

Review

# Global Challenges and Advancements in the Management of Pivotal Porcine/Swine Viral Diseases

TAEHO KWON<sup>1,2,3\*</sup>, GYU-SEO BAE<sup>4\*</sup>, EUNSU JEON<sup>4\*</sup>, PHILYONG KANG<sup>2</sup>, HEE CHANG SON<sup>2</sup>,  
YOU JUNG AN<sup>4</sup>, BON-SANG KOO<sup>4,5</sup>, SUN-UK KIM<sup>2,6</sup> and KYUNG-SEOB LIM<sup>2</sup>

<sup>1</sup>Primate Resources Center, Korea Research Institute of Bioscience and Biotechnology (KRIBB), Jeonbuk, Republic of Korea;

<sup>2</sup>Futuristic Animal Resource and Research Center, Korea Research Institute of Bioscience and Biotechnology, Ochang, Republic of Korea;

<sup>3</sup>Advanced Bioconvergence Department, KRIBB School, Korea National University of Science and Technology (UST), Daejeon, Republic of Korea;

<sup>4</sup>National Primate Research Center, Korea Research Institute of Bioscience and Biotechnology, Ochang, Republic of Korea;

<sup>5</sup>Department of Biomolecular Science, KRIBB School of Bioscience, Korea National University of Science and Technology (UST), Daejeon, Republic of Korea;


<sup>6</sup>Department of Functional Genomics, KRIBB School of Bioscience, Korea National University of Science and Technology (UST), Daejeon, Republic of Korea

## Abstract

Porcine/swine viral diseases pose substantial challenges to the global pig industry by affecting animal health and economic stability. This comprehensive review examines four major viral diseases impacting swine populations worldwide: Porcine reproductive and respiratory syndrome (PRRS), African swine fever (ASF), classical swine fever (CSF), and porcine circovirus type 2 (PCV2). We investigated the etiology, epidemiology, clinical signs, and diagnostic methods for each disease, thereby providing an in-depth understanding of their complexities. Additionally, we

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\*These Authors contributed equally to this work.

 Bon-Sang Koo, DVM, Ph.D., National Primate Research Center (NPPRC), Korea Research Institute of Bioscience and Biotechnology (KRIBB), Yeongudanji-ro, Ochang-eup, Cheongwon-gu, Ochang, Cheongju 28116, Republic of Korea. E-mail: porco9@kribb.re.kr; Sun-Uk Kim, Ph.D., Futuristic Animal Resource and Research Center (FARRC), Korea Research Institute of Bioscience and Biotechnology (KRIBB), Yeongudanji-ro, Ochang-eup, Cheongwon-gu, Ochang, Cheongju 28116, Republic of Korea. E-mail: sunuk@kribb.re.kr; Kyung-Seob Lim, DVM, Ph.D., Futuristic Animal Resource and Research Center (FARRC), Korea Research Institute of Bioscience and Biotechnology (KRIBB), Yeongudanji-ro, Ochang-eup, Cheongwon-gu, Ochang, Cheongju 28116, Republic of Korea. E-mail: dvmlim96@kribb.re.kr

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assessed their global distribution, transmission dynamics, and the economic repercussions they entail. We also discuss current management and control strategies, including vaccination, biosecurity measures, and regulatory policies. Special attention is given to the evolving nature of these diseases, with a focus on emerging strains, new insights into their pathogenesis, and the latest advancements in vaccine development. This review intends to be a valuable resource for veterinarians, researchers, and policymakers, presenting a thorough and current overview of the challenges and developments in managing these swine viral diseases at the international level.

**Keywords:** Porcine, swine viral diseases, porcine reproductive and respiratory syndrome, African swine fever, classical swine fever, review.

## Introduction

The global swine industry is continually threatened by a spectrum of viral diseases that substantially affect animal health and economic stability (1, 2). Diseases such as porcine reproductive and respiratory syndrome (PRRS), African swine fever (ASF), classical swine fever (CSF), and porcine circovirus type 2 (PCV2) stand as formidable challenges, necessitating vigilant scientific and veterinary monitoring. Although these diseases vary in etiology and clinical presentation, they universally present considerable obstacles to pig farming across the globe (3, 4). The recent emergence of novel strains, shifting epidemiological trends, and the constant threat of outbreaks have underscored the need for comprehensive understanding and proactive management of these viral hazards (5-7). Amidst increasing global interconnectedness through trade and travel, the imperative for effective disease control and prevention strategies is more pronounced than ever (8).

This review undertakes an exhaustive analysis of the complex issues surrounding PRRS, ASF, CSF, and PCV2 within the global pork industry. We dissect the virological foundations, transmission pathways, and clinical impacts of these diseases, as well as their geographical spread, prevalence, and significant economic impacts. Additionally, the article evaluates contemporary strides in disease management, spotlighting improvements in diagnostic methods and vaccination approaches.

By providing an in-depth scrutiny of these viral diseases, their evolving nature, and the concerted efforts to mitigate their impact, this article aims to serve as an

indispensable resource for veterinarians, researchers, and policymakers. It is designed to foster an informed, collaborative approach to the global challenges presented by swine viral diseases.

## Porcine Reproductive and Respiratory Syndrome (PRRS)

PRRS is predominantly attributed to the porcine reproductive and respiratory syndrome virus (PRRSV), the primary causative agent of the disease (9). PRRSV impairs the function of alveolar macrophages or modulates innate immune responses through alterations in non-structural proteins, leading to an imbalance of inflammatory cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-10 (IL-10). Consequently, suppression of the immune response in the lung occurs, along with changes in the expression of CD163, the primary viral receptor, affecting the virus's pathogenicity and replication (10, 11). The virus is characterized by its genetic diversity, presenting a spectrum of strains and genotypes that differ in virulence and pathogenicity (12). Consequently, certain strains are known to precipitate more severe manifestations of the disease (13). In 2006, an atypical PRRS known as highly pathogenic PRRS (HP-PRRS) emerged in China, characterized by a discontinuous deletion of 30 amino acids in non-structural protein 2 (NSP2). The disease was associated with high fever exceeding 40°C, neurological symptoms, shivering, and erythematous rash, with severe pathological changes observed in multiple organs (14).

Swine populations devoid of previous PRRSV exposure are particularly vulnerable (9). Lack of pre-existing immunity in a herd can expedite both the incursion and propagation of the virus (15). Subpar biosecurity measures are a significant risk factor for the introduction and proliferation of PRRSV within and among swine herds. This risk is compounded by the failure to prevent the ingress of infected animals, the use of contaminated equipment, or the movement of personnel without appropriate decontamination procedures (16). Management practices that entail the commingling of pigs from diverse origins are also implicated in heightening transmission risks (9). Moreover, environmental stressors, such as high population density and adverse living conditions, can amplify the severity of diseases. Ambient factors like temperature and humidity are known to affect the survival of virus and transmissibility (17), with certain locales reporting seasonal surges in PRRS incidents. The overall health and immune competence of the swine population are critical determinants of disease severity, as pigs with weakened immune defenses are more prone to severe outcomes (18).

*Clinical signs.* PRRS presents a spectrum of clinical signs in affected swine (Table I), varying from subtle to severe, and not all pigs may exhibit the full range of symptoms (9, 14). Respiratory issues, such as coughing, sneezing, labored or rapid and shallow breathing, along with nasal discharge, are common respiratory manifestations (19). Reproductive complications are also characteristic of PRRS, including late-term abortions, stillbirths, mummified fetuses, decreased farrowing rates, and the birth of weak or underdeveloped piglets (19, 20). Although the exact pathophysiological mechanism has not been fully elucidated, macrophages expressing sialoadhesin (Sn) and CD163, which play crucial roles in PRRSV replication, have been most frequently observed in the endometrium and placenta during late gestation. It has also been confirmed that the virus can cross the placenta of infected mothers and be detected in fetal organs such as the liver, spleen, and lungs (21, 22). In addition to these

symptoms, pigs with PRRS often show signs of fever, general weakness, and lethargy. Loss of appetite and subsequent weight loss are particularly detrimental in growing pigs (20). Some may develop edema, notably in the extremities and abdomen, and exhibit 'blue ear syndrome,' which is marked by the discoloration and inflammation of the ears (19).

Compromised immunity due to PRRS may predispose pigs to secondary bacterial infections, complicating their clinical state (15). Several models have been proposed to study the immunological changes, variations of clinical symptoms, reduced growth rates, and increased susceptibility to pneumonia caused by co-infections of PRRS with pathogens such as *Bordetella bronchiseptica* and *Haemophilus parasuis* within the context of porcine respiratory disease complex (PRDC) (23, 24). The disease's impact ranges from mild, subclinical infections to severe, acute outbreaks with significant mortality rates, especially in piglets. It's critical to recognize that these clinical signs can be influenced by factors such as the virulence of the PRRSV strain, the age and immune competency of the pigs, and existing farm management practices (15, 25).

*Distribution.* PRRS has a widespread presence, with reports of the disease across numerous countries on different continents (Table II). Initially identified in the United States in the late 1980s, PRRS has since become endemic in various regions of North America, particularly the United States, Canada, and Mexico, where it significantly affects the economic aspects of the swine industry (26). In Europe, PRRS has impacted swine herds in many countries, with documented cases in Spain, the Netherlands, Germany, and France, among others, each region contending with different virus strains (26, 27). Asia has also seen a prevalent spread of PRRS, with notable outbreaks in China, South Korea, Vietnam, Thailand, and the Philippines, where the disease has notably affected the pig farming sector (28, 29). In South America, countries such as Brazil and Argentina have reported challenges associated with PRRS in pig farming (30, 31). The disease is a concern in parts of Africa as well,

Table I. Clinical manifestations of porcine reproductive and respiratory syndrome (PRRS), African swine fever (ASF), classical swine fever (CSF), and porcine circovirus type 2 (PCV2), including porcine circovirus-associated disease (PCVAD) and porcine circovirus-associated reproductive failure (PCVAD-RF).

Disease	Clinical manifestations							
	Fever	Activity	Appetite	Respiratory	Reproductive	Neurological	Skin	Others
PRRS	Fever	Weak	Lose appetite	Coughing	Late-term abortions		Blue ear syndrome	Swelling in legs and abdomen
		Lethargy	Weight loss	Sneezing Labored breathing Rapid or shallow respiration Nasal discharge Coughing	stillbirths Mummified fetuses Reduced farrowing rates Weak or runty piglets Abortions			
ASF	Prominent and sudden fever	Lethargic and often lie down	Sharp decrease in appetite			Trembling reddening	Skin	Display signs of depression
		Reluctant to move Weak	Reduced food intake	Labored breathing	Birth of stillborn piglets	Lack of coordination Convulsions	Skin lesions often involve hemorrhaging	Vomiting and diarrhea with blood High mortality rate
CSF	High fever	Lethargic	Sharp decrease in appetite	Coughing	Abortions		Reddening	Displaying signs of depression High mortality rate
		Weak	Reduced food intake	Labored breathing	Stillbirths		Hemorrhages	High mortality rate
		Unwilling to move		Nasal discharge	Give birth to weak piglets		Bluish discoloration, on ears, snout, and lower abdomen	Per-acute form - pigs die suddenly without showing any clinical signs
PCV2-PCVAD	Often lying down	Weak	Progressive weight loss	Coughing			Yellowing	Diarrhea
		Lethargic	Reduced appetite	Labored breathing				Poor growth
		Decreased inclination to move or interact						Jaundice
PCV2-PCVAD-RF					Stillbirths			Anemia Sudden deaths
					Mummified fetuses			Higher mortality rates of piglets Increased likelihood of health problems in piglets
					Give birth to fewer piglets			

Table II. The global distribution of porcine reproductive and respiratory syndrome (PRRS), African swine fever (ASF), classical swine fever (CSF), and porcine circovirus type 2 (PCV2), including porcine circovirus-associated disease (PCVAD) and porcine circovirus-associated reproductive failure (PCVAD-RF), varies across different continents.

Disease	Global distribution					
	North America	South America	Asia	Europe	Africa	Oceania
PRRS	Initiated in United states Canada Mexico	Brazil Argentina	China South Korea Vietnam Thailand Philippines	Spain Netherlands Germany France	Kenya Uganda	Australia New Zealand
ASF	Not reported	Not reported	China Vietnam Philippines South Korea Cambodia	Poland Romania Germany Italy	Initiated in Kenya Sub-Saharan Africa	Not reported
CSF	Not reported in major countries	Brazil Argentina Columbia Ecuador	China Japan South Korea	Not reported	Nigeria Ghana Uganda Tanzania Kenya	Not reported
PCV2	United states Canada China	Brazil Argentina	South Korea Vietnam Thailand Philippines	Spain Netherlands Germany France	Country level data is not available	Australia New Zealand

with several countries observing PRRS cases (32). Even nations like Australia and New Zealand, which are typically vigilant about biosecurity, have not been spared, experiencing outbreaks that have prompted aggressive control and eradication measures (33).

*Transmission dynamics.* PRRS are complex, encompassing a range of factors that facilitate the spread of the virus both intra-herd and inter-herd. Within a single herd, PRRS can be transmitted through several pathways including direct contact between pigs, airborne aerosols, and indirect contact *via* contaminated equipment or fomites (Figure 1). Vertical transmission from sows to their offspring is also a significant route of spread. Additionally, the virus can be disseminated through boar semen, posing a risk during breeding procedures. Wildlife can also serve as a vector for the virus, further complicating control measures (12, 34).

*Direct transmission.* Direct pig-to-pig contact transmission. PRRS is principally spread through direct contact among

swine. Transmission typically occurs during interactions such as nose-to-nose contact, mounting behaviors, and grooming practices. High-density housing conditions, which often result in close proximity among animals, significantly increase the risk of virus transmission (20).

*Vertical transmission.* Vertical transmission of the PRRSV can occur when infected sows pass the virus to their offspring during gestation, leading to congenital infections. Furthermore, postnatal transmission is possible through the ingestion of infected colostrum or milk, which can expose piglets to the virus shortly after birth (35).

*Indirect transmission. Aerosol transmission.* The PRRSV has the capacity to become aerosolized and persist in the air for varying durations. Infected pigs can expel the virus into their surroundings *via* respiratory secretions, which can then be inhaled by susceptible pigs. This mode of transmission is particularly pertinent in enclosed spaces

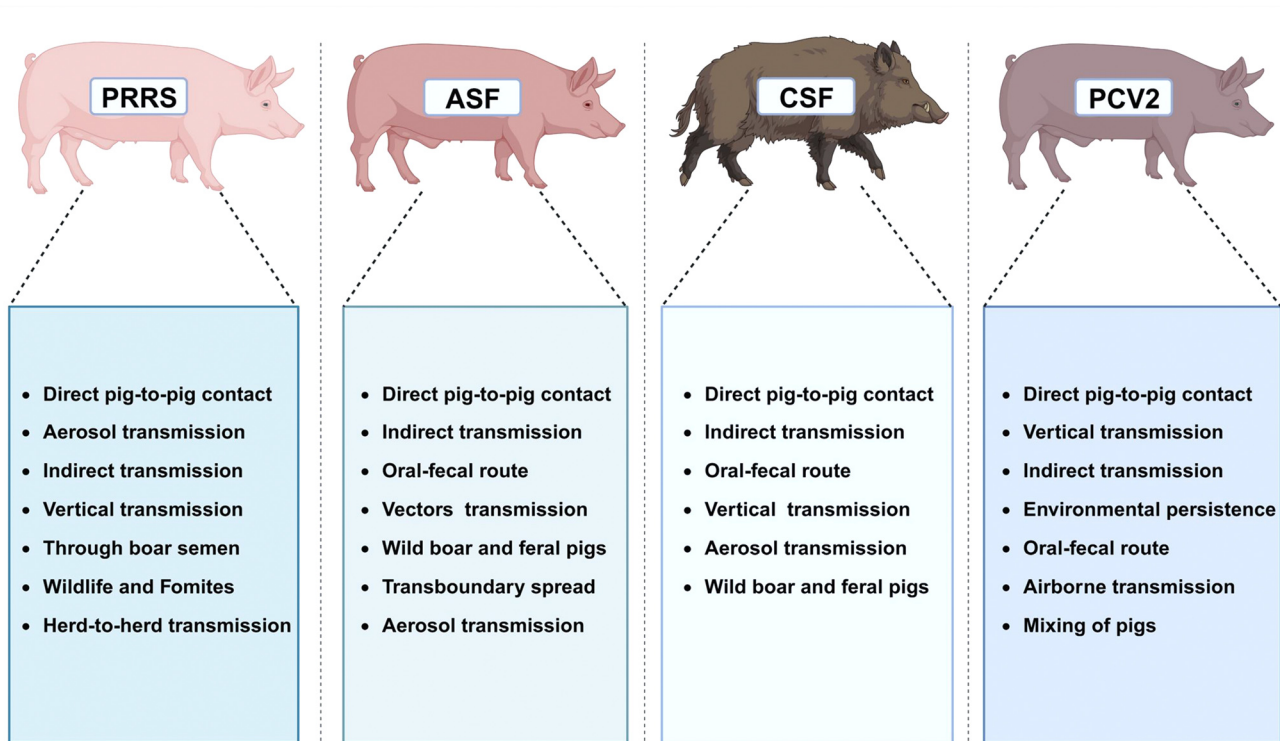


Figure 1. Transmission dynamics of porcine reproductive and respiratory syndrome (PRRS), African swine fever (ASF), classical swine fever (CSF), and porcine circovirus type 2 (PCV2). These diseases are spread among pig populations through various direct and indirect methods. Direct transmission includes pig-to-pig contact, while indirect pathways encompass aerosol transmission, vertical transmission (from sow to offspring), and oral-fecal routes. Additional vectors of disease spread include contaminated boar semen, contact with wild animals, and carrier vectors. Furthermore, the intermingling of pigs from different herds facilitates the spread of PRRS, ASF, CSF, and PCV2 diseases.

such as swine barns, where air circulation may facilitate the spread of the virus (12).

**Indirect transmission.** The PRRSV can survive outside of the host on various fomites, such as equipment, clothing, and vehicles, for a finite period. These contaminated inanimate objects, along with personnel who may have come into contact with the virus, can act as conduits for introducing PRRSV to previously uninfected pig herds. Therefore, indirect transmission is a critical focus in biosecurity protocols (36).

**Boar semen.** The presence of PRRSV in boar semen is a recognized risk factor for the transmission of the virus. Infected semen used during artificial insemination can serve as a vehicle for PRRSV, facilitating the spread of the

infection not only within a herd but also potentially to other herds (37).

**Wildlife and fomites as vectors.** Transmission of PRRSV via wildlife, including rodents and birds, is an acknowledged albeit less common route. These animals can mechanically transfer the virus, harboring it on their bodies or through their excreta. Additionally, PRRSV can be indirectly transmitted through contaminated feed and water sources, further underscoring the need for comprehensive biosecurity measures (36).

**Herd-to-herd transmission.** The movement of infected swine between farms is a primary vector for PRRSV spread from one herd to another. The introduction of these animals to uninfected populations, either through direct

purchase or the process of transportation, poses a significant risk for inter-herd transmission and is a crucial factor in the proliferation of the disease across different farming operations (38).

*Diagnosis.* Carrier animals are identified through enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) testing of serum samples from all animals. Despite its high success rate in eradicating PRRSV from chronically infected populations, this method has some drawbacks, including the high cost of diagnostics and the possible removal of animals that were previously exposed but no longer carry the virus. Herd closure has also demonstrated high efficacy in eliminating PRRSV. Testing and removal methods have proven effective in eradicating PRRSV from infected populations. This process focuses on testing the entire breeding herd to identify and eliminate carriers (39).

### **African Swine Fever (ASF)**

ASF is attributed to a distinct pathogen, the African swine fever virus (ASFV), which serves as the sole etiological agent of the condition. ASFV is categorized as a large, double-stranded DNA virus within the *Asfarviridae* family, representing one of the most structurally complex viruses capable of infecting animal species. The virus is characterized by considerable genetic diversity, encompassing a range of strains and genotypes that contribute to variability in virulence and pathogenicity. Consequently, this genetic variation influences the clinical outcomes and disease severity observed in ASF cases. Notably, ASFV demonstrates a robust resistance to a variety of environmental factors, including extremes of temperature and pH levels. Such resilience enables the virus to remain viable for prolonged durations in an array of materials and settings.

*Clinical signs.* The clinical manifestations of ASF exhibit a broad spectrum of severity and symptomatology (Table I), influenced by the strain of the virus, the age and general

health of the pigs, and any co-existing infections (40). A sudden, high fever is a quintessential sign of ASF and is often the initial indicator of infection (40, 41). Commonly, pigs infected with ASF display a marked reduction in appetite, leading to decreased food consumption. Such animals typically exhibit lethargy, weakness, and a reluctance to move, often lying down and showing signs of depression (42). Respiratory distress is also a notable symptom, characterized by coughing and difficult breathing (42). Dermatological manifestations include skin hemorrhages, particularly noticeable on the ears, abdomen, and extremities (43). Gastrointestinal disturbances, such as vomiting and diarrhea, occasionally with blood, are frequently observed and can result in dehydration and further debilitation (44). In some cases, neurological signs, including tremors, incoordination, and convulsions, may also manifest (45). Reproductive effects in sows can include abortions and the delivery of stillborn piglets (46). A defining feature of ASF is its high mortality rate; during acute episodes, death can occur swiftly after the onset of symptoms (41). A per-acute form of the disease may lead to sudden death without preceding clinical signs (40, 42). It is crucial to recognize that the presentation of ASF can range widely, and not every infected pig will necessarily display all of these symptoms.

*Distribution.* ASF has established a significant presence across the globe, with reports of outbreaks and varying degrees of prevalence in diverse regions (Table II) (45). The disease is endemic in many African countries, particularly within sub-Saharan Africa, where it was first identified in Kenya in the early 20th century. ASF continues to affect both domestic pigs and wild boar populations across the continent (47). In Europe, ASF has caused substantial economic losses and has led to the implementation of rigorous control measures to prevent further spread (47, 48). The advent of ASF in Asia has raised considerable alarm, with confirmed cases in nations such as China, Vietnam, the Philippines, South Korea, and Cambodia. This has led to significant depopulation of pigs and has severely disrupted the local swine industries (49). While ASF has not

yet been reported in North or South America, the proximity of outbreaks in the Caribbean and parts of South America has catalyzed the enactment of strict biosecurity protocols and increased vigilance (50). Additionally, ASF has been detected in countries like Papua New Guinea and several Pacific Islands, prompting concerted containment and eradication efforts. The disease's impact on wild boar populations poses an additional challenge for disease management and underscores the complexity of controlling ASF's spread (51, 52).

*Transmission dynamics.* The transmission dynamics of ASF encompass a multifaceted network of factors that facilitate the spread of the virus within and between domestic and wild swine populations (53, 54). Direct contact with infected pigs is a primary route, allowing for the efficient transmission of the virus. ASF can also be propagated through the consumption of contaminated feed or waste food products containing unprocessed pig meat or by-products. Indirect transmission *via* fomites, such as vehicles, equipment, clothing, and footwear, is especially problematic as the virus is known for its environmental resilience. Furthermore, the role of arthropod vectors, specifically soft ticks of the genus *Ornithodoros*, in transmitting ASFV, particularly in endemic regions, cannot be understated. These ticks can harbor the virus and facilitate its spread to healthy swine. Wild boar movements and interactions are additional critical components of the virus's ecology, contributing to its persistence and circulation in natural habitats. Given the complexity of these transmission pathways, the control of ASF requires integrated approaches that consider the interplay between animal husbandry practices, wildlife management, and biosecurity measures to mitigate the risk of ASFV introduction and dissemination (Figure 1).

*Direct transmission.* Direct pig-to-pig contact. Direct transmission of ASF predominantly occurs through contact between infected and susceptible pigs. The virus spreads more readily in conditions where pigs are in close quarters, such as overcrowded pens. Behaviors that involve physical

interaction, including mating and aggressive encounters, significantly enhance the opportunity for ASF to transmit from one individual to another (54).

*Indirect transmission.* The ASFV exhibits notable environmental tenacity, surviving for prolonged periods under various conditions. This durability facilitates indirect transmission through contaminated vectors such as feed, farming equipment, clothing, and vehicles. Consequently, stringent biosecurity protocols, alongside meticulous cleaning and disinfection practices, are imperative to curb the spread of ASFV (55).

*Oral-fecal route.* The oral-fecal route is a significant pathway for the transmission of the ASFV. Infection can occur when pigs ingest materials contaminated with the virus, such as feed or water. Additionally, the consumption of carcasses of infected pigs can also lead to the spread of ASFV within a population (54).

*Vectors transmission.* Certain species of soft ticks, particularly those belonging to the genus *Ornithodoros*, serve as biological vectors for the ASFV. These arthropods can harbor the virus and are capable of transmitting it to swine, a mode of spread that is notably prevalent in specific African territories (54).

*Wild boar and feral pig reservoirs.* Wild boars and feral pigs are capable of contracting African swine fever and becoming reservoir hosts of the virus. Their role in the epidemiology of ASF is particularly challenging for containment efforts, as these wild populations can facilitate the virus's incursion into domestic pig herds, complicating eradication strategies (54).

*Aerosol transmission.* Although not the predominant route, aerosol transmission of the ASFV is possible, particularly within dense and confined environments such as pig pens. This form of transmission can contribute to the intra-herd spread of ASFV and between closely situated animal enclosures (56).

*Transboundary spread.* The transboundary spread of ASF is facilitated by the illicit transport of infected pigs, the trade of contaminated pork products, and the movement of fomites across borders. Such activities pose a substantial risk for the international transmission of ASF, underlining the necessity for stringent border control practices and rigorous regulations governing international trade to prevent the spread of the virus (57).

*Diagnosis.* The available diagnostic tests for ASF can be categorized into virus detection tests and antibody detection tests. Virus detection methods include ASFV genome detection, which identifies the genetic material of the virus. Another method is virus isolation (VI) combined with the hemadsorption (HAD) test, which involves isolating the virus from a sample and using the HAD test to confirm its presence. Additionally, antigen detection techniques are used to identify specific proteins associated with the virus. However, antibody detection tests are used to determine if an animal has been exposed to the virus by detecting antibodies in the blood. These tests include the Antibody-ELISA, which is a widely used method for its accuracy and efficiency, as well as confirmatory antibody detection tests, which provide further validation of the presence of antibodies against the virus (58).

### **Classical Swine Fever (CSF)**

CSF, also known colloquially as Hog Cholera, is caused by the classical swine fever virus (CSFV). This pathogen is a small, enveloped virus with a single-stranded RNA genome, classified within the *Pestivirus* genus of the *Flaviviridae* family. CSFV is characterized by its genetic variability, presenting multiple genotypes and subtypes (59). The diversity among strains leads to differences in virulence and antigenic properties, influencing both the clinical severity of CSF and the immunological responses observed in affected swine populations (59, 60).

*Clinical signs.* The clinical manifestations of CSF (Table I) are variable and influenced by factors such as the strain of the virus, the age and health of the pigs, and any concurrent

infections (60). A prominent high fever is typically the initial indicator of CSF, often accompanied by lethargy, weakness, and depression (61). Infected pigs show a marked disinterest in food, leading to a decrease in intake (62). Severe cases of CSF may progress to neurological impairment, with symptoms including tremors, incoordination, convulsions, and even paralysis (62). Cutaneous signs are also indicative of CSF, with possible presentations including erythema, ecchymoses, or cyanosis, particularly noticeable on the ears, snout, and abdomen (60). Respiratory distress, characterized by coughing, dyspnea, and nasal discharge, may also be present (63). Reproductive issues in sows, such as abortions, stillbirths, or the birth of weak piglets, can occur due to transplacental virus transmission (63). A critical aspect of CSF is its potential for high mortality, which can lead to substantial losses within swine populations. The peracute form of the disease is especially devastating, as affected pigs may succumb rapidly without preceding clinical symptoms (64).

*Distribution.* CSF presents with varying prevalence across the globe, influenced by regional control initiatives and eradication programs (Table II) (65). In Europe, CSF has been a concern with recorded outbreaks and sporadic reemergence. Comprehensive surveillance and control strategies implemented by many European countries have led to successful disease containment and elimination in some areas (66). Asia has witnessed CSF outbreaks, particularly in countries such as China, Japan, and South Korea. In response, recent years have seen a ramping up of regional efforts towards enhanced control and surveillance (61, 67).

In Africa, CSF poses ongoing control challenges, with the disease remaining a significant threat to the swine industry (61). Although CSF is not endemic in North or South America, historical outbreaks have prompted the establishment of vigilant biosecurity protocols to forestall the virus's introduction (68). Additionally, wild boar populations in certain areas are susceptible to CSF, acting as potential virus reservoirs and complicating control measures directed at wild swine (59, 69).

*Transmission dynamics.* The transmission of CSF is facilitated primarily through direct contact between infected and susceptible pigs. This direct transmission is a significant risk factor for disease spread, especially in densely populated swine operations. Indirect pathways, including exposure to contaminated feed, farming equipment, or transport vehicles, also play a crucial role in introducing the virus to naïve herds. Wild boars, serving as a natural reservoir of the virus, pose an additional risk for transmission to domestic pig populations. They can spread the virus through environmental contamination and by straying into areas in close proximity to domestic swine operations (Figure 1) (50, 70).

*Direct transmission.* Direct pig-to-pig contact. Direct transmission is the principal route for the spread of CSF, occurring when infected and susceptible pigs engage in physical activities such as mating, fighting, or other social behaviors that are common within herds. The risk of transmission is exacerbated by close contact, which is often unavoidable in crowded pen conditions, thereby facilitating the virus's spread (60).

*Vertical transmission.* Vertical transmission of the CSFV occurs when the virus is passed from infected sows to their offspring. This can happen in utero, during the birthing process, or postnatally through the ingestion of contaminated colostrum and milk, which presents significant implications for the management of breeding herds (71).

*Indirect transmission.* The CSFV has the ability to persist in the environment, which enables its indirect transmission *via* contaminated feed, farm equipment, clothing, and vehicles. Such transmission underscores the importance of stringent biosecurity protocols, alongside thorough cleaning and disinfection practices, as critical preventative measures against the spread of CSF (72).

*Oral-fecal route.* The CSFV can be transmitted through the oral-fecal route when pigs ingest materials contaminated with the virus. This includes consumption of feed or water

that has been exposed to CSFV. Additionally, the virus can spread when pigs consume the carcasses of animals that have succumbed to CSF, further perpetuating the infectious cycle within a population (73).

*Aerosol transmission.* Although not as prevalent as other modes, aerosol transmission of the CSFV can transpire, particularly in enclosed or densely populated swine environments. This pathway of transmission may facilitate the spread of the virus within a facility, emphasizing the need for adequate ventilation and air quality control in pig housing (60).

*Wild boar and wildlife reservoirs.* Wild boar and feral pig populations are susceptible to infection with the CSFV and can act as reservoirs for the disease. Their interactions with domestic pig populations, through both direct and indirect contact, can lead to the transmission of the virus, thus posing a significant risk for the introduction and spread of CSF within commercial swine operations (74).

*Diagnosis.* Nucleic acid detection methods, including real-time (RT)-PCR and gel-based RT-PCR, are widely used to identify viral nucleic acids with high sensitivity in both individual and pooled samples. However, diagnosing low-virulence strains, which are only present in the blood for a brief period, can present difficulties. Virus isolation, achieved through culturing the virus in porcine cell cultures, plays a key role in research and genotyping, but it is time-consuming and less sensitive than RT-PCR. Antigen detection techniques, such as immunofluorescence (IFA), peroxidase staining, and ELISA targeting the Erns antigen, are used to identify viral antigens. Although ELISA is quick and can be automated, its lower sensitivity makes it unsuitable for testing individual animals. Antigen detection *via* cell cultures yields rapid results but has limited sensitivity and requires experienced laboratory staff for proper interpretation. Serological methods like ELISA and virus neutralization tests (VNT) detect antibodies that typically appear 2-3 weeks after infection and can persist throughout the animal's life, helping to identify past

infections. However, cross-reactivity with other *pestiviruses*, such as bovine diarrhea virus, and suboptimal sample quality can cause false positives (75).

## Porcine Circovirus Type 2 (PCV2)

PCV2 is the causative agent of several syndromes collectively known as PCV2-associated diseases (76). This virus falls within the genus *Circovirus* of the *Circoviridae* family and is characterized as a small, non-enveloped virus with a single-stranded DNA genome (76). Three primary genotypes of PCV2 have been recognized: PCV2a, PCV2b, and PCV2d, each exhibiting distinct genetic profiles (76). The genotypic diversity of PCV2 is associated with variations in virulence and pathogenicity, which, in turn, influence the spectrum of clinical presentations observed in infected swine (77).

*Clinical signs.* The clinical presentation of PCV2 infections in swine is influenced by a variety of factors, including the animals' age, immune competence, concurrent infections, and the specific virulence of the PCV2 strain involved. PCV2 is implicated in a spectrum of pathologies known as porcine circovirus-associated disease (PCVAD), which can range from subclinical to severe. Moreover, PCV2 is associated with reproductive failures, designated as PCVAD with reproductive failure (PCVAD-RF), presenting additional complexities in breeding herds (Table I) (76, 78).

*Porcine circovirus-associated disease (PCVAD).* PCVAD manifests through a spectrum of clinical symptoms in pigs, often becoming evident during the nursery and growing-finishing phases. Affected pigs typically endure progressive weight loss and stunted growth. Respiratory distress is also common, characterized by symptoms such as coughing and difficulty breathing. Gastrointestinal issues, including diarrhea and a decrease in appetite, may exacerbate the condition by contributing to further weight loss (78). Liver involvement in some cases can lead to jaundice, presenting as a yellowish discoloration of the skin and mucous membranes (79). The disease often results in a general state of weakness and lethargy, with

pigs showing little motivation to move or engage with their surroundings. Additionally, anemia may manifest, with pale skin and mucous membranes being indicative signs. In the most severe cases, PCVAD can lead to sudden mortality within the pig population (78).

*Porcine circovirus-associated reproductive failure (PCVAD-RF).* Reproductive performance in sows infected with PCV2 can be significantly compromised, evidenced by increased incidences of stillbirths and mummified fetuses (80). It is also common for affected sows to produce smaller litters than expected (80). Additionally, piglets born from PCV2-infected sows tend to have reduced vitality, which correlates with elevated neonatal mortality and a greater propensity for health complications (81). These reproductive difficulties underscore the detrimental effects of PCV2 on both the fertility of breeding sows and the survivability of their progeny.

*Distribution.* PCV2 has a worldwide prevalence, impacting swine populations across the globe (Table II) and representing a significant economic concern within the industry (82). In North America, both the United States and Canada have recognized the virus as a critical issue, prompting the establishment of targeted management practices to mitigate its effects (82). European countries have also experienced widespread PCV2 incidence, with nations such as Spain, the Netherlands, Germany, and France reporting varying strains and genotypes endemic to each region (82, 83). In Asia, prominent swine-producing countries like China, South Korea, Vietnam, Thailand, and the Philippines have encountered PCV2 outbreaks, which have had considerable repercussions for their swine sectors (82, 84). Similarly, in South America, countries such as Brazil and Argentina have reported PCV2 cases, reflecting the virus's extensive reach (82). PCV2 infections have been noted in some African regions, adding to the global spectrum of the virus's impact (85, 86). Australia and New Zealand have not been exempt from PCV2 challenges, facing outbreaks that have necessitated proactive control and management responses (82).

*Transmission dynamics.* PCV2 is highly contagious and can be transmitted through a multitude of routes. Direct transmission between pigs is common, occurring *via* nose-to-nose contact, or through contact with contaminated bodily fluids. Indirect transmission can result from exposure to contaminated fomites such as feeders, drinkers, and other equipment within a swine facility. Additionally, vertical transmission from sows to piglets can occur, either in utero or through the ingestion of infected colostrum and milk. The virus's resilience in the environment also facilitates its spread, as PCV2 can remain viable for extended periods on surfaces and materials, leading to further opportunities for disease propagation (Figure 1) (76).

*Direct transmission.* Direct pig-to-pig contact. PCV2 is primarily transmitted through direct contact between infected and susceptible pigs. This can occur through various activities within swine populations, such as nose-to-nose contact, social interactions, and mating. Close proximity in crowded conditions facilitates transmission (87).

*Vertical transmission.* Vertical transmission of PCV2 from sows to piglets constitutes a significant pathway for the virus's dissemination within swine herds. Infected sows can pass PCV2 to their offspring during gestation or postnatally through colostrum and milk. This mode of transmission plays a crucial role in the maintenance and spread of PCV2 infections, impacting both individual animal health and overall herd immunity (88).

*Indirect transmission.* PCV2 can also be transmitted indirectly *via* fomites. Objects such as farm equipment, clothing, and even personnel can become vectors for the virus, inadvertently facilitating its transfer between pigs or different pen environments. This form of transmission is of particular concern within swine facilities, where stringent biosecurity measures are essential to prevent the spread of infection (87).

*Oral-fecal route.* The fecal-oral route is a notable transmission pathway for PCV2. Ingestion of fecal matter

from infected pigs, or intake of feed and water that has been contaminated with the virus, can facilitate the spread of PCV2 among swine populations. This route highlights the critical need for maintaining high standards of hygiene and feed quality control in swine management practices (89).

*Airborne transmission.* Though not the primary route, airborne transmission of PCV2 is possible when the virus becomes aerosolized. Such transmission is more likely to occur in environments where pigs are housed in close quarters or where ventilation is inadequate. This aerosolized spread underscores the importance of proper air management systems in facilities to minimize the risk of PCV2 transmission (87).

*Environmental persistence.* The durability of PCV2 in various environmental contexts contributes significantly to its transmission. The virus can remain viable for extended periods on contaminated surfaces, within water supplies, and across different areas within swine operations. This persistent nature of PCV2 in the environment underscores the potential for indirect transmission and the importance of rigorous sanitation practices within pig rearing and handling facilities (90).

*Mixing of pigs.* The introduction and propagation of PCV2 can be significantly influenced by the movement and intermingling of swine populations. Practices such as trading at auction yards, transportation logistics, and the commingling of pigs during events or upon introduction to new herds are known to facilitate the spread of the virus. These activities can expose susceptible pigs to PCV2, highlighting the need for stringent biosecurity measures during any event that requires pig mixing (91).

*Diagnosis.* PCV infections, particularly those caused by PCV-2, are diagnosed using a combination of clinical signs, histopathology, and molecular techniques. Diagnosis of systemic diseases like PCV-2 systemic disease (PCV-2-SD) involves clinical signs such as weight loss and skin paleness, along with histopathological evidence of lymphocyte depletion and moderate to high viral loads in

tissues. For subclinical infections (PCV-2-SI), there are no noticeable signs, and histological lesions are minimal. The qPCR is an important tool for detecting viral presence in various tissues and fluids, helping to distinguish clinical from subclinical cases. Although qPCR is often used for diagnostic purposes, its application is particularly valuable for monitoring, given the widespread nature of the virus. PCR thresholds, like those in serum or tissue, correlate with disease severity, but PCR alone may not be sufficient without supporting clinical evidence. For reproductive diseases, such as PCV-2 reproductive disease (PCV-2-RD), viral loads in tissues like the heart and liver of stillborn piglets are indicative, but additional methods such as immunohistochemistry (IHC) may be required for confirmation. While antibody detection methods, such as ELISA, are useful for monitoring herd exposure, they cannot definitively diagnose active infection due to the interference of vaccination-induced antibodies. Thus, antibody testing serves more for surveillance purposes rather than disease diagnosis.

### **Economic Consequences of Swine Viral Diseases**

The economic impact of PRRS, ASF, CSF, and PCV2 on the swine industry is considerable, affecting both individual farms and the global market (Figure 2) (92). These diseases can lead to diminished production outputs due to increased mortality, impaired growth rates, and reproductive challenges, directly resulting in lower yields of meat products and fewer piglets for future breeding, thereby reducing producers' revenues (60). The costs associated with disease management, including diagnostics, medications, and veterinary services, place a significant financial strain on producers (93, 94).

Outbreaks often necessitate depopulation and culling, leading to the loss of genetically valuable breeding stock and market-ready pigs, while also triggering trade restrictions that limit market access and diminish export revenues (42, 95). Rebuilding herds post-culling involves substantial investment in new, disease-free stock (96).

Producers must also fund enhanced biosecurity measures to prevent disease reintroduction, including facility improvements and comprehensive surveillance systems (97, 98). Market fluctuations due to culling and export bans can further drive down pork prices, negatively affecting income (99). The ripple effects of these diseases extend beyond primary production to related sectors, including feed, transportation, and processing, with losses felt across the supply chain (100). Investment in research for better disease understanding and development of control measures also constitutes a significant financial commitment (101).

Collectively, the economic ramifications of PRRS, ASF, CSF, and PCV2 necessitate robust prevention strategies and international cooperation to mitigate their impact on the swine industry and associated economies.

### **Public Health Significance**

*Impact on public health.* While PRRS, ASF, CSF, and PCV2 are not zoonotic and do not typically pose a direct threat to human health, there remains the potential for these viruses to give rise to zoonotic pathogens through genetic reassortment or mutations (Figure 3A). Vigilant surveillance and robust biosecurity measures are essential to mitigate such risks (45). In the therapeutic management of these diseases, antibiotics are often utilized to combat secondary bacterial infections in pigs. However, the overuse and misuse of antibiotics in animal husbandry can lead to the emergence of antibiotic-resistant bacteria, which is a growing public health concern. This resistance can compromise the effectiveness of antibiotics, which are critical in treating human diseases, underscoring the need for judicious use of these medications in agriculture (93).

*Impact on food security.* The incursion of PRRS, ASF, CSF, and PCV2 within swine populations can significantly reduce pork production (Figure 3B). This decline poses a threat to food security, particularly in countries where pork is a key component of the dietary protein intake (93). Disease outbreaks often prompt international trade

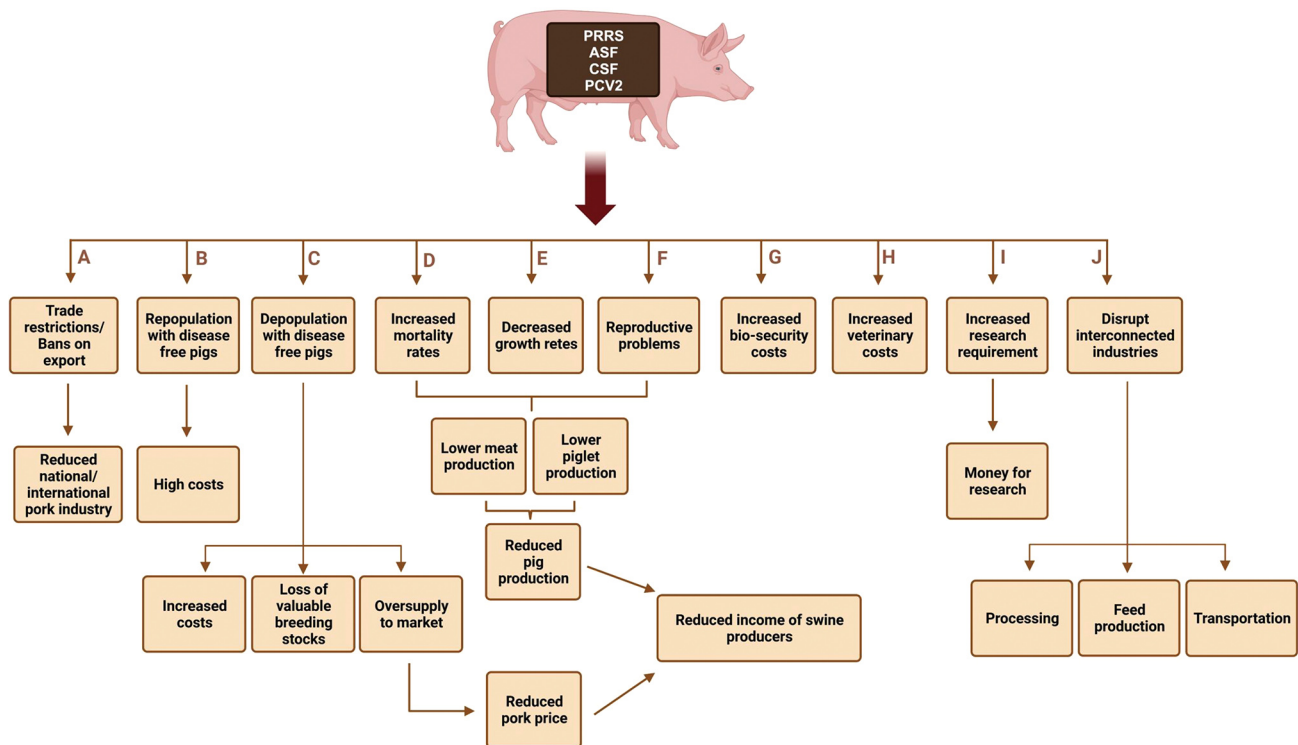


Figure 2. Economic impact of porcine/swine viral diseases. The presence of porcine reproductive and respiratory syndrome (PRRS), African swine fever (ASF), classical swine fever (CSF), and porcine circovirus type 2 (PCV2) can have multifaceted negative effects on the swine industry's economy. (A) Trade restrictions imposed due to these diseases adversely affect pork operations both domestically and internationally. (B) Significant financial investment is required for restocking farms with healthy pigs following outbreaks. (C) The necessity of pig depopulation and culling to mitigate disease risk leads to increased costs and the loss of valuable breeding stock. This action, coupled with an oversupply of meat, can result in a decrease in pork prices. (D) Higher mortality rates, (E) diminished growth rates, and (F) reproductive complications caused by these viral infections decrease meat and piglet production, thereby reducing revenue for swine producers. Additionally, these diseases escalate expenditures related to (G) biosecurity measures, (H) veterinary care, and (I) research efforts. (J) The ripple effect of these infections extends to related sectors, including transportation, feed production, and processing industries.

restrictions and the imposition of export bans, which can disrupt the global pork supply chain, leading to market volatility (102). This reduction in pork production can drive up pork prices and, consequently, affect the affordability and accessibility of animal protein for consumers (102). A contraction in pork supply tends to elevate prices, potentially making pork less affordable and accessible to consumers and impacting overall food security (102).

*Environmental impact.* Farms grappling with PRRS, ASF, CSF, or (PCV2 may face significant waste management

challenges (103, 104). Inadequate disposal of carcasses and contaminated materials can exacerbate environmental degradation, potentially affecting soil and water quality (104). While the primary concern of these diseases lies within the swine industry, their broader indirect effects can extend to public health and food security. Efficient management of these diseases, coupled with rigorous enforcement of biosecurity protocols and active international collaboration, is crucial. These measures are not only vital for safeguarding swine populations but also for protecting environmental integrity, human health, and global food security (Figure 3C).

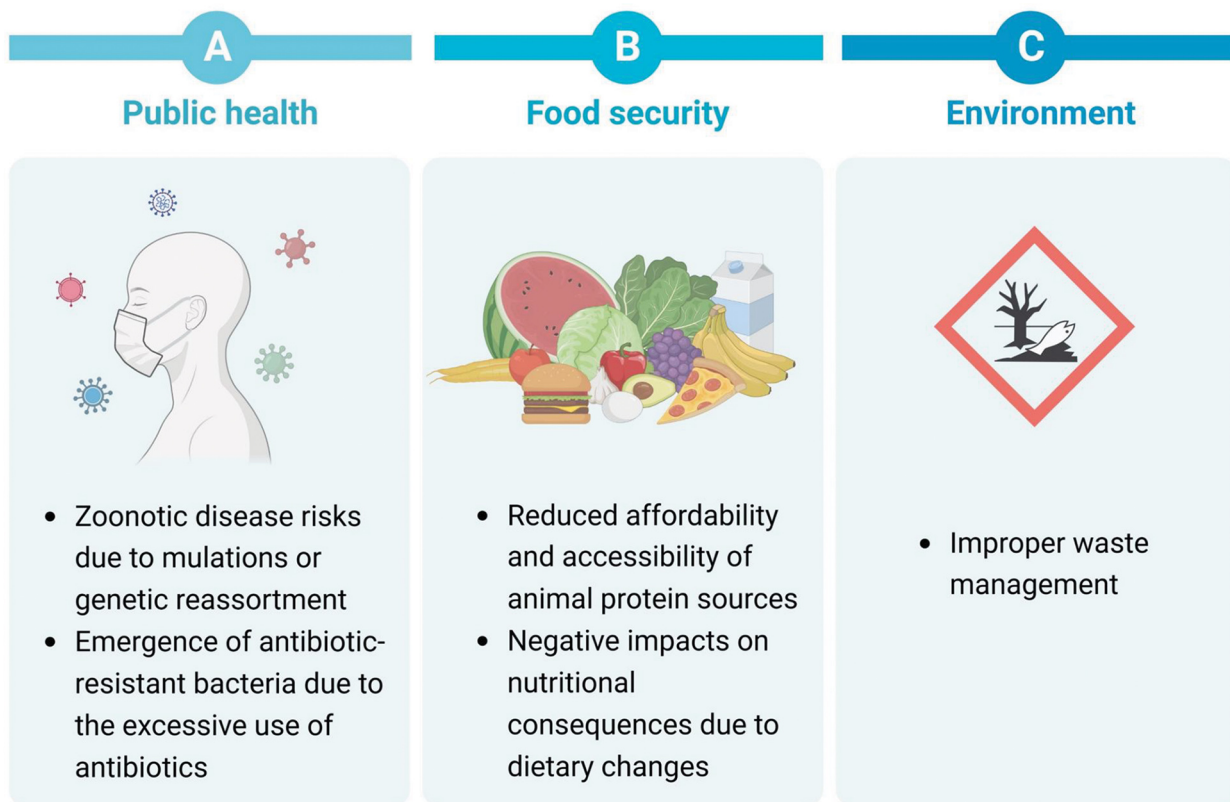


Figure 3. Indirect effects of porcine reproductive and respiratory syndrome (PRRS), African swine fever (ASF), classical swine fever (CSF), and porcine circovirus type 2 (PCV2) on the environment, food security, and public health. These infections have detrimental effects on the environment, food security, and public health. The impact of these swine diseases extends beyond direct animal health concerns. (A) The potential for zoonotic transmission or the emergence of antibiotic-resistant bacteria poses significant public health risks. (B) The reduced pork supply caused by these diseases can lead to higher prices, making this protein source less affordable. This situation may force consumers to alter their protein sources, potentially impacting nutritional outcomes. (C) The disposal of diseased animal carcasses and related waste products presents challenges in waste management, often leading to improper handling and environmental contamination.

### Current Strategies for Disease Management and Control

Depending on the particular virus involved, different swine viral infections might require different management and control strategies due to their unique features and routes of transmission. Nonetheless, a few universal guidelines and procedures are frequently used to treat a variety of swine virus illnesses (Figure 4).

*PRRS*. The management of PRRS relies heavily on stringent biosecurity measures. This includes controlled access to

swine facilities, extensive disinfection processes, and vigilant monitoring of visitors to prevent viral incursion (105). Vaccination plays a pivotal role in mitigating the severity of PRRS, with both modified-live and killed vaccines being utilized to protect swine populations (105-107). PRRSV replicates in monocyte and macrophage lineages and exhibits immune evasion mechanisms through antigen presentation inhibition, reduced cell surface expression of viral proteins, shielding of neutralizing epitope, and down regulation of interferon production. Therefore, next-generation vaccines must induce a comprehensive immune response and adapt

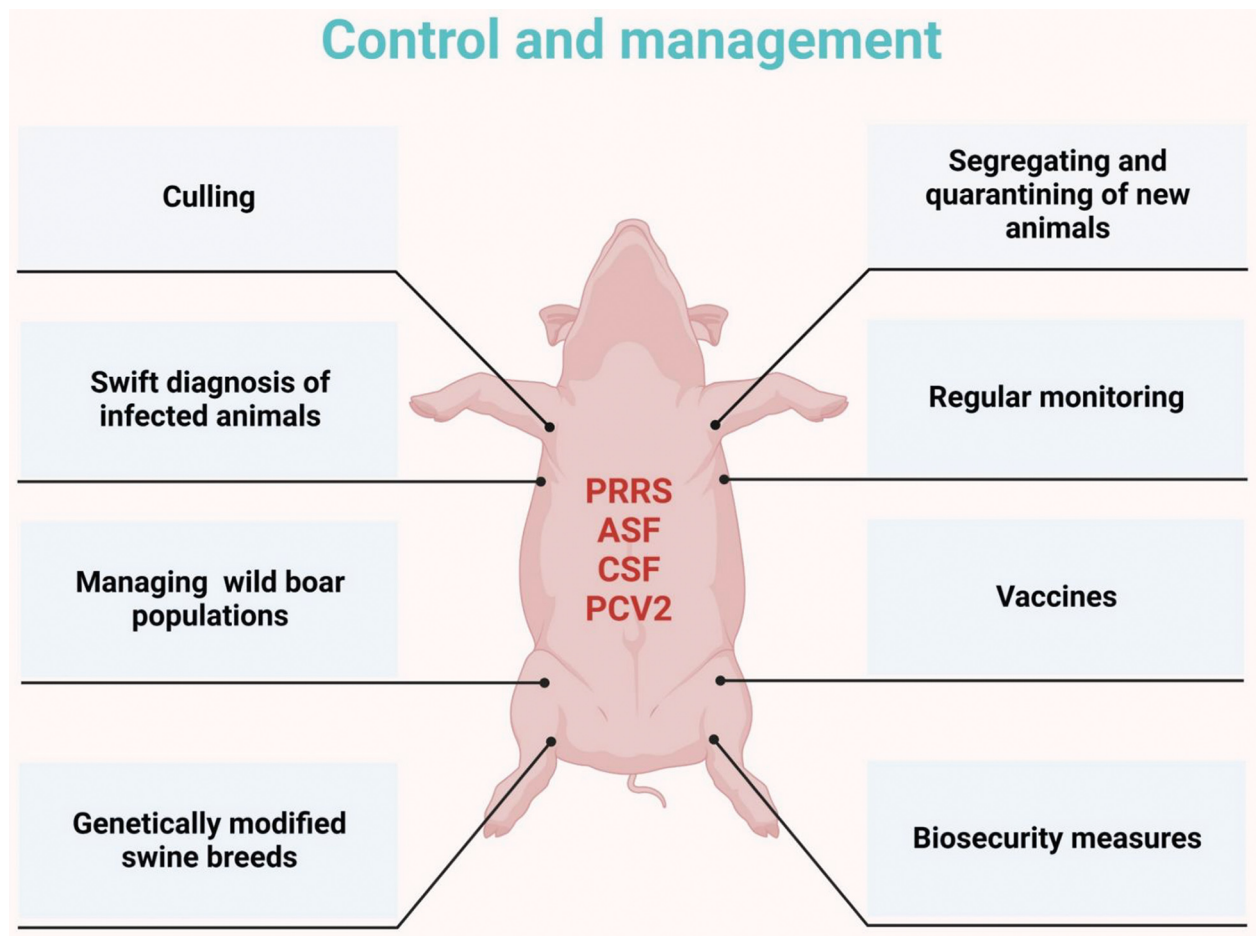


Figure 4. Strategies for management and control of porcine reproductive and respiratory syndrome (PRRS), African swine fever (ASF), classical swine fever (CSF), and porcine circovirus type 2 (PCV2) in porcine/swine. Effective management and control of these viral diseases in swine populations involve a range of approaches. These include implementing stringent biosecurity measures, utilizing vaccinations, conducting regular health monitoring of animals, and isolating and quarantining new or suspected infected animals. Additionally, the development of genetically modified swine breeds resistant to these diseases, effective management of wild boar populations to prevent disease transmission, rapid and accurate diagnosis of infections, and strategic culling of affected animals are crucial components of these control strategies.

vaccination strategies based on the prevalent genotypes in specific regions (108). Additionally, global studies on commercially available modified live vaccines (MLVs) comparing their ability to generate neutralizing antibodies, cellular and humoral immune responses, and protection against North American and European strain co-infections indicate varying efficacy depending on the vaccine strain. This highlights the need to select vaccines tailored to the specific strain present in a region or farm (109, 110). Constant herd monitoring is crucial for the

early detection of PRRS and prompt response to outbreaks (111). The biosecurity protocol extends to the segregation and quarantine of new stock to prevent potential virus introduction (112). Moreover, genetic advancements are being pursued to breed PRRS-resistant swine, complementing research efforts aimed at deepening our understanding of PRRS virology (113-115).

**ASF** The containment of ASF necessitates stringent biosecurity protocols. Critical measures include strict

regulation of swine movements, thorough disinfection practices, and the disposal of contaminated materials to curb the spread of the virus (116). Control of wild boar populations is also vital due to their potential role as reservoir hosts for ASF (117). While vaccine development is a priority, ASFV has a large genome containing numerous genes associated with virulence and immune-related functions, making it prone to frequent mutations, which complicates vaccine commercialization. Additionally, pigs infected with the virus exhibit high susceptibility and rapid mortality, making it challenging to develop animal models for immunological evaluation, assessment of candidate vaccines' neutralizing antibody responses, and evaluation of potential side effects. For these reasons an effective ASF vaccine has yet to gain broad acceptance, making research in this area a high priority (118). International regulatory efforts focus on preventing ASF dissemination through trade, with rapid diagnosis and culling of infected animals being crucial for halting transmission (52).

*CSF*. Combatting CSF involves a proactive approach anchored in immunization and biosecurity. Live attenuated vaccines are widely used to confer immunity to swine populations (119-122). Comprehensive biosecurity measures, such as quarantine, isolation of new or sick animals, and rigorous disinfection protocols, are critical for preventing the spread of CSF (68). Educational initiatives are also crucial, aiming to enhance the detection and removal of infected animals to establish CSF-free environments (68). Continuous surveillance programs are essential for the early detection of CSF, allowing for timely and effective outbreak management (68).

*PCV2*. Management of PCV2-associated diseases incorporates a holistic strategy that extends beyond vaccination. While PCV2 vaccines are critical for reducing both the clinical impact of the virus and the associated economic losses (123, 124), a strong emphasis is also placed on stringent biosecurity to block the virus's entry into herds. Herd management practices focus on maintaining animal health through proper nutrition and

stress reduction, acknowledging the role of stress in exacerbating PCV2 effects (103). Research initiatives are ongoing to decipher the complexities of PCV2 strains and to improve vaccine effectiveness. This is complemented by regular diagnostic testing to monitor infection prevalence and to inform intervention strategies (125). Controlling secondary infections, which can complicate PCV2 cases, is also an integral part of a comprehensive disease management plan (125). As disease landscapes evolve, so do the strategies to combat them. The efficacy of control measures is contingent upon various factors, including disease virulence, herd demographics, and environmental conditions. Hence, a dynamic and multidisciplinary approach is essential, combining diligent surveillance, continued research, and global cooperation to effectively manage and mitigate the threat of PCV2 and other swine diseases.

## **Conclusion**

This review elucidated the critical nature and far-reaching impact of PRRS, ASF, CSF, and PCV2 on the swine industry. These viral diseases contribute to significant economic losses, raise animal welfare issues, and carry implications for public health and global food security. An in-depth examination has revealed the complex etiology, clinical signs, distribution patterns, and transmission mechanisms of these diseases, underscoring the multifaceted challenges they present. Despite concerted control and management efforts, including stringent biosecurity, vaccination, and research into genetic resistance, these diseases persist as a global threat. Future strategies require ongoing research and development to enhance prevention and control tactics. Cross-sectoral collaboration is imperative in fostering a robust response to these diseases, safeguarding both swine health and the agricultural economy. In essence, the intertwined nature of swine health with public health and food security necessitates a united front, with continuous engagement across all stakeholders to fortify the industry against these pervasive challenges.

## Conflicts of Interest

The Authors declare that they have no competing interests in relation to this study.

## Authors' Contributions

TK, GSB, EJ, BSK, SUK and KSL designed, researched, and wrote the manuscript. TK, GSB, EJ, PK, HCS, YJA, BSK, SUK and KSL participated in the discussion. BSK, SUK and KSL supervised and reviewed all the research. All Authors have read and agreed to the published version of the manuscript.

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