean and PED for MUM was found, which is in concurrence with our study. Although Olanratmanee et al. [16]

reported an increase ($P < 0.05$) in SB from 4.5% (Clean) to 6.2% (PED), we found no differences between both disease statuses.

To our knowledge, there are no studies comparing differences in reproductive performance between sows infected with PRRSV and PEDV. Due to the differences in the diseases, PRRSV infecting piglets in utero and PEDV not infecting piglets until birth, the expectation would be for that there would be significant difference for AB, birth, and weaning traits. For all traits in this study, except TB, PED and PRRS were shown to be significantly different. Based on the indicator traits for these two diseases, it is not too surprising that they were found to be different. PRRS is known to decrease NBA as well as born dead traits, PED has been shown to cause decreases in NW, and both have been shown to cause increases in AB, although we have observed decreased AB during PED in our data analysis. With an increase in born dead and decrease in NBA that is seen in PRRS, it makes sense that the NW would decrease, but not as much as with PED because the mortality rate for PEDV infected piglets is much higher than for PRRS.

One limitation to this study is that since this is commercial data, we do not know which strains of PRRSV or PEDV were present at the farms. Although we are unaware of the strains, this data is representative of what is present in the overall industry. In addition, we must point out that the performance data used for statistical analysis was used to split the data set into disease statuses, based on the biological impact of these diseases on performance. However, Lewis et al. [10] showed that this strategy was successful in splitting data into Clean and Diseased (i.e. PRRS) statuses and capture the effects of the disease. A similar strategy has been used by others, which further validated the approach by Lewis et al. [5,7,8]. Finally, one of the objectives of this study was to estimate the impact of PRRS and PED on reproductive

performance of sows, and thus, we were able to do so, providing estimates of the differences in performance.

Genetic Parameters within Disease Status

Heritabilities for reproductive traits are generally low, which is what was observed in this study. In general, heritabilities were similar to those previously reported in reproductive sows in Clean environments, which have been largely discussed in several studies [5,8,10], and thus, we will not focus attention in the absence of diseases. Heritability estimates within the PRRS status were low, but higher than those reported during the Clean status. To our knowledge, there are no reports in the literature that include heritability estimates for AB in PRRSV-challenged animals. Heritability estimates for NBA (0.14 ± 0.07), NBD (0.18 ± 0.12), and NW (0.11 ± 0.09) were within the ranges of estimates reported by Lewis et al. [10], Serão et al. [8], and Herrero-Medrano et al. [5]. The estimate for TB (0.16 ± 0.08) in the current study was comparable to the estimate reported by Lewis et al. [10]. Estimates of heritability for SB during PRRS by Lewis et al. [10] and Serão et al. [8] were lower than the what was estimated in the current study. Overall, heritability estimates during PRRS were higher when compared to the absence of disease (i.e. Clean) which is also observed by Lewis et al. [10] and Serão et al. [8]. Standard errors during the PRRS status were generally large, as compared to the Clean status, but this was expected because the PRRS dataset was much smaller than the Clean dataset in this study. In our study, we observed an increase in both additive genetic and residual variances during PRRS compared to the Clean status, with a proportionally greater increase in the additive genetic variance, which resulted in the higher heritability estimates found in PRRS as compared to Clean (data not shown). The larger additive genetic variances and greater heritability in the PRRS status as

compared to the Clean status indicate that the genetic differences between animals are more revealed when a disease is present, differently than in an environment without the occurrence of diseases, such as the nucleus herds [5]. Therefore, selection for improved performance under PRRSV infection must be done during the presence of the disease for animals to fully express their genetic potential.

To our knowledge, there are no studies that reported genetic parameters for reproduction traits in sows infected with PEDV. The heritability estimates during PED were comparable to those found in the Clean status, with the exception of AB, TB, and NW, which were higher during PED than during Clean. This overall similarity with the Clean status was expected; infection with PEDV should not have an impact on reproductive performance in sows, as the disease does not infect piglets in utero, so there should be no decrease in TB or increase in the born dead traits with PEDV infection. Since there should be no impact of PED on TB, it was surprising to find that the heritability of TB during PED was estimated to be 0.26 ± 0.05, which was higher than what was found in Clean (0.11 ± 0.02). The moderate heritability estimate for AB (0.41 ± 0.06) was also surprising, since PED is only known for high mortality in piglets. However, this heritability indicates that there is opportunity to select for improved AB in PEDV-infected pigs, which is in accordance with the phenotypically lower AB during PED compared to Clean and PRRS sows. Less surprising was the heritability that was found for NW during PED (0.15 ± 0.05), which was higher than what was estimated during Clean (0.02 ± 0.01) or PRRS (0.11 ± 0.09). Similar to PRRS, there was an increase in both additive genetic and residual variance, with the increase in additive genetic variance being greater, which resulted in increased heritabilities in this study. It is also important to note that during disease, there would be a decrease in cross fostering to limit the spread of disease. When there is a lot of cross fostering

and this information is not accurately recorded, genetic variation for of NW cannot be fully captured accurately because the sow and the piglets in her litter are not necessarily related, but more genetic variance can be captured with the increased relatedness of the litter when there is a decrease in cross fostering and thus an increase in heritability of NW can be seen. Although there was an increase in heritability for AB and NW from Clean to PED, the use of these traits for selection purpose during PEDV infection would be challenging. At both the nucleus and commercial levels, AB can be a challenging trait to collect accurately and there is added difficulty in analysis due its binary nature. At the commercial level, there is a high frequency of cross-fostering and limited records kept on these transfers, making genetic evaluations for NW a challenging task to be performed. An added challenge for identifying animals with variation in NW during PEDV infection is the nearly 100% piglet mortality [3,4]. Nonetheless, our results indicate traits during PRRSV or PEDV infection are, in general, numerically more heritable than in a clean environment.

Genetic and phenotypic correlations were estimated within each of the disease statuses. For the Clean status, most correlations were low, with high genetic and phenotypic correlations for NBD with SB and PROP, and for MUM with PROP, which makes sense since these traits all measure mortality. The low genetic correlations that were found between traits with NW in this study could be due to the lack of traceable cross-fostering information from these animals, which did not allow us to properly account for the foster dam information in the statistical analysis of the data.

During PRRS, the genetic correlation estimates between traits were in general greater than for those in the Clean status. There were also much larger standard errors estimated during PRRS than in Clean. This must be due to the few records for the PRRS status as compared to the

Clean status, as well as to the large variation seen during PRRS as compared to Clean for many of the traits. Some traits had opposing genetic correlations between Clean and PRRS, like NBA with SB and NBD which was negative in PRRS and positive during the Clean environment. This pattern indicates that the relationship between born dead traits with NBA is genetically favorable during PRRS as compared to their relationship during Clean. The relationship with NBA and NBD was also much higher than in Clean. Other traits, like NBD with SB and PROP, had genetic correlations that were similar to those that were estimated during Clean. These results indicate that selection for improved performance recorded during a PRRS outbreak in one trait would result stronger changes in other correlated traits, compared to the Clean status. Therefore, selection under Clean status would differ from that under PRRS status. To our knowledge, there are no reports available in the literature providing correlation estimates within PRRS status.

Within the PED disease status, the genetic correlations between AB with NBD and NW, and between SB with NBD were similar in size and direction to their corresponding phenotypic correlations. The genetic correlations between MUM with SB and NW were larger than their corresponding phenotypic correlations, but were the same directionally. The standard errors for the genetic correlations for between MUM with SB, NBD, NBD, PROP, and NW and between PROP and NBA are extremely high. The high genetic correlation between AB and NBD could be due to the similarity in how these traits express performance (i.e. piglets born dead), although one accounts for the number of dead piglets (NBD) and the other does not (AB). This difference between the two may be reflected in their low phenotypic correlations. Compared to the Clean status, much of the genetic correlations were in opposite directions for PED. Comparisons between Clean and PED show that correlated response to selection in a Clean environment for these traits would be different that the response during PED. Also for PED, the standard errors

were much larger than for Clean, probably due to the lower number of animals used for the PED analysis and greater residual variance.

There were problems with convergence for models to estimate the relationship of MUM with PROP, NBD, and TB for PRRS, between PROP with NBD and TB with MUM for PED, and between SB and PROP for the Clean status. Within PRRS and PED, it is possible that these problems could be caused by the low number of animals that are within the disease statuses, and the limited number of animals represented in each farm. It is also problematic to estimate genetic correlations for traits where the heritability is not different than zero, like MUM for all disease statuses and PROP for PED, which could also be contributing to these convergence problems.

Genetic Parameters between Disease Status

Overall, the moderate to high positive correlations between Clean and PRRS statuses found in this study indicated that the underlying genetic mechanisms of these traits are similar between healthy and PRRSV-infected animals, suggesting that selection for improved performance under a PRRS disease status would not negatively affect performance during a Clean environment. In general, estimates found in this study were similar to those found in independent studies. For NBA, the genetic correlation between Clean and PRRS was 0.82 ± 0.12, which was comparable to the estimate by Rashidi et al. [7], but higher than the estimates reported by Herrero-Medrano et al. [5] and Lewis et al. [10]. Genetic correlation between SB in Clean and PRRS was moderate (0.65 ± 0.15) and comparable to the correlation reported by Lewis et al. [10]. There was also a moderate correlation between Clean and PRRS disease status for NBD, 0.47 ± 0.23, which was comparable to the estimate reported in Lewis et al. [10], but lower than the estimates reported by Rashidi et al. [7] and Herrero-Medrano et al. [5]. Herrero-

Medrano et al. [5] reported a genetic correlation for NW between the Clean and PRRS status that is comparable to our estimate of 0.59 ± 0.22. The NW estimate reported by Lewis et al. [10] was much lower than what was estimated in the current study, with a genetic correlation of 0.27 ± 0.25 between Clean and PRRS. Genetic correlations for AB were not reported in other studies, but were found to be high between the Clean and PRRS disease statuses, 0.99 ± 0.30. Genetic correlations for TB between disease statuses were also not reported in other studies, but these were also found to be high between Clean and PRRS, 0.88 ± 0.08. Standard errors for many of these genetic correlations were large, most likely due to animals not having records in both environments. This is especially true for AB, where many animals that aborted were removed from the studied herds before having performance recorded under PRRSV-infection.

The expectation for genetic correlations between Clean and PED was that they would be high, since the reproductive performance was, in general, not significantly different between these statuses, with the exception of NW and AB. To our knowledge, there are currently no studies comparing genetic parameters between Clean and PED. Genetic correlations between Clean and PED disease statuses were positive moderate to high for most traits, with the exception of NBD, which had a low genetic correlation (0.11 ± 0.59). There was a significant difference in NBD between these two statuses, and although we may not understand why PED would show a lower NBD than in Clean, this low genetic correlation corroborates with this finding, indicating that, indeed, NBD between Cleaned and PED statuses are different. Nonetheless, the large SE associated with this estimate makes it hard to properly conclude on their genetic relationship. The high genetic correlations between Clean and PED statues for AB, NBA, and SB may be reasonable since PEDV infects the piglet only after birth, so they are born healthy and mortality is high post-infection [3,4]. With the high post-natal piglet mortality

caused by PEDV, it is encouraging that the genetic correlation between Clean and PED was positive and moderate, suggesting that selection for improved NW during Clean would not have a negative impact on NW during PEDV infection.

The genetic correlation estimates between PRRS and PED were more variable than for the previous comparisons. In addition, the standard errors of these estimates were much larger than for the other disease status comparisons, but this should be due to the low number of animals that had records during both statuses. This might also have contributed with the convergence problems we observed for MUM. An added possible practical problem with this trait could be that this trait may not be properly distinguished during recording of the data among the farms due to different staff and different procedures on the farms. Because of these convergence issues, we also estimated these correlations using a sire model (data not shown). The same convergence issues still occurred, and this analysis resulted in the same overall conclusions, but with estimates with much greater SE. Additionally, we used the sire model to investigate potential non-linear relationships between statuses within a trait (data not shown). Sire estimated breeding values (EBVs) for a given trait between statuses were very linearly correlated, with the exception for AB between PRRS and PED. For this trait, PED sire EBVs tended to plateau at high PRRS sire EBVs. However, this dataset consisted of only 100 sires, and with the large SE of estimates, further studies are needed to better understand the relationship between these diseases at the genetic using a sire model. Nonetheless, positive high genetic correlations between PRRS and PED were found for NBA, SB, NBD, and PROP, indicating that reproductive performance will be reflective of the genetic merit of the individual regardless of whether performance was recorded in PRRS or PED. This is of major importance to the swine industry because of the increased interest in breeding a more robust pig that excels in both the

Clean and dirty environments. If selection was done for an increase in performance during PRRS, this would also result in increased performance in PED. Moreover, the very low genetic correlation between PRRS and PED for NW might be due to the major impact that PEDV has on NW, and thus, the genetic control for this trait between the two diseases should be quite different. Nonetheless, these results for NW indicate that genetic improvement for response to one disease would not impact the response the other disease.

Conclusions

Phenotypic and genetic differences were observed in commercial sows as a function of disease status (PRRS, PED, or Clean) in this study. Mean performance under PRRS was different than for performance recorded in Clean and PED affected environments. In contrast, PED and Clean statuses had more similar phenotypic performance. The greater heritability and additive genetic variance estimates obtained during PRRS and PED statuses compared to Clean indicate that selection for improved reproductive performance under these diseases is possible. The high genetic correlations obtained between PRRS and PED statuses indicate that selection for improved reproductive performance under one disease would also be favorable for the other disease. In addition, genetic correlations between Clean and Diseased environments were overall positive, and thus, the reproductive performance in PRRS and/or PED would also be informative of the animal's genetic merit during Clean. Overall, our results indicate that there is an opportunity to select for improved reproductive performance during PRRS and PED outbreaks in commercial sows.

References

1. Lunney JK, Fang Y, Ladinig A, Chen N, Li Y, Rowland B, et al. Porcine Reproductive and Respiratory Syndrome Virus (PRRSV): Pathogenesis and Interaction with the Immune System. Annu Rev Anim Biosci. 2016;4.
2. Holtkamp DJ, Kliebenstein JB, Neumann EJ, Zimmerman JJ, Rotto HF, Yoder TK, et al. Assessment of the economic impact of porcine reproductive and respiratory syndrome virus on United States pork producers. J Swine Heal Prod. 2013;21:72–84.
3. Song D, Park B. Porcine epidemic diarrhoea virus: a comprehensive review of molecular epidemiology, diagnosis, and vaccines. Virus Genes. 2012;44:167–75.
4. Stevenson GW, Hoang H, Schwartz KJ, Burrough ER, Sun D, Madson D, et al. Emergence of Porcine epidemic diarrhea virus in the United States: clinical signs, lesions, and viral genomic sequences. J Vet Diagn Invest. 2013;25:649–54.
5. Herrero-Medrano JM, Mathur PK, ten Napel J, Rashidi H, Alexandri P, Knol EF, et al. Estimation of genetic parameters and breeding values across challenged environments to select for robust pigs. J Anim Sci. 2015;93:1494–502.
6. Lewis CRG, Ait-Ali T, Clapperton M, Archibald AL, Bishop S. Genetic Perspectives on Host Responses to Porcine Reproductive and Respiratory Syndrome (PRRS). Viral Immunol. 2007;20:343–58.
7. Rashidi H, Mulder HA, Mathur P, Van Arendonk JAM, Knol EF. Variation among sows in response to porcine reproductive and respiratory syndrome. J Anim Sci. 2014;92:95–105.
8. Serão NVL, Matika O, Kemp RA, Harding JCS, Bishop SC, Plastow GS, et al. Genetic analysis of reproductive traits and antibody response in a PRRS outbreak herd. J Anim

Sci. 2014;92:2905–21.

9. Bertolini F, Harding JCS, Mote B, Ladinig A, Plastow GS, Rothschild MF. Genomic investigation of piglet resilience following porcine epidemic diarrhea outbreaks. Anim Genet. 2017;48:228–32.

10. Lewis CRG, Torremorell M, Galina-Pantoja L, Bishop SC. Genetic parameters for performance traits in commercial sows estimated before and after an outbreak of porcine reproductive and respiratory syndrome. J Anim Sci. 2009;87:876–84.

11. Hurvich C, Tsai C. Regression and time series model selection in small samples. Biometrika. 1989;

12. Komijn RE, van Klink EGM, Van der Sande WJH. The possible effect of weather conditions on the spread of the “new” pig disease in the Netherlands. new pig Dis Porc Respir Reprod Syndr A Rep Semin held Brussels 29 30 April 1991 Organ by Eur Comm (Directorate Gen Agric. 1991.

13. Gilmour AR, Gogel BJ, Cullis BR, Welham SJ, Thompson R. ASReml User Guide Release 4.1. VSN International Ltd. Hemel Hempstead. 2015.

14. Karniychuk UU, Nauwynck HJ. Pathogenesis and prevention of placental and transplacental porcine reproductive and respiratory syndrome virus infection. Veterinary Research. 2013.

15. Dastjerdi A, Carr J, Ellis RJ, Steinbach F, Williamson S. Porcine epidemic diarrhea virus among farmed pigs, Ukraine. Emerg Infect Dis. 2015.

16. Olanratmanee E on, Kunavongkrit A, Tummaruk P. Impact of porcine epidemic diarrhea virus infection at different periods of pregnancy on subsequent reproductive performance in gilts and sows. Anim Reprod Sci. 2010;122:42–51.

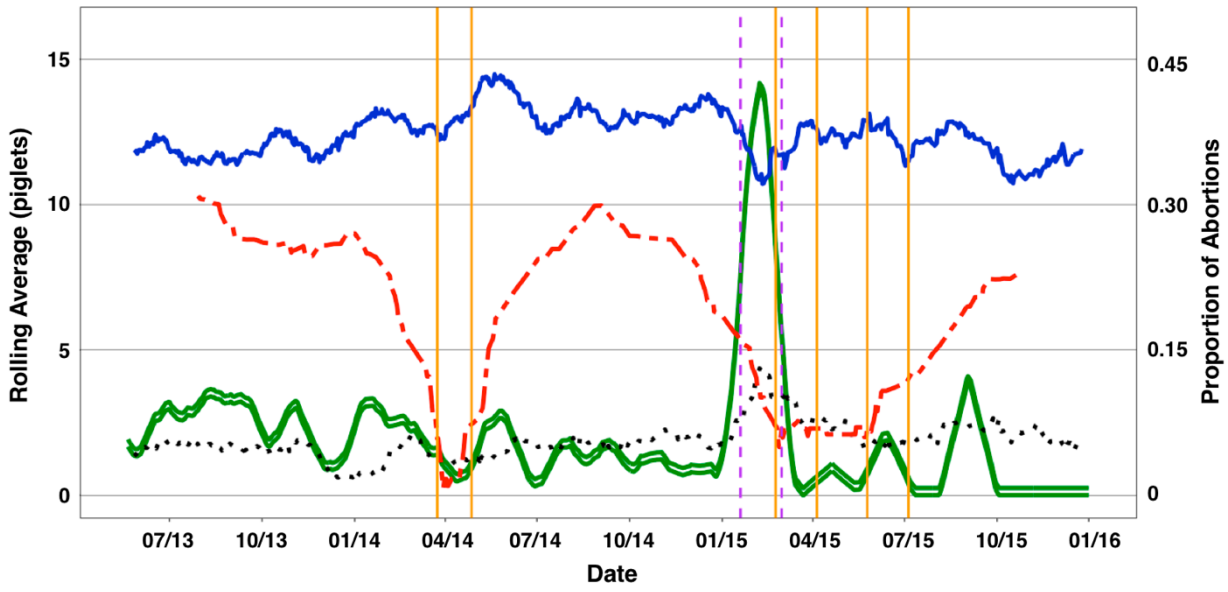

Figure 2.1 Example of visualization of the performance data using rolling averages (RA) across time (month and year) for one of the farms used in the study. Traits included for visualization were: abortions (AB; green open line), number born alive (NBA; blue solid line), number born dead (NBD; black dotted line) and number weaned (NW; red dashed line). The primary y-axis represents the RA for NBA, NBD, and NW and the secondary y-axis represent the RA for proportion of AB. A 30-day RA was used to visualize all traits. RAs allowed to capture changes in performance due to infection with Porcine Epidemic Diarrhea (PED) or Porcine Reproductive and Respiratory Syndrome (PRRS). Decreases in NW indicated PED whereas PRRS was identified with increases in AB and NBD, and with decreases in NBA. Consecutive vertical lines of the same color represent the initial disease windows that were identified: PRRS (purple dashed line) and PED (orange solid line).

Table 2.1: Summary statistics of the raw data

Trait[1]	*n*	Mean	SD	Min	Max
AB, %	20,558	4.06	19.73	-	-
TB	21,197	14.16	3.32	3	25
NBA	20,540	12.86	3.25	0	25
SB	20,540	0.90	1.31	0	15
MUM	20,540	0.39	1.02	0	20
NBD	20,540	1.29	1.75	0	20
PROP	20,540	0.09	0.12	0	1
NW	20,043	9.31	3.67	0	16

[1]AB, Percent of abortions; TB, Total number of piglets born; NBA, Number of piglets born alive; SB, Number of stillborn piglets; MUM, Number of mummified piglets; NBD, Number of piglets born dead; PROP, Proportion of piglets born dead; NW, Number of piglets weaned.

Table 2.2: Summary statistics for time windows during the different disease statuses[1]

	Clean (Windows=31)			PRRS (Windows=8)			PED (Windows=15)		
Trait[2]	Length (SD)	Records	Mean (SD)	Length (SD)	Records	Mean (SD)	Length (SD)	Records	Mean (SD)
AB, %	36.8 (30.3)	18,564	2.8 (16.5)	5.8 (2.5)	309	24.9 (43.3)	5.9 (2.3)	1,685	5.7 (23.1)
TB	37.4 (30.4)	18,653	14.2 (3.3)	10.6 (3.1)	970	14.7 (3.6)	5.9 (2.3)	1,574	14.0 (3.2)
NBA	38.2 (30.7)	17,708	12.9 (3.2)	12.4 (4.3)	1,258	12.0 (3.8)	5.9 (2.3)	1,574	12.7 (3.1)
SB	38.4 (30.9)	18,190	0.5 (0.5)	7.0 (4.1)	776	0.7 (0.6)	5.9 (2.3)	1,574	0.4 (0.5)
MUM	36.7 (30.8)	18,307	0.2 (0.4)	8.1 (2.9)	659	0.4 (0.6)	5.9 (2.3)	1,574	0.2 (0.5)
NBD	37.8 (30.8)	18,307	0.6 (0.6)	8.1 (2.9)	659	0.9 (0.8)	5.9 (2.3)	1,574	0.6 (0.6)
PROP	36.9 (31.1)	17,974	0.1 (0.1)	9.7 (4.0)	992	0.1 (0.2)	5.9 (2.3)	1,574	0.1 (0.1)
NW	36.8 (30.3)	17,732	9.9 (3.1)	11.0 (4.6)	751	8.0 (3.7)	5.9 (2.3)	1,560	3.9 (4.7)

[1]Clean, Clean status (no presence of PRRS and PED); PRRS, porcine reproductive and respiratory syndrome; PED, porcine epidemic diarrhea;

[2]AB, Abortion; TB, Total number of piglets born; NBA, Number of piglets born alive; SB, Number of stillborn piglets; MUM, Number of mummified piglets; NBD, Number of piglets born dead; PROP, Proportion of piglets born dead; NW, Number of piglets weaned;

Window, number of outbreak windows identified; Length, average length (weeks) of individual outbreak windows; Records, number of records analyzed; Mean, raw means of the records within each trait for the disease windows.

Table 2.3: Least squares means (SE) of traits by disease status[1]

	Disease Status			
Trait [2]	Clean	PRRS	PED	*P*-value
AB,%	2.9^{b} (0.2)	38.8^{a} (0.9)	1.6^{c} (0.5)	<0.01
TB	14.12^{a} (0.07)	14.21^{a} (0.12)	14.14^{a} (0.10)	0.66
NBA	12.65^{a} (0.06)	11.53^{b} (0.10)	12.71^{a} (0.10)	0.03
SB [3]	0.60^{b} (0.01)	0.84^{a} (0.02)	0.59^{b} (0.02)	<0.01
MUM [3]	0.20^{b} (0.01)	0.46^{a} (0.02)	0.22^{b} (0.01)	<0.01
NBD [3]	0.81^{b} (0.01)	1.32^{a} (0.03)	0.82^{b} (0.02)	<0.01
PROP	0.08^{b} (0.01)	0.13^{a} (0.01)	0.09^{b} (0.01)	<0.01
NW	9.51^{a} (0.05)	8.34^{b} (0.13)	5.58^{c} (0.10)	<0.01

[a,b,c] Means lacking the same superscript are different at *P*-value < 0.05;

[1]Clean, Clean status (no presence of PRRS or PED); PRRS, porcine reproductive and respiratory syndrome; PED, porcine epidemic diarrhea;

[2]AB, Abortion; TB, Total number of piglets born; NBA, Number of piglets born alive; SB, Number of stillborn piglets; MUM, Number of mummified piglets; NBD, Number of piglets born dead; PROP, Proportion of piglets born dead; NW, Number of piglets weaned;

[3]Results are back-transformed from natural log + 1.

Table 2.4: Genetic parameters[1] for the Clean status[2]

Trait[3]	AB	TB	NBA	SB	MUM	NBD	PROP	NW
AB[4]	**0.07** **(0.05)**	NC	-0.83 (0.35)	0.02 (0.45)	-0.51 (0.85)	-0.08 (0.47)	0.27 (0.44)	-0.35 (0.53)
TB	-	**0.11** **(0.02)**	0.95 (0.02)	0.47 (0.10)	0.22 (0.23)	0.47 (0.11)	0.29 (0.14)	0.34 (0.15)
NBA	-	0.87 (0.01)	**0.09** **(0.02)**	0.17 (0.13)	-0.08 (0.24)	0.17 (0.14)	-0.02 (0.16)	0.46 (0.15)
SB	-	0.29 (0.01)	-0.10 (0.01)	**0.07** **(0.01)**	0.61 (0.22)	0.99 (0.01)	NC	-0.39 (0.15)
MUM	-	0.19 (0.01)	-0.12 (0.01)	0.15 (0.01)	**0.01** **(0.01)**	0.72 (0.15)	0.75 (0.16)	-0.32 (0.35)
NBD	-	0.33 (0.01)	-0.14 (0.01)	0.86 (0.01)	0.60 (0.01)	**0.05** **(0.01)**	0.99 (0.02)	-0.32 (0.18)
PROP	-	0.09 (0.01)	-0.38 (0.01)	NC	0.60 (0.01)	0.88 (0.01)	**0.03** **(0.01)**	-0.43 (0.20)
NW	-	0.08 (0.01)	0.13 (0.01)	-0.07 (0.01)	-0.04 (0.01)	-0.07 (0.01)	-0.31 (0.03)	**0.02** **(0.01)**

[1]Estimates of heritability (diagonal), and genetic (above diagonal) and phenotypic (below diagonal) correlations;
[2]The Clean status was defined as the period of time when no disease was actively present;
[3]AB, Abortion; TB, Total number of piglets born; NBA, Number of piglets born alive; SB, Number of stillborn piglets; MUM, Number of mummified piglets; NBD, Number of piglets born dead; PROP, Proportion of piglets born dead; NW, Number of piglets weaned;
[4]AB was treated as a quantitative variable and was assumed to have no residual covariance when estimating correlations between this and other traits;
NC = Not converged.

Table 2.5: Genetic parameters[1] for the PRRS status[2]

Trait[3]	AB	TB	NBA	SB	MUM	NBD	PROP	NW
AB[4]	**0.17** **(0.11)**	-0.08 (0.20)	-0.22 (0.20)	0.01 (0.22)	NC	0.66 (0.21)	0.37 (0.28)	-0.48 (0.24)
TB	-	**0.16** **(0.08)**	0.86 (0.14)	-0.18 (0.37)	NC	-0.61 (0.42)	-0.36 (0.42)	0.09 (0.41)
NBA	-	0.74 (0.02)	**0.14** **(0.07)**	-0.49 (0.32)	-0.50 (0.75)	-0.91 (0.24)	-0.67 (0.27)	0.33 (0.41)
SB	-	0.29 (0.04)	-0.23 (0.03)	**0.16** **(0.10)**	0.33 (0.92)	0.94 (0.22)	0.92 (0.39)	-0.68 (0.36)
MUM	-	NC	-0.35 (0.03)	0.24 (0.04)	**0.03** **(0.05)**	NC	NC	-0.61 (1.09)
NBD	-	0.27 (0.04)	-0.40 (0.03)	0.83 (0.01)	NC	**0.18** **(0.12)**	0.85 (0.26)	-0.85 (0.30)
PROP	-	-0.02 (0.04)	-0.63 (0.02)	0.62 (0.02)	NC	0.85 (0.01)	**0.09** **(0.08)**	-0.99 (0.36)
NW	-	0.10 (0.04)	0.33 (0.03)	-0.21 (0.04)	-0.23 (0.04)	-0.30 (0.04)	-0.31 (0.03)	**0.11** **(0.09)**

[1]Estimates of heritability (diagonal), and genetic (above diagonal) and phenotypic (below diagonal) correlations;
[2]PRRS, porcine reproductive and respiratory syndrome;
[3]AB, Abortion; TB, Total number of piglets born; NBA, Number of piglets born alive; SB, Number of stillborn piglets; MUM, Number of mummified piglets; NBD, Number of piglets born dead; PROP, Proportion of piglets born dead; NW, Number of piglets weaned;
[4]AB was treated as a quantitative variable and was assumed to have no residual covariance when estimating correlations between this and other traits;
NC = Not converged.

Table 2.6: Genetic parameters[1] for the PED status[2]

Trait[3]	AB	TB	NBA	SB	MUM	NBD	PROP	NW
AB[4]	**0.41 (0.06)**	-0.15 (0.10)	-0.05 (0.19)	0.02 (0.21)	-0.14 (0.87)	0.12 (0.42)	NC	0.35 (0.12)
TB	-	**0.26 (0.05)**	0.95 (0.05)	-0.12 (0.29)	NC	0.17 (0.50)	-0.14 (0.88)	0.26 (0.19)
NBA	-	0.85 (0.01)	**0.07 (0.05)**	-0.23 (0.45)	0.49 (1.43)	-0.04 (0.77)	-0.20 (1.01)	0.14 (0.28)
SB	-	0.30 (0.03)	-0.09 (0.03)	**0.06 (0.04)**	-0.85 (1.34)	0.87 (0.36)	NC	-0.07 (0.36)
MUM	-	NC	-0.15 (0.02)	0.14 (0.02)	**0.01 (0.03)**	-0.35 (1.49)	-0.19 (2.12)	-0.83 (1.67)
NBD	-	0.35 (0.02)	-0.16 (0.02)	0.81(0.01)	0.67 (0.01)	**0.02 (0.03)**	NC	-0.58 (0.81)
PROP	-	0.17 (0.03)	-0.38 (0.02)	NC	0.65 (0.01)	NC	**0.03 (0.03)**	-0.22 (0.49)
NW	-	0.05 (0.03)	0.08 (0.03)	0.01 (0.03)	-0.02 (0.03)	-0.02 (0.03)	-0.05 (0.03)	**0.15 (0.05)**

[1]Estimates of heritability (diagonal), and genetic (above diagonal) and phenotypic (below diagonal) correlations;
[2]PED, porcine epidemic diarrhea;
[3]AB, Abortion; TB, Total number of piglets born; NBA, Number of piglets born alive; SB, Number of stillborn piglets; MUM, Number of mummified piglets; NBD, Number of piglets born dead; PROP, Proportion of piglets born dead; NW, Number of piglets weaned;
[4]AB was treated as a quantitative variable and was assumed to have no residual covariance when estimating correlations between this and other traits;
NC = Not converge

Table 2.7: Variance components[1,2] for the Clean, PRRS, and PED statuses[3]

	Clean		PRRS		PED	
Trait[4]	σ_u^2	σ_e^2	σ_u^2	σ_e^2	σ_u^2	σ_e^2
AB	0.17	3.29	5.34	3.29	14.88	3.29
TB	1.13	8.30	2.09	10.78	2.65	7.56
NBA	0.88	8.28	1.87	11.56	0.75	8.96
SB	0.02	0.24	0.06	0.32	0.015	0.25
MUM	0.001	0.15	>0.001	0.37	>0.001	0.19
NBD	0.02	0.32	0.10	0.46	0.005	0.37
PROP	>0.001	0.01	0.003	0.03	>0.001	0.03
NW	0.17	6.87	1.29	10.01	1.78	10.14

[1]Estimates of additive genetic (σ_u^2) and residual (σ_e^2) variances;
[2]Variances expressed as %^{2} on the logistic scale for AB, and as piglets^2 for all other traits;
[3]Clean, no disease actively present, PRRS, porcine reproductive and respiratory syndrome, PED, porcine epidemic diarrhea;
[4]AB, Abortion; TB, Total number of piglets born; NBA, Number of piglets born alive; SB, Number of stillborn piglets; MUM, Number of mummified piglets; NBD, Number of piglets born dead; PROP, Proportion of piglets born dead; NW, Number of piglets weaned;

Table 2.8: Estimates of genetic correlations (SE) between disease statuses[1]

	Disease Status		
Trait [2]	Clean-PED	Clean-PRRS	PED-PRRS
AB	0.99 (0.36)	0.99 (0.63)	0.38 (0.14)
TB	0.78 (0.09)	0.88 (0.08)	0.63 (0.18)
NBA	0.79 (0.14)	0.82 (0.13)	0.92 (0.35)
SB	0.96 (0.25)	0.60 (0.15)	0.68 (0.40)
NBD	0.10 (0.56)	0.54 (0.29)	0.62 (0.68)
NW	0.67 (0.12)	0.62 (0.20)	-0.22 (0.26)

[1]Clean, Clean status (no presence of PRRS or PED); PRRS, porcine reproductive and respiratory syndrome; PED, porcine epidemic diarrhea;

[2]AB, Abortion; TB, Total number of piglets born; NBA, Number of piglets born alive; SB, Number of stillborn piglets; NBD, Number of piglets born dead; NW, Number of piglets weaned.