Title: Review of literature for epidemiology and control of Porcine Reproductive and Respiratory Syndrome virus (PRRSV) in North America: lessons learned and knowledge gaps – **NPB #13-242**

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Abstract:

Objective—To describe the current knowledge on porcine reproductive and respiratory syndrome (PRRS) control and epidemiology in North America.

Animals or sample—Systematic review of the literature on PRRS epidemiology in North America

Procedures— The review was largely based on authors experienced and supported by a number of literature searchers. We described features related to PRRS control and elimination at the farm and regional levels and subsequently summarized knowledge gaps on PRRS epidemiology in North America.

Results—Much has been learned about the epidemiology of PRRS in North America. There are, however, important features of the disease that are yet-to-be elucidated, including those related with accuracy of diagnostic tests, effect of vaccine on virus diversity, and evaluation of control strategies at a regional level.

Conclusions and clinical relevance— Coordinated actions of producers and practitioners, in the absence of a regulatory framework, will be required to control and eventually eliminate the disease.

Introduction

In 1989, a syndrome characterized by reproductive disorders in sow herds and respiratory disease in growing pigs was first reported in the southeastern United States (US) and disease reports rapidly followed throughout North America [1, 2]. A number of known pathogens were initially implicated as the cause of this disease and the major breakthrough came in 1991 when a virus, initially referred to as Lelystad virus, was identified in The Netherlands [3, 4]. Subsequently, Koch's postulates were fulfilled when experimental aerosol exposure to sows with cell cultured Lelystad virus reproduced the clinical manifestation of the disease [4, 5]. In the United States, a prototype virus referred to as VR2332, which was isolated from continuous cell lines, was first identified in 1992 [3, 6, 7]. Although several names were originally applied to this syndrome, the designation of Porcine Reproductive and Respiratory Syndrome (PRRS) was chosen at the 1st International Symposium on Emerging and Re-emerging Pig Diseases in St Paul, Minnesota in 1991 [7]. A retrospective analysis of samples in the United States suggested no evidence of the PRRSV prior to 1980, whereas 1/26 herds were positive in 1985, and nearly 63% of samples were positive in 1988 [8]. In Canada, it has been suggested that PRRS antibodies were present as early as 1979, although clinical signs were not recorded until the mid to late 1980's [9]. The European strain is referred to as type I PRRS virus and the North American strain as type II. Most PRRSV infections in the US are due to type II viruses [10] and type I viruses remain a relatively unimportant component of PRRS outbreaks in North America [11].

Cost of PRRS virus was estimated for the United States to be approximately $560 million in 2005 and $664 million in 2011 [12, 13]. PRRS incidence has been difficult to estimate because differentiating new PRRSV introductions from resident or vaccine strains is technically challenging and expensive [14-16]. A coordinated action item from an American Association of Swine Veterinarians PRRS task force, referred to as National PRRS Incidence project, was initiated in 2011. In this project, voluntary participants agreed to share PRRS status of their sow herds using standardized terminology for status and new infection [17, 18]. Also agreeing to share retrospective data to 2009, this project now has four years of incidence data being reported across 14 production companies, 374 sow farms, and 1.2 million sows [19]. This project has revealed striking repeatability of the annual PRRS epidemics in the participating herds. For each assessed year (2011-2013), the incidence has exceeded the annual average in mid-October, signaling the onset of an epidemic of PRRS virus. The highest and lowest incidence rates occur in late winter and mid-summer, respectively.

This paper describes the current knowledge on PRRS control and epidemiology.
The review was largely based on authors experienced and supported by a number of PubMed searches (Figure 1). We first reviewed aspects related with the molecular epidemiology, within-farm transmission,

and between-farm spread of the PRRSV. Subsequently, we described features related to the control and elimination of the disease at the farm and regional levels. Finally, we summarized knowledge gaps yet-to-be elucidated on PRRS epidemiology in North America.

Figure 1: Results of PubMed searches conducted in May 29, 2014. Number of articles retrieved a) per search criterion, and b) per year Note that categories are not mutually exclusive, so that one given paper may belong to more than one category, and that some papers may not actually refer to porcine reproductive and respiratory syndrome
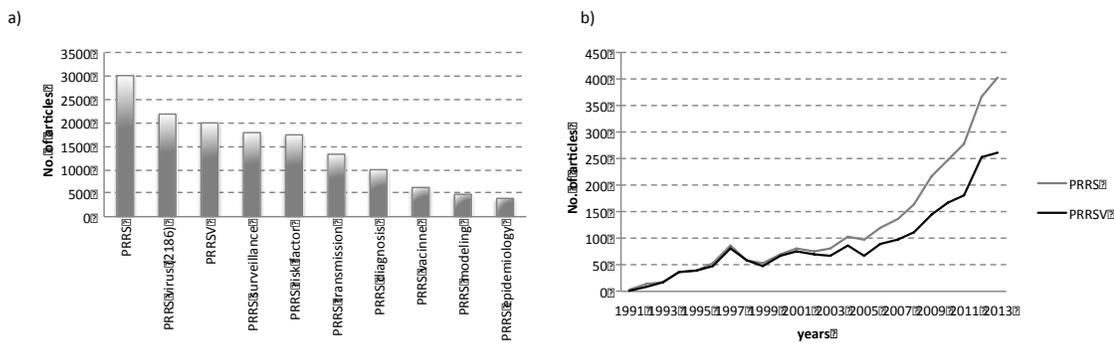
2.   Molecular epidemiology of PRRSV

Similar to other viruses of the *Arteriviridae* family, the PRRSV is species-specific, is highly resistant to cold temperatures, and is highly variable, due to its high mutation rate and potential for recombination [20]. High variability of the PRRSV is an important feature that offers unique opportunities to advance the study of PRRS through the investigation of epidemiological features at the molecular level [21]. The PRRSV genetic variability has been used to establish associations between PRRSV and epidemiological features of the outbreaks at different geographical (global and continental, regional, local, and farm) scales.

At global and continental scales, molecular epidemiology has been used to differentiate between PRRSV incursions associated with European and American strains, providing a hypothesis for the emergence and evolution of the virus, and to characterize circulating strains at a continental level [22-24].

At a regional scale, molecular methods have been used to assess the number of genetic groups circulating and to describe the circulation pattern in a country or region. For example, in the United States, Bayesian methods applied to an extensive collection of PRRSV sequences demonstrated that PRRSV spread reflects the movement of live pigs in the country with multiple introductions from Canada being detected [23, 25]. Similar descriptive studies have been conducted over the last five years in Canada [26, 27], China [25, 28-30], Korea [31], Denmark [32], Italy [33], Vietnam [34], and Thailand [35].

At a local scale, molecular methods have been used to discriminate between novel and pre-existing strains as a prerequisite to identifying factors associated with virus spread. Results have been inconsistent. In a study conducted in 316 PRRS-infected farms in Ontario, restricted fragment length polymorphism (RFLP) was used

to identify related strains and demonstrate that sharing herd ownership, gilt source, and market trucks accounted for most of the virus spread. Spatial proximity, which could be a proxy for airborne transmission, did not substantially contribute to PRRSV spread [36]. Furthermore, an early study conducted in the Midwest found that genetic similarity of isolates correlated better with time than with geographical distance, suggesting that PRRSV infection is uncommon through local transmission and, instead, typically occurs via long-distance contacts. Genetic distances between PRRSV isolates collected from the same farms at different times increased as the time separating the collection events increased [37]. Similarly, genetic variation was better explained by temporal, compared to spatial variation, in a study conducted in Italy [38]. In contrast, PRRSV identified in environmental samples were related (<1.2% nucleotide difference) to experimentally inoculated grow-to-finish pigs located far away, suggesting that PRRSV airborne dispersion may occur through long distances [39]. Furthermore, genetic relation was found to vary in time and space [40]. In line with this hypothesis, molecular epidemiology has been used to demonstrate that air filtration significantly reduced the incidence of PRRSV new strains incursions in sow farms located in a pig densely populated region of the United States [41]. An extensive analysis of ORF 5 sequences from 226 field cases originating from Quebec herds and submitted over a 4-year period (March 1998-July 2002) suggests that both statements, namely, that long distance and local transmission may be important. In this study, introduction of pigs and geographical location were associated (19% and 33% increase of risk, respectively) with PRRSv spread. Many (40%) of the outbreaks in which local spread was suspected were located within 3 km from an infected farm and aerosol transmission was suspected in many of them [42]. The relative contribution of alternative transmission routes on PRRSV spread, in relation to alternative production types, management companies and system, and regional demographic (such as farm density) and epidemiological (such as incidence) conditions is yet to be elucidated, and is prerequisite for the development of a system for forecasting PRRSV incursions in a region.

At a farm scale, molecular epidemiology has been used to demonstrate persistence and rate of incursion of PRRSV strains, which is prerequisite for identifying internal or external breaks in biosecurity. In 41/226 PRRSV-infected farms in Quebec, more than one strain were detected over a 3 months-to-4 years period. Results also suggested that PRRSV may persist in a farm up to 3.5 years displaying as little as 2% variation in ORF5. In 78% of the herds with multiple submissions, genetically different strains were identified [42]. The genetic variability observed among farms, among pigs within farms, and within individual pigs accounted for 92.94, 3.84, and 3.22% of the total variability in a study conducted in the Midwest [43].

3.   **Within-farm transmission of PRRSV**

Routes of shedding that have been described for PRRSV include saliva, nasal secretions, semen, urine, feces, and mammary secretions in lactating sows [7, 44-47]. Consequently, PRRSV transmission may occur through

multiple common routes including intranasal, oral, or intramuscularly [48, 49]. It has been suggested that the amount of shedding depends on strain type, with less virulent strains (such as MN 30100 or VR2332) shedding less than virulent strains (such as MN-184) by all routes including aerosol [50-52]. Although duration of infection and shedding vary widely, prolonged infection is a hallmark of PRRS virus as with other viruses in the *Arteriviridae* family. Persistent infection was first suggested in 1992 when transmission occurred 99 days post infection (DPI) in a sow [53]. Another study reported detection in oropharyngeal samples until 220 days after challenge-exposure [44]. In a second study this group reported that the virus could be detected in tonsils up to 56 DPI and in other tissues until 119 DPI [54]. Additional studies have shown that much longer persistence may occasionally occur in individual pigs [55, 56]. That said, there appears to be little evidence for persistence beyond 200 days as supported by field experiences with herd closure [57, 58]. Therefore, it has been suggested that the term prolonged is a better term than persistent in describing PRRS infections [56, 59].

Vaccination appears to help reduce shedding of PRRS virus. In one study, vaccination prior to challenge with homologous virus reduced the number of infected pigs at 127 days post infection and administration of 2 or 3 doses reduced viral shedding after 97 DPI [60]. Another study reported that vaccination after challenge with heterologous virus reduced the duration of shedding but did not reduce the viral load in the tissues and when subsequently challenged with another heterologous strain, vaccinated pigs had fewer clinical signs and better performance, but no difference in shedding [61]. More recently, another study has reported that air-surrounding pigs vaccinated 8 and 26 days after experimental challenge with a heterologous virus had reduced detection of aerosolized virus [62].

Minimal infectious dose (ID_{50}) appears to vary by isolate and studies have suggested ranges from $1 \times 10^{0.26}$ $TCID_{50}$ for MN-184 to $1 \times 10^{3.1}$ $TCID_{50}$ for VR2332.11 [63]. Additionally, route of exposure seems to play a role and higher doses may be required for oral vs. intranasal exposure ($1 \times 10^{5.3}$ and $1 \times 10^{4.0}$ respectively) and lower doses in intramuscular exposure (as few as 20 viruses) [64, 65].

In general, the PRRSV is highly susceptible to inactivation by heat and drying and infectious virus was not recovered from a variety of common surfaces and materials beyond day zero at temperatures from 25-27°C. At temperatures between -20°C and -80°C, PRRS can be stable for months to years, but infectivity is quickly lost when the pH of the solution is below 6.0 or above 7.5 [3, 66, 67]. Further, stability has recently been evaluated in manure and as expected, survival depended on time and temperature [68].

Those features influence the value of the basic reproductive ratio (Ro), which is the number of secondary infections that occurs in a fully susceptible population given contact with one infectious individual through the duration of the infectious period. Average values of Ro=2.6-3.0 (CI95%: 1.5-6.0) have been estimated for

PRRSV transmission [69, 70]. Characterization of the value of Ro is important to model disease spread and, ultimately, identify cost-effective disease control strategy. For example, disease modeling has recently been used to identify that herd size was negatively associated with probability of achieving stabilized status and repeated mass vaccination with gilt acclimatization was better than single exposure for control [71].

Various studies estimated transmissibility using diagnostic testing over time [70, 72, 73]. However, those studies were conducted in farms with a demographic and epidemiological condition different to those observed in North America and for that reason, conclusions are difficult to generalize.

In one of the few simulation studies conducted under conditions observed in the United States, Jeong et al [71] constructed a stochastic model based on 3 age groups in sows and pigs until 3 weeks of age. Similarly to other models, this was also the SIRS model with the added compartment of maternally immune pigs. It was assumed that pigs with maternal immunity are not likely to have the maternal immunity wane over the duration of the suckling period. In this simulation study, piglets born to the infectious sows were also assumed to be infectious. For the R_0, the authors used estimates of minimum, most likely and maximum values as a combination of reports from other studies and expert opinion [71]. Briefly, R0 in sow population was assumed to have values of 0.14, 3, and 3.2 for the minimum, mean and maximum, respectively. The R0 in the population of suckling pigs was assumed have values of 7.3, 9.8 and 13.1 for the minimum, mean and maximum, respectively. The baseline scenario in the simulation model by Jeong et al represented the absence of control measures, and it was followed by 4 scenarios of control measures including different combinations of herd closure, mass immunization, and gilt acclimation. Acclimatized gilts were assumed to have period of infectivity that was 70% of the duration in un-acclimatized gilts. Vaccine efficacy was assumed to be 92.5%. The scenarios evaluated were herd closure + single mass immunization, 2) closure and gilt acclimation + repeated mass immunization, 3) acclimation + single mass immunization, and 4) acclimation with repeated mass immunization.
The outcome that was measured in this model was the likelihood of achieving the stable status, defined as absence of PCR-positive (i.e. infectious) nursing pigs at weaning. It was concluded that the larger magnitude of R_0 and larger herd size both had negative effect on the likelihood of achieving the stable status. Based on the results of this paper, herd closure together with acclimation and repeated mass immunization was the scenario that resulted in the highest level of iterations with achieved stability. This was followed by gilt acclimation with repeated mass immunization, and gilt acclimation with a single mass immunization. Sensitivity analysis for the models having control measures included suggested that the recovery rate (i.e. duration of infectiousness) in sows was the factor influencing the likelihood of achieving the stability, and this varied between vaccinated and unvaccinated sows – depending on the model.

Authors argued that repeated mass immunization (ie every 15 weeks) was more effective strategy of minimizing the frequency of infectious animals at 200 weeks than was single mass immunization, and therefore did not recommend the use of the latter strategy for PRRS control.

4. **Between-farm spread of PRRSV**

Between-farm spread of PRRSV may occur through a number of routes, including 1) live pigs or semen; 2) vehicles; 3) people; 4) tools, equipment, and supplies; 5) food and water; 6) non-swine animals and insects; 7) air.

4.1. Live pigs or semen

Transmission of PRRSV via semen from infected boars has been well documented [74-76]. Introducing semen from potentially infected sources has been identified as an important risk factor [77, 78]. Practices to reduce the risk associated with semen include testing of semen or serum from boars for the presence of PRRSV RNA by PCR prior to use of the semen. Testing serum by PCR is more sensitive and detects PRRSV in infected boars earlier than testing semen by PCR [79-82]. A novel method of blood collection from boars using blood-swabs has been validated to enable testing of serum that overcomes the challenges of collecting blood from boars using traditional venipuncture [79-82]. Pooling individual samples of blood from boars for testing has been evaluated. A reduction in sensitivity of detection with as few as 3 samples per pool were reported [79, 80] with the loss of sensitivity being greater at the onset of viremia [81, 82]. Results from simulation models have demonstrated the need for intensive testing strategies for timely detection of infections in boars [81, 82].

When swine are moved, the pigs represent the most significant carrying agent. Live swine routinely moved include replacement gilts and boars, weaned pigs, growing pigs moved between production sites, cull animals, and market pigs. Risk factors related to entry of gilts include the number of gilts purchased and entered [78]. Practices to reduce risks associated with entry of gilts include purchasing gilts from negative sources and isolation prior to entry [73, 77, 78, 83]. Acclimation of gilts to provide immunity to the PRRSV by intentionally exposing them to either wild-type PRRSV or vaccination followed by a period long enough to assure they are no longer shedding virus has also been reported to reduce spread of the virus [83-86].

4.2. Vehicles

Risks associated with livestock trailers and practices to reduce the risks have been studied relatively extensively. It has been demonstrated that a sufficient amount of live virus remained in unwashed trailers contaminated after carrying infected weaned pigs to infect PRRSV negative pigs [87]. PRRSV can survive in feces 120 hours at 4^0C, which is long enough Linhares *et al* (2012) to present a risk given typical schedules and

conditions under which pig movements occur. All of the studies evaluating sanitation practices to reduce the risk of contaminated livestock trailers include washing as the first step. However it has been demonstrated that washing alone is not sufficient [88-91]. Sanitation practices reported to reduce the risk associated with contaminated trailers include a combination of disinfection (Tek-Trol; Biotek Industries, Atlanta, Georgia, USA) and drying [88]. Overnight drying of trailers following washing has also been shown to reduce the risk associated with contaminated trailers [88-91]. Disinfection with a quaternary ammonium and glutaraldehyde combination (Synergize; Preserve International, Atlanta, Georgia, USA) applied with a hurricane fogger was shown to be effective [89]. In another study that evaluated the efficacy of commercially available disinfectants at 4oC it was found Synergize, and another quaternary ammonium and glutaraldehyde combination (Aseptol 2000; SEC Repro, Quebec), prevented transmission of PRRSV in experimentally contaminated model trailers [90]. In the same study, it was demonstrated that at -20^0C, Synergize mixed with a 10% solution of propylene glycol or 40% methanol solutions eliminated the virus from the model trailers. Using thermal assisted drying technologies to heat and dry washed livestock trailers have also been evaluated and shown to reduce the risk of transmission. Heating trailers to 71^0C for 30 minutes [91] and applying thermal assisted drying for 2 hours to allow the trailer to dry were reported to be effective [92].

4.3.   People

Mechanical transmission of PRRSV has been described via boots and coveralls of personnel after being in contact with infectious virus but much more frequently in cold than in warm weather [93-97]. However, failure of people to transmit PRRSV after interacting with experimentally infected PRRSV pigs followed immediately by interactions with naïve sentinel pigs has also been reported [98]. Practices to reduce the risks associated with drivers have been studied including disposable plastic boots [99], and boot baths with 6% sodium hypochlorite (bleach) [99]. In one study several combinations of practices were shown to be effective at preventing transmission. The practices included changing boots, coveralls and washing hands; changing boots, coveralls, showering and 12 hours of downtime; and changing boots, coveralls, showering and no downtime [95].

4.4.   Tools, equipment, and supplies

Mechanical transmission of PRRSV via fomites has been demonstrated [100] with higher frequency in cold weather [93, 94]. Reported practices to reduce the risks associated with tools, equipment and supplies include plastic bagging inside a box for equipment and supplies that may come into contact with PRRSV at any time prior to entry into a farm [99].

4.5.   Food and water

Surveys of fresh pork meat samples collected in 2004 from slaughter plants in Canada tested positive for PRRSV by PCR [101], However a similar study conducted in Canada in 1997 found no meat samples positive by PCR [102]. Similarly, mixed results have been reported when evaluating the transmission of PRRSV by fresh pork meat. Results of some study support that negative pigs can be infected when fed fresh pork from PRRSV infected pigs [101, 103, 104]. In others, viral RNA could be found by PCR in pork muscle from PRRSV infected pigs; however, no transmission of PRRSV to recipient pigs via consumption of the pork was observed [105].

4.6. Non-swine animals and insects

Several insects have been studied to determine if they act as potential mechanical or biological vectors for PRRSV including houseflies, mosquitoes and stable flies. It has been demonstrated that houseflies (*Musca domestica*) can harbor virus [106] and mechanically transmit PRRSV from infected pigs to naïve pigs [97, 106-108]. Mosquitoes (*Aedes vexans*) can serve as a potential mechanical vector for PRRSV [109, 110]. In a single study, stable flies (*Stomoxys calcitrans*) failed to transmit PRRSV to naïve pigs after feeding on the blood of pigs infected with PRRSV [111]. Installations of insect screens and insecticides to reduce risks associated with insect carrying agents have been evaluated. In one study it was demonstrated that insect screens over sidewalls and inlets of a finishing facility significantly reduced the number of flies and fly bites compared to rooms treated with pyrethroid-based insecticides without screens or the rooms with neither intervention [112].

Studies to determine if non-domesticated animals and birds, including mice, rats, mallard ducks, prairie dogs and avian species can transmit PRRSV have been reported but results are inconsistent. Attempts to detect PRRSV or antibodies to PRRSV from experimentally infected Prairie dogs (*Cynomys ludovicianus*) were unsuccessful and it was concluded that prairie dogs were an unlikely reservoir for PRRSV [113]. In one study that compared the susceptibility of Muscovy ducks, Mallard ducks, guinea fowl, and chickens to PRRSV it was found that PRRSV could frequently be isolated from the feces and intestinal tracts of Mallard ducks and sporadically in the feces of guinea fowl and chickens [114]. In the same study it was also demonstrated that PRRSV could be detected in Mallards exposed to the PRRSV contaminated feces of other Mallards and that PRRSV could be transmitted to pigs through the PRRSV contaminated feces of Mallards. In another study, however, efforts to detect PRRSV in the feces and tissue of mallard ducks exposed to PRRSV infected pigs or to transmit PRRSV from experimentally inoculated ducks to pigs were both unsuccessful [115]. Mice and rats have also been investigated as potential reservoirs for PRRSV. The virus could not be isolated by virus isolation from mice and rats collected from an endemically infected pig farm nor could virus be detected from mice or rats after being experimentally inoculated with PRRSV [116].

4.7. Air

Several studies have been conducted to evaluate the potential role of aerosol transmission of PRRSV from one population of pigs to another. Early studies failed to find evidence of aerosol transmission. In a study conducted in early May in Minnesota, transmission was not observed from a barn containing pigs experimentally infected with PRRSV to PRRS naïve pigs located in a trailer outside the barn [115]. Aerosol transmission was again not observed in a study conducted with a similar design except the trailer with the naïve pigs was simply located in front of the exhaust fans outside the barn for 5 days [95]. More recent studies have provided evidence that aerosol transmission of PRRSV can occur. Models with a box containing a mister to aerosolize PRRSV connected to a second box housing a cyclonic collector to collect air samples subsequently tested for the presence of live virus by virus titration[117]; models with a box containing a nebulizer to aerosolize PRRSV connected to a second box housing PRRSV naïve pigs [118, 119] and models with a duct connecting PRRSV positive donor and PRRSV naïve recipient pigs [120, 121] have all been used to demonstrate that aerosol transmission may occur. In a study involving a population of pigs experimentally infected with PRRSV and naïve populations of recipient pigs, virus titration was used to demonstrate that live virus may be shed in aerosol, may travel and survive for at least 120 meters and may infect PRRSV naïve recipient pigs located 120 m from a population [122]. Weather conditions favorable for aerosol spread of the virus, including wind direction from donor to recipient pigs, higher barometric pressure and lower humidity, were also identified in this study. The quantity of virus being shed through aerosol may vary for different isolates and more pathogenic isolates may be more likely to be transmitted by aerosol [50, 120, 123].

Filtration of incoming air to reduce the risk of aerosol transmission of PRRSV has been evaluated in a number of experimental studies. The most consistent reduction in the risk of aerosol transmission of PRRSV has been reported for high-efficiency particulate air (HEPA) filters, with and without large particle pre-filters [118, 121]. Various fiberglass and electrostatic filters typically used in household or industrial applications, with alternative minimum efficiency reporting value (MERV) ratings, have been evaluated with mixed results. Several studies with different experimental models evaluating two-stage filtration systems with the second stage involving one or more filters with a MERV rating of 16 successfully prevented aerosol transmission of PRRSV [118, 122, 124]. In one study, however, three of four fiberglass filters with a MERV rating of 16 and one with a MERV rating of 14 evaluated in the study failed to filter concentrations of aerosolized PRRSV up to 1×10^7 TCID$_{50}$/L [117]. In several related observational studies of negative pressure ventilated large breeding herds in southern Minnesota and Northern Iowa involving non-filtered breeding herds and herds filtered with either MERV 14 or MERV 16 filters, a significant reduction in the risk of PRRS outbreaks over the study period was reported for the filtered farms [41, 125-127]. A capital budgeting analysis was performed to estimate the payback period for filtering breeding herds, based on the results of an observational study [41]. Point estimates of the payback

period for farms filtered with a conventional attic filtration system was 5.35 years and for a combination attic and sidewall system, which is more expensive to install, the payback was estimated at 7.13 years [128].

A two stage filtration with a single fiberglass pre-filter with a MERV 4 rating and a single electrostatic filter with a MERV rating of 12 resulted in a reduction in risk but the reduction was significantly less than that achieved with HEPA filters [118]. The same result was achieved in a companion study that evaluated a double fiberglass pre-filter with a MERV 4 rating and a double electrostatic filter with a MERV 12 rating [119]. A 95% DOP, 0.3um system using a filter with a MERV rating of 15 also reportedly resulted in a significantly lower reduction in risk relative to HEPA filters in the same study. Polypropylene filters impregnated with antimicrobial compounds (Noveko International, Montreal, Canada) in a 15 or 20 layer configuration successfully filtered PRRSV in aerosolized concentration of up to 1×10^7 TCID50/L, however a 10 layer configuration was successful only for concentrations up to 1×10^6 TCID50/L [117].

Use of a quaternary ammonium and glutaraldehyde combination (Synergize; Preserve International, Atlanta, Georgia, USA) disinfectant in an evaporative cooling system (EVAP) failed to filter aerosolized PRRSV in one or more replicates even for the lowest concentration of virus, 1×10^1 TCID50/L, tested [117]. Radiation lamps emitting ultraviolet light (UVC classification) have been evaluated but failed to reduce the risk of aerosol transmission of PRRSV [118].

5.   Control and elimination programs at the farm level

Classification of a herd's PRRSv infection status is a useful tool in the control and elimination of PRRS as standardized definitions allow for accurate measurements of virus impact such as prevalence and incidence over time. Such a classification has been designed by a group in the American Association of Swine Veterinarians PRRS task force which outlines criteria for five different status categories ranging from positive unstable (1), through positive stable (2a or 2b), provisionally negative (3) and negative (4) [17]. Briefly, herds are classified as status 1 during the active, acute phase of the infection when weaned piglets are tested positive for PRRS virus by PCR. After four monthly negative consecutive tests are achieved over a 3-month period a herd is classified as either stable status 2a if the long term decision is to control, rather than eliminate the virus, or 2b if the decision is to eliminate the virus. Herds are classified as status 3 after replacement animals have been introduced to the herd and remained sero-negative (by ELISA) for a period of at least 60 days. Finally, status 4 is achieved by complete herd roll over, depopulation repopulation program or a period of 12 months since the beginning of status 3 and animals must be confirmed sero-negative by ELISA.   Additionally, a standardized case definition is useful to reduce the effect of bias. Recently an effort was undertaken to outline a decision making process to determine if a virus recovered from a population of pigs is the same or different from

historical strains [18]. Together, these components make up the first step in classifying herds, and have been applied extensively in the National PRRS Incidence Project [19].

PRRS control starts in the sow herd with the intention of weaning pigs with low prevalence, ideally zero prevalence of PRRS virus at weaning. There are two fundamental strategies to accomplish this. Herds in high-density regions where infection pressure is high may prefer an approach that is based on maintaining a uniform level of immunity through vaccination and/or strategic exposure to live virus from the herd (Class IIa). This approach is based on the rationale that some immunity in a herd is better than no immunity, even if the level of cross-protection among different viruses is not complete [129].

The second strategy (Class IIB, III or IV) has the goal of eliminating PRRS virus from the sow herd. PRRSV elimination may be accomplished in several ways. Whole herd depopulation and repopulation is the most effective means of eliminating virus from a herd, however, the disruption in production comes at a financial cost [130, 131]. Long-term financial gains from this method are only realized if there are PRRS free replacement pigs available and the farm remains uninfected. Modifications of the whole herd depopulation strategy have been described including partial depopulation, test and remove and herd closure [57, 132-134]. The most common of these methods are partial depopulation and herd closure. Test and removal methods have important financial and logistic considerations and are rarely applied in the swine industry except on boar stud farms [135, 136].

Herd closures have been evaluated previously [57]. Recently a large prospective observational study was conducted to understand factors influencing the times required to eliminate PRRSv from a sow herd and to re-achieve production [58]. Overall, the median time to negative pig production was 27 weeks, however there was considerable variation among herds in the study [58].

At the initiation of a herd closure program, three methods have been used for achieving homogenous immunity in the sow herd. These include vaccinating all sows with live virus PRRS vaccine, challenge-exposing sows with serum containing live virulent PRRS virus recovered from the herd or exposing sows to 'feedback' material produced from tissues of infected piglets [84, 137, 138]. Linhares *et al.* (2014) compared herds that were exposed to serum to those that received MLV vaccine and reported that exposure to field virus through serum promoted virus elimination from the sow herd while exposure to vaccine virus promoted a quicker return to baseline production [58, 129].

Exposure to live virus obtained from infected pigs raises the concern of the unintentional spread of other pathogens [139]. Unwilling to take risk of unintentional introduction of pathogens into breeding herds, many veterinarians are adopting the use of commercial vaccine as the preferred method of homogenizing immunity in breeding herds and while several commercially available killed vaccines are marketed around the world, current evidence suggests limited efficacy and have instead been suggested as a means of boosting immunity after exposure to live virus [140, 141].

6.   Control and elimination programs at a regional level

At the country level, eradication has been successful for in Chile, Sweden and South Africa [142-146], although Chile and Sweden have been re-infected. Each of these situations was perhaps 'ideal' for elimination due to several factors, including relatively low prevalence, clustered outbreaks, small swine industries, government - producer veterinarian cooperation and perhaps attributes of the virus that favor eradication. In countries where these ideal circumstances do not exist, the goal may be to keep the virus out of uninfected farms and regions with an emphasis on biosecurity and control it in regions where it exists.

Large scale epidemiological studies available in the peer-review literature are frequently conducted with a sample of swine herds with the aim to investigate risk factors for presence or spread of PRRSV or a specific PRRSV strain. An alternative design has been the inclusion of entire regions in disease control programs (DCP), in which a large proportion of herds was included. The DCP could be implemented as an organized response of veterinary services to incursion of PRRSV in a country (Sweden) or as a voluntary program which is founded on cooperation between producers and veterinary services. Evaluation of disease status, outbreak investigations, targeted epidemiological studies, development of communication strategies, and recently mapping of PRRS status have frequently been included as part of such programs.

6.1. Observational studies

Despite the importance of PRRS in swine populations, observational studies investigating factors contributing to its presence or spread between herds are relatively infrequent. Spread of PRRSV among herds has been evaluated using a variety of approaches and case definitions. Some studies relied on serological evidence of PRRSV circulation in various herd types [147]. Others used broad classification based on PRRSV types (European versus North-American) on the basis of serology [77], genotypes on the basis of RFLP patterns [85, 148], classification based on phylogenetic trees and different cut-off points to categorize variants into different groups [149-151], or matrices of similarities to assess correlation between similarity of nucleotide sequences and spatial and other proximities among herds [40, 152-154]. The analytical approach varied among studies as well. Some relied on descriptive statistics[147, 149], contingency tables [150], Cox's proportional hazard

models [77, 151], generalized additive models and methods to detect spatial and space-time clustering and clusters commonly used in spatial epidemiology [148], statistical individual-level infectious disease transmission models [85], Mantel correlation test [40, 152-154] and linear regression based on permutation approach [154]. As a part of such investigations, one of the largest uncertainties continues to be importance of area spread (also commonly referred to as local spread), which is often discussed in the context of airborne transmission. Several epidemiological studies reported area spread and have argued that aerosol transmission played a critical role in transmission [77, 150]. In other studies, existence of area spread could not be identified [85, 147]. Furthermore, several authors reported the possibility of area spread for some discrete genotypes, although such spread was not identified as the dominant mechanism of spread [148, 149], or could in some cases be explained by common sources of animals [148]. Few studies investigated membership in important networks such as ownership [85, 148, 149, 153, 154], sources of animals and semen [77, 85, 147, 148], or different transportation or service networks [85]. Membership in different networks should be considered more thoroughly, either in the context of outbreak investigations, or stand-alone descriptive network analysis, or in the context of PRRSV transmission between herds. Although studies of pig movements are starting to emerge, an important component should also be evaluation of trucking networks. As an illustration, one study reported that three farms shared one truck when monthly and weekly networks of farms and trucks were evaluated in a pilot study in four Canadian regions. On a daily basis, the truck involved in shipment was used for at least one additional shipment in >50% of shipments [155].

In a cross-sectional study of 103 UK swine herds during 2003 and 2004, a sow herd size of <250 sows and having distance of >2miles to the nearest pig site were factors that increased the odds of being negative for exposure to PRRSV [73]. The larger distance to the nearest pig herd was however positively associated with being a nucleus or a multiplier herd, and with being a herd size <250 sows. Thus, cause and effect was not possible to separate in this analysis. The pig-level quantitative ELISA response was evaluated on a subset of data in two different hierarchical models. In the model based on 16 herds that had PRRSV sero-negative young pigs, presence of quarantine facilities on farm was associated with lower level of serological response, adjusting for other factors in the model. Moreover, in the model based on 25 herds that had PRRSV seropositive young pigs, factors that were associated lower ELISA titers were: purchase of gilts, longer length of isolation period for purchased stock (with =>6 days as the category with longest quarantine), and =>48 hours of pig-free time for farm visitors. Interesting perspectives were gained in this study just by examining the serological profile of herds according to major age groups present on the site. It has been argued that smaller isolated herds are likely to experience the fadeout of infection, whereas persistently infected herds are more likely to be larger herds in pig-dense areas with ongoing introduction of infectious pigs.

An approach of within-herd examination of prevalence and serological profiling should be considered more frequently although it should be recognized that this could have limited utility in many North American herds. Nonetheless, alternative strategies could be used to investigate spread of PRRSV in sow herds in the early phases of the outbreak, before control measures are implemented.

In another cross-sectional study of risk factors for PRRSV circulation in UK swine herds, Velasova et al [156] reported >15,000 pigs in 10 km radius, collecting dead pigs (as opposed to incineration), use of live PRRSV vaccine, and weaning age of 21-27 days (as opposed to weaning at >=28 days of age) as risk factors for PRRSV circulation.

Management of dead stock has been identified in other studies as well. Lambert et al [157], identified access to the site by a rendering truck to be positively associated with the PRRSV status of sow herds in a Quebec region, as well as absence of shower at entrance. The latter two variables were identified to have population attributable fractions of 0.10 and 0.27, and because they are manageable at the herd level were identified as modifiable factors. Other risk factors were herd size of >300 heat producing units, and less than 2.5 km distance to the nearest pig site.

Mortensen et al [77] used time-matched nested case-control study design and a proportional hazard model to evaluate association with factors preceding the introduction of vaccine-like PRRSV US strain into sow herds over two intervals of exposure and using different functional forms of covariates. The outcome was defined based on serological response to the representative viruses after excluding PRRS-EU positive sites from eligible controls with a rationale that PRRS positive status could change management practices. Factors associated with the risk of introducing the PRRSV-US strain were herd size (expressed as the log of heat producing units), introduction of animals from herds positive for this strain, purchasing semen from boar studs positive for this strain during a risk interval, and cumulative exposure due to infection of neighboring herds with PRRSV-US. The latter variable was calculated as a composite variable constructed from number of animals housed in PRRSV-US positive herds within 3 km radius and by taking into consideration their time of positivity and actual distance. Such cumulative neighboring exposure was associated with the hazard of experiencing the outbreak and led authors to conclude that area spread was an important factor associated with the spread of PRRSV-US among herds. It was also argued that the only factor linked with such spread could be aerosol transmission of this strain between herds. The authors also looked at herd density and pig density calculated using 5 km radius. However, this exposure was not associated with the risk of becoming infected with this strain.

Rosendal *et al.* (2010) evaluated spatial trends, spatial clustering and clusters of different PRRSV genotypes in Ontario swine herds, using RFLP patterns based on ORF5 sequence [27]. Detection of spatial or space-time

clusters was followed by exploration of common sources of animals and potential fomites. Out of all field RFLP genotypes investigated, significant space-time clustering was detected only for RFLP type 1-18-4. This could be interpreted as existence of local spread. However herds that influenced detection of clustering also had common sources of animals. Similarly, out of all field RFLP genotypes investigated, significant spatial clustering was detected only for genotype 1-3-4. In this case however, no obvious common linkages among herds could be identified. Non-significant spatial and space-time clusters of different genotypes were investigated and in many cases, there were obvious linkages between herds [148].

A follow up study of genotype 1-18-4 based on individual-level models for infectious diseases has also been published [85]. Management practices, spatial proximity and membership in different networks of ownership and service providers were considered either individually or simultaneously. Two separate models were considered; one for sow herds and the other for all herds. Dates on confirmatory diagnosis from a diagnostic laboratory were used to convert data on individual herds into SIR type of data for each herd, where period of infectiousness was estimated from the data or assumed to be fixed and of different duration. In addition, uncertainty about the exact period of PRRSV genotype introduction into a herd was accounted for. Using such an approach, networks important for the spread of the genotype were herd ownership, gilt sources, and transportation of market pigs. Spatial proximity could not be identified as one of the important factors. Acclimation of gilts using different approaches was identified as factor that decreases the risk of herds becoming infected as well as transmission of this genotype to other herds. Transportation of culled animals was also identified as important factor for the model that included all herds, although this network has not been included in the final model [85].

Using phylogenetic analysis of ORF5 nucleotide sequences and =>98% as a cutoff point to declare different strains, Larochelle et al [149] investigated epidemiological linkages between herds with identical strains. In the analysis where more than one common link was possible, authors reported that 11 outbreaks with a total of 24 strains were attributed to the introduction of infected piglets, whereas 9 outbreaks with 11 strains were linked with replacement gilts. Possibility of area spread among herds in different ownership located within 3 km distance was reported for 15 strains. In their study area, spread was defined as "herd-to-herd transmission without any apparent pig or human contact". The authors also reported that 40% and 37% of all herds where the area spread was suspected were located within 3 kms, and between 3 and 10 kms, respectively. Aerosol transmission was suspected in several cases in this study.

In a longitudinal study of breeding sites Holtkamp *et al.* [151] reported significant association between risk of introduction of PRRSV and external biosecurity score. Median time to reported outbreak in herds with high

external risk index was 12.7 weeks, whereas median time in herds with low index was 107 weeks. Other important factors contributing to shorter time to PRRS outbreak were establishing a new herd during winter season and new site start up (as opposed to establishing herd through depopulation-repopulation). No association between the internal biosecurity and time to outbreak could be detected.

Le Potier et al [147] reported findings from a DCP in a region in France that is well aligned with many contemporary regional PRRS programs in North American regions. Conducted in the early phases of PRRS spread and low prevalence situation, this program resulted in further decrease in PRRSV prevalence to below 2%. Disease investigations that resulted from this program suggested that 56% of possible sources of PRRS cases were due to introduction of infected gilts and piglets, 19% due to contaminated semen, 21% due to fomites or slurry, and 3% due to other causes or remained unknown. The authors reported that herds within 500 meters from the outbreak PRRS site had herd PRRS prevalence of 45%, whereas prevalence for herds over 1km was only 2%. Authors concluded that airborne transmission was infrequent except for sites within very close proximity.

Using well defined inclusion criteria Alonso *et al.* [150] investigated incidence of new introduction in air-filtered and non-filtered herds, where novel incursions were defined on the basis of comparison of newly detected PRRSV variants to the previously detected ones. A range of different cutoff points was used to define a novel introduction. Regardless of the cutoff point used, the incidence of new PRRSV introductions was lower in herds under air filtration. The risk of novel PRRSV genotype used was between 2.3 and 10 fold higher in non-filtered herds and increased linearly with cut-off value used to define novel introduction. The authors suggested that 3-5% cutoff point was the most useful decision rule to define the novel introduction for the purposes of their study. Authors also used estimated that, on the basis of 5% cutoff point, 80% of novel PRRSV introductions could be attributable to airborne spread in the target population (herds with good biosecurity in pig dense areas).

6.2. Disease control programs for PRRS

Results published on the basis of disease control programs for PRRS are not very common in the peer-reviewed literature. There are several early descriptions of PRRS control programs [77, 147] reporting the results of disease control program aimed at elimination of PRRSV after its incursion in a completely susceptible population, and recent descriptions mostly coming from North America [158, 159].

The study by Mortensen et al [77] offers a perspective on utilization of PRRS registers and other animal health databases in Denmark for the purposes of a specific epidemiological study in 1996. Several points could be of

use for the design of databases of use in regional control programs. For example, neighborhood exposure for each site was calculated on the basis of documented movement of animals from PRRSV-US positive herds into neighboring herds. Additionally, an epidemiological questionnaire that was used was in the study collected information about the actual sources of semen and breeding animals.

Le-Potier et al [147] described PRRS disease control program - "PRRS agreement" - in the "Pays de la Loire" region in France starting in early 1993. The authors described the development of a voluntary program, structure and evolution of leadership organization, financial background, and actual methodology used to investigate PRRS at the regional level and eliminate infection from affected herds. Many current issues for North American regions involved in regional disease control programs have been described in this report including surveillance and outbreak investigation, definition of priority herds, control measures implemented in priority herds (based on depopulation-repopulation), and certification and testing requirements following the implementation of control measures.

Carlsson et al [144] described incursion and elimination of PRRSV during summer of 2007 in Sweden. As a part of this report, authors described legal foundations for outbreak response, regular surveillance, outbreak investigation and surveillance strategies to ascertain freedom from infection after outbreak has been contained. Outbreak investigations relied on assessment of management practices and detailed trace in and trace out data from infected herds. Interestingly, the period under consideration for tracing was 4-6 months prior to the detected infection for each herd and was based on the abattoir data, transport records, central register of holdings, and the pig movement database. PRRS in Sweden has been included in the Swedish Law of Epizootics, which requires all clinical suspicions for PRRSV to be analyzed diagnostically (for virus). The authorities investigated two clusters of disease and concluded that the most likely source of transmission between herds was combination of pig transport to abattoir, contact through people, animal movement, and sharing equipment between sites or other type of short-distance transmission between two very close sites. The eradication of PRRSV in this instance was achieved through stamping out method. Authors argued that a prerequisite for successful eradication was early detection which was dependent on effective surveillance. In addition, they stressed importance of good collaboration and a common objective among stakeholders.

Most recently, several North American regions have shown different level of activities related to regional PRRS control [83, 160]. An important part of communication strategies has been mapping of PRRS status and different PRRSV genotypes. This can be achieved in a variety of different ways and could include development of static mapping or dynamic and interactive mapping which also includes time dimension and which is becoming more available in recent times. Mapping of disease serves to provide good visualization and is

excellent communication tool. Nonetheless, it also serves the purpose of accurate collection of data. Provide accurate data for mapping could prove useful for the purposes of traceability and establishment of PRRS databases and registers. Such databases existed in other regions in the early phases of PRRS incursion, and could prove to be essential for PRRS investigation and control.

7.   Surveillance and testing

Effective PRRSV surveillance is based on clearly defining the population of interest, the objective of testing, and the approach that can achieve the objective in the population of interest at the lowest cost. Cost is invariably a major factor in veterinary surveillance. If PRRSV control and elimination is the goal, the surveillance plan must be capable of providing quantifiable evidence of progress and guide final eradication efforts. In the ultimate scenario, surveillance must be capable of efficiently proving that a state, region, or country is PRRSV-free.

Contemporary surveillance methods are a relatively recent invention that continues to evolve. "Representative sampling", testing a subset of animals, rather than the entire population, was the first step towards more efficient surveillance. First described in 1895 [161], representative sampling was not applied to swine surveillance until the late 1970's when statistical sampling in the U.S. PRV eradication program replaced the whole-herd testing used in the "hog cholera" eradication program. (The standard of collecting 30 samples is a legacy of this era). Indeed, the statistical sampling approach described by Cannon and Roe (1982) in *Livestock Disease Surveys: A Field Manual for Veterinarians* established a methodology that served the swine industry well for decades [162]. Improving on this approach, Cameron and Baldock (1998) developed formulas to calculate sample sizes for surveillance based on imperfect diagnostic tests [163] and Cannon (2001) derived fast approximation formulas for this calculation [164]. The application of this classic approach to PRRSV surveillance in commercial swine populations is thoroughly reviewed elsewhere [165, 166].

This earlier work provided a strong theoretical basis for surveillance, but changes have occurred in the industry that challenge the ability of the traditional approach to be effective:

a. *Subpopulations:* Animals on farms are spatially separated by age, production stage and/or function, with little interaction between these subpopulations. Non-uniform distribution of disease among segregated subpopulations, a consequence of physical segregation, should be expected, but is rarely accounted for in surveillance designs.

b. *Dynamic population change:* Subpopulations change rapidly, but non-uniformly, in space (buildings) as

they progress through the production cycle. A finishing barn on a typical farm will experience ~250% annual population change as groups of animals are placed, grow, and go to market. In sow herds, ~40% of females are replaced annually [167]. The constant introduction of new, immunologically susceptible animals promotes the circulation of pathogens.

c. *Connectivity of metapopulations:* In the U.S., large numbers of young pigs are moved from breeding farms into feeding operations located in the Corn Belt because it is more efficient to move young pigs to the feed than the reverse. In 2011, nearly 40,000,000 live swine (and the pathogens they carried) were moved across state lines. In addition to pigs farrowed in the U.S., this included ~6,000,000 live feeder or weaned pigs imported chiefly from Canada and shipped to grow-out facilities in the Corn Belt [168, 169]. This pattern of moving animals closer to food sources provides an efficient network for the rapid dissemination of PRRSV and other pathogens.

Very unlike the herds of the 1980's and 1990's in which statistical sampling was first applied, the current industry consists of large, physically segregated pig populations with high population turnover rates. These conditions favor pathogens because herd immunity is tenuous and unstable [170]. In addition, the transport of large numbers of animals between sites provides the means for pathogens to rapidly reach geographically distant populations. Under such conditions, a new statistical sampling methodology capable of accounting for the heterogeneous hierarchies within systems (sites, barns, animals) and the need for repeated sampling over time needs to be developed. Such work is in progress.

Serum is the traditional *ante mortem* surveillance specimen, but other specimens may be collected from individual animals for testing, e.g., semen and blood swabs. Testing costs may be reduced by "pooling" samples prior to testing. Technically, a pooled sample is a composite sample created by combining two or more discrete samples into one for testing [171]. In veterinary medicine, "pools" are usually formulated for diagnostic testing by combining individual samples in approximately equal portions [172]. The issues in detection related to pooled samples, e.g., the effect of sample dilution on test performance, are complex but the approach is common practice [173, 174].

Regardless of the type of specimen, the primary roadblock to more extensive and routine surveillance has been the inconvenience and cost of collecting and testing statistically appropriate numbers of specimens from individual pigs. One alternative is the use of oral fluid specimens. These samples are (1) are collected by a single person, (2) can be collected as frequently as desired without stress to pigs or people, and (3) provide a higher probability of analyte detection with fewer samples than serum [175]. The biological basis of oral fluid-

based testing is well established and the approach is used extensively in human diagnostic medicine [176]. Oral fluid-based assays are capable of excellent diagnostic performance, e.g., the diagnostic sensitivity and specificity of a commercial serum antibody ELISA modified to detect PRRSV IgG antibodies in pen-based oral fluid specimens was estimated at 94.7% (95% CI: 92.4, 96.5) and 100% (95% CI: 99.0, 100.0), respectively [177, 178]. A shortcoming of oral fluid samples has been the effort of collecting oral fluids from individually housed animals.

PRRSV infection does not produce pathognomonic clinical signs. For this reason, diagnostic testing is mandatory, i.e., syndromic surveillance is not an option. The choice of testing technology, i.e., nucleic acid or antibody-based testing, is an important consideration in surveillance. Testing flexibility is desirable because, in the event of an uncertain test result, it allows for follow-up testing using the alternate technology. In this case, both serum and oral fluid specimens are be suitable for nucleic acid (PCR) or antibody-based testing, but each diagnostic methodology presents advantages and disadvantages. The detection of nucleic acid reflects the circulation of pathogens in the present; an important issue from the point of view of timeliness. However, nucleic acid assays are more expensive than antibody-based assays and test performance has been an issue [179, 180]. Antibody is abundant in serum, readily detected in oral fluid [176], and the cost of antibody assays is significantly lower than PCR-based assays. In contrast to nucleic acid, antibody provides a prolonged window of detection because it reflects both recent and past exposure history. At the farm level, antibody assays are compatible with continuous monitoring of population immune status using a control-chart approach. On the other hand, point-in-time detection of pathogens or nucleic acid may be useful for pathogen characterization and/or vaccine development. Ultimately, the selection of which approach to use should be dictated by the purpose of testing.

Surveillance cannot be successful without a clear vision, but surveillance also requires technical capability and capacity. This includes the availability of tests that are reliable, accurate, and highly reproducible between laboratories [177-179], as well as laboratories capable of meeting standards of quality assurance and quality control. Above all, surveillance must be simple, flexible, and accepted by its users; else it will not be done [181].

8. Knowledge gaps

As a result of the literature review here, authors have identified a list of yet-to-be elucidated aspects of PRRS epidemiology, namely:

1. What is the most cost-effective control strategy at the regional level?

2. Is there a way to differentiate resident strains from new incursions?

3. What can we do to identify the most accurate diagnostic tests and laboratories and discourage the use of tests that do not meet the required standards? Nearly all the controlled studies ("ring trials") of the tests commonly used in PRRSV testing have shown either high variability in performance among laboratories or lower performance than we have come to expect.

4. What is the relative contribution of alternative transmission routes on PRRSV spread?

5. How can we shorten the time to achieve stability in sow herds?

    a. May we develop better control strategies in the early phases of the outbreak in a sow herd?

    b. Might a one time, early wean strategy, such as is performed to control PED, shorten the time to achieve PRRS virus stability?

6. Does vaccination at the regional level affect ensuing virus diversity and spread?

7. Is there an inexpensive and rapid test to differentiate between vaccine and field virus?

8. What is the optimum surveillance strategy for herds and regions?

9. What is the contribution of filters vs added biosecurity that accompanies filtering to reducing a sow farm's risk of infection?

10. Why did the incidence of PRRS decrease in 2013/14 and what will it be next year?

11. Is there any association between incidence of PRRS and other infectious diseases, such as PED in sow herds?

12. What number and distribution of herds do we need to maximize potential of the national incidence project and area regional control projects?

13. Is there a role for adding location to the national incidence project and area regional control projects to better understand spatial clustering of PRRS and associated risk factors?

14. What are the carrying agents (gilts, trucks, people, fomites, air) most frequently involved in outbreaks caused by the new PRRSV introductions?

15. Is the probability of success in controlling PRRS influenced by yet-to-be investigated social and economic factors?

Conclusions

Despite time and money invested on research over the last 25 years and substantial advances made to understand the epidemiology of PRRSV, there is still a need to elucidate critical aspects of the disease epidemiology. It may be accepted, however, that only coordinated actions of producers and practitioners, in the absence of a regulatory framework, will be required to control and eventually eliminate the disease.

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