Systematic review of transmission factors, management interventions, and elimination techniques related to porcine epidemic diarrhea (PO-002754)

Eric Neumann
Epi-Insight USA, LLC
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Industry Summary:

While PEDV eradication may not be feasible at a national level, improved biosecurity protocols, feed decontamination, and enhanced surveillance can help reduce transmission and economic losses. Vaccines can play a role in disease control but currently do not provide complete immunity and therefore other complementary control strategies are required for an industry level control program. Future research should focus on improving biosecurity compliance, information-sharing during outbreaks, and epidemiological modelling to understand role of current vaccines during an eradication program.

Key Findings:

The findings of this systematic review highlight that while PEDV eradication may be theoretically possible under idealized conditions, significant barriers remain. The high transmissibility, environmental resilience, and inability to achieve sterilizing immunity suggest that long-term endemic management is a more practical objective. Instead of full eradication, a risk-based control strategy may offer a more viable approach, emphasizing:

- Enhanced transport biosecurity measures, particularly for slaughterhouse and livestock trailer sanitation.
- Continued investment in vaccines, not as eradication tools but as means of reducing shedding and clinical disease severity.
- Industry-wide adoption of standardized feed biosecurity protocols to prevent future reintroductions.
- Surveillance programs to detect emerging variants early and adjust control measures accordingly.
- Government – industry partnership to drive compliance with surveillance and animal movement requirements likely to be necessary for organized control (or eradication) programs.

While the goal of complete PEDV eradication remains aspirational, strategic control measures can significantly reduce economic losses and prevent large-scale outbreaks, ensuring the long-term sustainability of swine production systems.

Keywords:

Porcine epidemic diarrhea virus, systematic review, swine, disease eradication, epidemiology

Scientific Abstract:

Background

Porcine epidemic diarrhea virus (PEDV) is a highly contagious enteric coronavirus that has caused severe economic losses in the swine industry worldwide. The virus spreads rapidly through fecal-oral transmission and contaminated fomites. Despite extensive research on vaccines, biosecurity, and inactivation strategies, PEDV remains endemic. This systematic review evaluates the key epidemiological factors relevant to the feasibility of PEDV eradication.

Methods

A systematic review of peer-reviewed literature published since 1990 was conducted using multiple bibliographic databases. Studies were selected based on their relevance to PEDV transmission, biosecurity interventions, and disease control measures, including vaccination, antiviral strategies, epidemiological modeling, and inactivation methods. Data from eligible studies were synthesized to provide an overview of current knowledge and gaps.

Results

The review identified key risk factors including viral shedding duration, transportation-related contamination, and feed-based transmission, all of which complicate eradication efforts. Epidemiological modeling suggests that localized control measures can reduce outbreaks, but national-level eradication remains challenging. Biosecurity measures, heat inactivation, and chemical disinfectants are helpful adjuncts to controlling viral spread but transportation networks remain a weak point in PEDV containment.

Introduction:

Porcine epidemic diarrhea virus (PEDV) is an enteric coronavirus that has significantly impacted the global swine industry. First reported in the United Kingdom in 1971 and isolated in Belgium in 1978, PEDV has since spread worldwide, causing severe outbreaks characterized by high morbidity and mortality, particularly in neonatal piglets.[1] The virus belongs to the genus Alphacoronavirus in the Coronaviridae family and shares similarities with other porcine coronaviruses, such as transmissible gastroenteritis virus (TGEV) and porcine deltacoronavirus (PDCoV).[2] Despite its long history, PEDV re-emerged as a major threat in the 2010s, with highly virulent strains causing devastating outbreaks in Asia, North America, and Europe.[3]

PEDV has undergone significant genetic evolution, leading to distinct genogroups: GI (classical strains) and GII (variant strains). Early GI strains, including the prototype CV777, caused sporadic outbreaks with moderate clinical severity. However, since 2010, GII strains, particularly GIIa and GIIb, have spread globally, exhibiting increased virulence with higher mortality.[4] The virus appears to have first re-emerged in China in 2010 then rapidly spread across Asia before reaching North America in 2013, where on infected herds it caused nearly 100% morbidity and up to 95% mortality in piglets. The disease subsequently spread to Europe, with outbreaks in Germany, Belgium, and other countries.[3,5]

PEDV primarily affects the small intestinal epithelium, leading to severe villous atrophy, diarrhea, dehydration, and malabsorption. The disease is most severe in neonatal piglets, where mortality can exceed 80%, while older pigs exhibit milder symptoms with lower fatality rates. The virus typically enters the host through the fecal–oral route, infecting enterocytes and leading to rapid viral shedding. Additionally, PEDV has been detected in the nasal cavity and semen, suggesting the potential for aerosol and reproductive transmission.[6,7] GII variants have evolved mechanisms to evade the host immune response that are unique from classical PEDV strains, making disease control more challenging.[8]

Efforts to control PEDV have focused on biosecurity, vaccination, and herd immunity as the virus is highly contagious, spreading through contaminated feces, feed, water, and fomites. Biosecurity measures, including strict sanitation protocols, vehicle disinfection, and feed monitoring, are essential for reducing viral transmission. While vaccines against classical and emergent PEDV strains have been developed, their performance in field settings have been variable.[9]

The economic impact of PEDV has been substantial. The disease is not reportable in the U.S. so actual losses as measured in terms of productivity or economics are only available from modelling estimates. The early years (2013–2014) of the U.S. outbreak were thought to involve losses of around 8 million pigs with additional costs to swine producers as a result of non-lethal morbidity in affected pigs.[10] Understanding the full economic costs of the outbreak are difficult to estimate as the high mortality rate contributed to real (and anticipated) shortages in pork supply, which appeared to have resulted in higher live hog prices across the industry and offset much of the direct losses borne by affected farmers.[11,12]

The persistence and evolution of PEDV highlight the need for continuous surveillance, genetic monitoring, and enhanced biosecurity practices to mitigate future outbreaks. The high mutation rate and potential recombination events[13,14] underscore the importance of developing more broadly protective vaccines and understanding PEDV-host interactions for long-term disease control or eradication at herd, regional, or national levels.

Objectives:

The objective of this systematic literature review was to summarize the existing knowledge about PEDV transmission, epidemiological risk factors for infection with the virus, and the availability and efficacy of control measures or tools that can contribute to regional or national eradication of the virus from the U.S. Gaps in the knowledge that would contribute to an argument against implementation of a regional or national eradication strategy will be discussed.

Materials & Methods:

A systematic review of the published literature was conducted according to a pre-defined protocol[15] with modifications to the protocol incorporated as required based on learnings from the initial stages of searching. The literature review and was registered with Systematic Reviews for Animals & Food (https://syreaf.org/).

The objective of the review was to summarize the peer-reviewed published literature on epidemiological factors related to PEDV transmission within and between farms, the components of farm and industry biosecurity plans that may reduce the likelihood of virus transmission, and disease control measure that could contribute to elimination of the virus from farms or the US industry.

Information sources and search strategy

Search strategies were developed using medical subject headings (MeSH) whenever possible and included text words as necessary to locate relevant materials. The following electronic publication databases were searched: MEDLINE, Elsevier (SCOPUS interface), the USDA National Agricultural Library (AGRICOLA interface), CAB Abstracts, and international theses and dissertations (ProQuest, Open Access Theses and Dissertations, and EBSCO OpenDissertations interfaces).

A Boolean search string suitable for use with MEDLINE was developed then modified as necessary for use in the other publication databases to identify relevant content published since January 1, 1990:

> "porcine epidemic diarrhea virus"[MeSH Terms] OR "porcine epidemic diarrhea"[Text Word] OR "porcine epidemic diarrhoea"[Text Word] AND ("1990/01/01"[Date - Publication] : "3000"[Date - Publication]) AND (transmi* OR biosecur* OR intervention OR eliminat* OR eradicat* OR epidemiolo* OR control OR spread OR disinfec* OR clean* OR hygien* OR prevalence OR vaccin* OR ((feces OR fecal OR faec*) AND (PCR OR "polymerase chain reaction" or "virus isolation"))) AND ("english"[Language])

Initial searches were completed on November 18, 2024, and updated on December 20, 2024. Search results from the bibliographic databases were downloaded as Research Information Systems (RIS) files then uploaded into commercial SaaS software (Covidence; Veritas Health Innovation Ltd, Melbourne, Australia) to aid in management of the review process and data extraction.

Eligibility criteria

Studies were selected according to the criteria outlined below (**Table 1**), consistent with the Population, Outcome, and Study design (POS) framework recommended under the Preferred Reporting Items for Systematic review and Meta-Analysis protocol (PRISMA-P).[15]

Table 1. Eligibility criteria for inclusion in the systematic review of transmission factors, management interventions, and elimination techniques related to porcine epidemic diarrhea.

Criteria	Description
Population (P)	*Sus scrofa* (for field and epidemiological studies)
	Laboratory animals permitted for in vitro and studies of vaccines, immunologic studies, etc.
	Only studies involving PEDV were included. Other studies related primarily to other porcine coronaviruses were excluded.
Outcome (O)	Studies with outcomes related to virus transmission within and between farms, biosecurity, disease control measures (including vaccines, compounds thought to have antiviral effect, and medications or treatments that could reduce severity of clinical signs), virus inactivation, and other outcomes relevant to understanding the potential for regional or national eradication of PED. Studies may have included either natural or experimental infections with PEDV.
Study design (S)	Randomized controlled trials, controlled clinical trials, prospective and retrospective comparative cohort studies, and case-control studies. Case studies will be included only if there are at least two intervention/affected sites and two control sites.
Language	English
Location	No restriction
Time period	January 1, 1990, to present
Type of evidence	Peer-reviewed articles and theses

Selection process

Records from the bibliographic databases were downloaded as Research Information Systems (RIS) files and then uploaded into Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia). Covidence's deduplication tool was used to remove duplicate records before screening with additional duplicates deleted manually as they were detected. A first-stage screening of each record's title and abstract was performed by two reviewers (EN, WH), with consensus required for a

study to be advanced to the second-stage screening. Records were reviewed utilizing the following questions as a screening tool: (1) Does the study describe or evaluate epidemiological aspects of PED that are related to transmission, biosecurity interventions, and elimination techniques in swine? (YES=include, NO=exclude, UNCLEAR=include), (2) Is there a concurrent comparison group? (YES=include, NO=exclude, UNCLEAR=include), and (3) Is the full text available in English? (YES=include, NO=exclude). The criteria were tested by both reviewers on the first 25 records to ensure clarity and consistent understanding of the criteria.

A second-stage, full-text screening was then conducted on each of the records that were identified as eligible after the first-stage screening. Each record was screened by only one of the two reviewers (EN, WH). Each record was evaluated against the following criteria in order to determine if it should be advanced into the data extraction phase of the study: (1) Is the full text available and comprised of > 500 words?; (2) Does the study assess PED interventions relevant to PED transmission (i.e. biosecurity measures, transportation methods, etc.) which could include either commercially oriented (proprietary vaccines, tools, equipment, methods) or non-commercially oriented (biosecurity steps, staff training, etc.) interventions?; (3) Is at least one of the study outcomes relevant to understanding the feasibility of PED eradication?; (4) Is there a relevant concurrent comparison group and was the study conducted under an eligible study design?

Data extraction and synthesis

A data collection template was designed in the Covidence software to facilitate extraction of key features and outcomes from each study. The studies were grouped into the following categories prior to data extraction (rather than completing data extraction in random order) to facilitate the reviewer's understanding of the important factors related to study type and outcome: Airborne transmission, antivirals and other therapies, biofeedback and purposeful virus exposure, colostrum and management of passive immunity, immune cross-protection, epidemiological modelling, feed risk, host resistance, viral inactivation, viral shedding, transportation risks, vaccine development and use, and the role of wildlife. Data extracted from the studies was then used to develop the narrative-based systematic review.

Results:

Search results

After two separate searches of the literature had been completed (at two different times), a total of 9,968 records were identified, of which 7,951 were duplicates, resulting in 2,017 to be reviewed by title and abstract in the first-stage screening (**Figure 1**). One-thousand four-hundred and sixty-one records were excluded during the first-stage screening resulting in manuscript retrieval and full-text review of 555 eligible records in the second-stage screening. One-hundred forty-three of these were excluded, mostly due to wrong study outcomes (n=65) and ineligible study designs (n=47). Data extraction was then completed for 412 records.

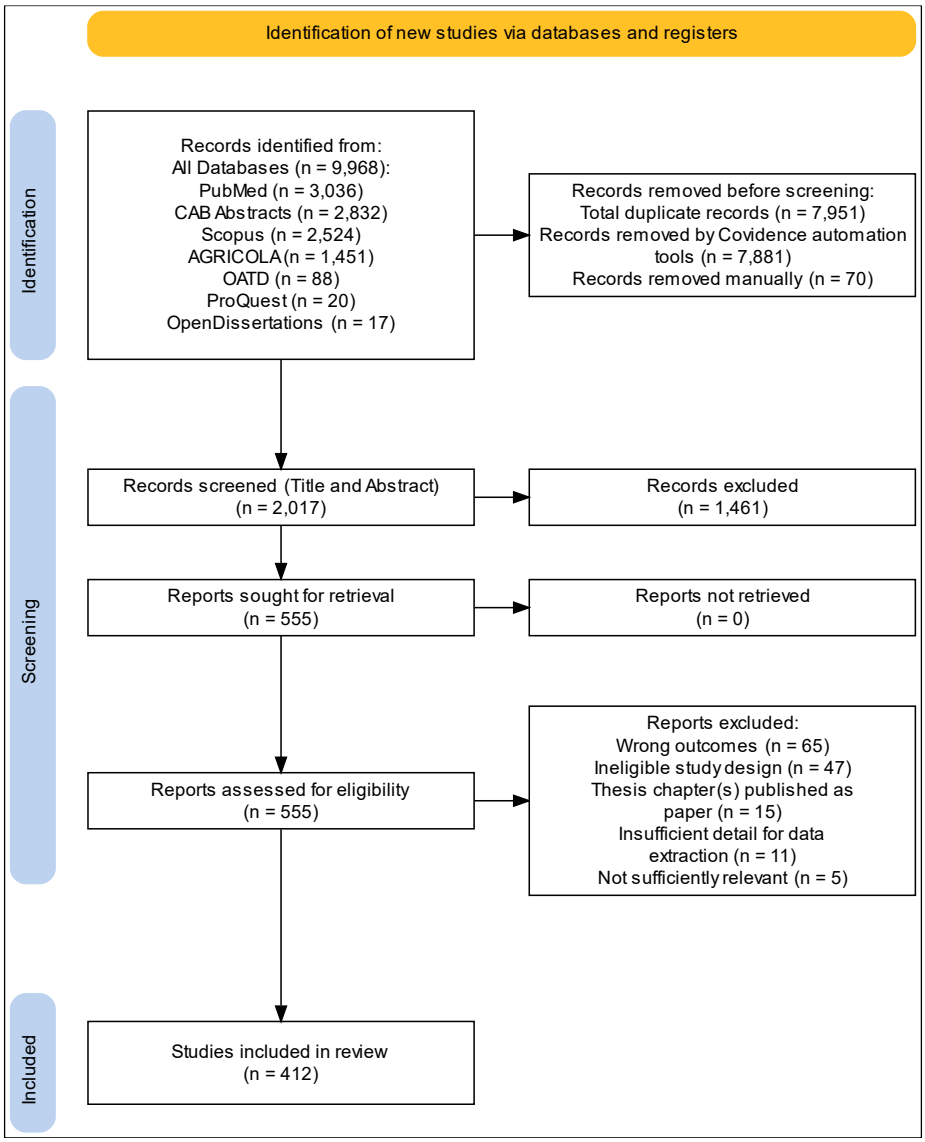

Figure 1. PRISMA flow diagram describing quantitative results of systematic literature review of transmission factors, management interventions, and elimination techniques related to porcine epidemic diarrhea.

The overwhelming majority of eligible studies were reported from countries in Asia (56%) or North America (36%), with substantially less reporting from Pacific, European, or South American countries (8%). The effect of the U.S. PED outbreak starting in 2013 with carry-on effects in much of the world in subsequent years is apparent in the volume of published papers by year. Of the 412 eligible records, only 7% were published between 2010 and 2013 with the remaining 93% of papers published between 2014 and 2024. The category of study type was not equally distributed with papers related to “Antivirals and other therapies” or “Vaccine development and use” accounting for 54% of the eligible studies (**Table 2**).

Table 2. Distribution of eligible papers stratified by study category.

Study category	Number	Proportion
Airborne transmission	4	1%
Antivirals and other therapies	104	25%
Biofeedback and purposeful virus exposure	13	3%
Colostrum and management of passive immunity	20	5%
Epidemiological modelling	41	10%
Feed risk	36	8%
Host resistance	4	1%
Viral inactivation	31	7%
Viral shedding	31	7%
Transportation risks	6	1%
Vaccine development and use	123	29%
Role of wildlife	11	3%
Grand Total	**424**[a]	100%

[a] **Total is greater than the number of eligible papers (n=412) due to some papers being classified into more than one category.**

Airborne transmission

Though the potential for airborne transmission of some livestock viruses such as foot-and-mouth disease virus, influenza virus, Aujeszky's disease virus, and others are well-understood, the significance of aerosol spread for PEDV is less clear.[16] Experimental evidence shows that the virus is present in the nasal cavity and oropharynx of infected pigs, at least transiently during infection, and there is potential for airborne spread.[7] Though the virus is thought to transmit most efficiently by the fecal-oral route, it seems the fecal–nasal route may also play a role, particularly in confined spaces such as farrowing or nursery facilities.[17] However, inducing successful experimental airborne transmission has not been reliably achieved even over short distances.[18]

Farm-to-farm airborne transmission of PEDV appears possible but again, its significance in perpetuating endemic or epidemic spread has not been demonstrated. Experimental infection of 7-8 week old pigs housed in a controlled environment resulted in recovery of infectious virus from the air for at least 63 hours post-inoculation and from airstreams outside the research facility at distances up to 16 kms (10 miles).[19] Though direct evidence of aerosol transmission between farm sites is lacking, empirical evidence is available. During a 2013 outbreak of PED in the U.S., temporal climatological data from a cluster of infected farms was analyzed.[20] The researchers hypothesized that if airborne dissemination played a role in the outbreak, the direction of disease spread should correlate with the predominant wind direction. Using two different analytical methods, their hypothesis was strongly supported.

The available studies collectively support the hypothesis that PEDV can become airborne and remain infectious in a concentration that creates risk for nearby farms; there is some evidence that some strains spread more efficiently through aerosols than others.[17] However, as data presented below will show, this risk should be considered low relative to the substantial evidence supporting the importance of oral-fecal transmission between pigs and through contaminated fomites.

Antivirals and other therapies

While vaccination efforts continue to evolve, alternative strategies, including antiviral compounds, probiotics, plant-derived therapeutics, and immuno-modulatory agents, have gained increasing attention for their potential to mitigate PEDV infection.

Interferons

Interferons have been explored for their broad-spectrum antiviral effects. Interferons (IFNs) serve as critical first-line antiviral defenses by activating a cascade of interferon-stimulated genes (ISGs) that inhibit viral replication and enhance host immunity. Given their broad-spectrum activity, exogenous IFN administration has been explored as a potential antiviral strategy against PEDV. The most extensively studied IFNs in PEDV research are Type I interferons (IFN-α, IFN-β) and Type III interferons (IFN-λ3), both of which exert their effects through distinct receptor-mediated pathways. While Type I IFNs elicit systemic immune responses, Type III IFNs target mucosal surfaces, making them particularly relevant for enteric infections like PEDV. A notable study by Shen, et al. (2016) focused on porcine IFN-λ3 (poIFN- λ3), evaluating its molecular characteristics and antiviral properties

against PEDV.[21] The study successfully cloned and expressed poIFN- λ3 in *Escherichia coli* and demonstrated that recombinant poIFN- λ3 significantly inhibited PEDV replication in Vero E6 cells in a dose- and time-dependent manner. Pre-treatment with poIFN- λ3 before PEDV exposure induced the highest observed level of inhibition observed and supported IFN-λ's potential as a prophylactic antiviral strategy in piglets.

A major advantage of IFN-λ therapies is their mucosal specificity. Unlike Type I IFNs, which trigger systemic immune activation and inflammation, IFN-λ primarily targets epithelial cells lining the intestine, where PEDV replicates. This reduces the risk of cytokine storms or immune overactivation, making IFN-λ -based therapies safer for neonatal piglets.

Beyond direct IFN administration, researchers have also investigated host antiviral proteins that are induced by interferon signaling. Wu, et al. (2020) examined the antiviral effects of viperin, a broad-spectrum antiviral protein whose expression is upregulated by IFN signaling.[22] The study found that PEDV infection increased viperin expression in porcine intestinal epithelial (IPEC-J2) cells, and that overexpression of viperin significantly reduced PEDV replication. Mechanistically, viperin was shown to interact with the PEDV nucleocapsid (N) protein, interfering with viral assembly and release. The study concluded that viperin represents a key IFN-induced antiviral effector against PEDV, suggesting that targeting IFN-stimulated pathways could enhance host resistance. Despite their potential, interferon-based antiviral strategies face several challenges: Viral immune evasion due to PEDV's ability to suppress IFN signaling, particularly through actions of non-structural proteins that can block upregulation of interferon-stimulated genes expression; PEDV strain variation that can contribute to differing levels of IFN susceptibility; and finally the fact that recombinant IFNs are expensive to produce and their oral or intranasal administration for swine can be challenging due to degradation in the gastrointestinal tract.

Miscellaneous chemicals

Other chemical antivirals that have been investigated, likely related to the early suggestions that they may have potential for treatment of COVID, include lithium chloride (LiCl) and ivermectin. Li, et al. (2018) demonstrated that LiCl inhibited PEDV replication and entry *in vitro* in a dose-dependent manner, significantly reducing viral RNA and protein expression.[23] Additionally, the study noted that LiCl inhibited PEDV-induced early and late-stage apoptosis, suggesting that its antiviral mechanism may involve the modulation of cell death pathways. After screening an FDA-approved drug library, Wang, et al. (2023) identified ivermectin (IVM) as a potent antiviral agent against PEDV.[24] The study demonstrated that IVM inhibited PEDV RNA synthesis, protein expression, and viral progeny production. IVM was most effective during the late stages of infection, where it interfered with the extracellular shedding of virions. Moreover, a combination of IVM and niclosamide exhibited an enhanced antiviral effect, highlighting its potential for combination therapy approaches.

Plant-based extracts or chemicals

Numerous papers have reported on the antiviral effects of plant-based extracts on PEDV and at least two recent reviews are available on the topic.[25,26] Within this group of antiviral chemicals, flavonoid and alkaloid compounds are frequently cited. Liang, et al. (2024) investigated flavonol, a polyphenolic compound widely found in tea, vegetables, and citrus fruits, demonstrating that it effectively inhibited PEDV RNA synthesis, protein expression, and viral progeny production in a dose-dependent manner.[27] Notably, flavonol was shown to interfere with viral attachment and internalization phases, suggesting its potential for preventing viral entry into host cells. A study by Xiang, et al. (2024) identified berbamine, a naturally occurring alkaloid, as a potent anti-PEDV compound.[28] Screening of a natural product library using molecular docking techniques revealed that berbamine selectively targeted PEDV replication-associated non-structural proteins (Nsp3 and Nsp16). In piglet trials, oral administration of berbamine significantly reduced clinical signs and viral shedding, suggesting strong *in vivo* efficacy.

A common feature of studies of these plant-origin compounds is the use of what is frequently termed "essential oils" or "plant extracts" which typically refers to simple alcohol or water extracts of plant matter and that results mixtures of chemicals that have poorly defined make-up or unknown concentration of the active molecule(s). As an example, Kim (2012) examined the antiviral effects of *Artemisia dubia* essential oil, finding that its application to infected Vero cells resulted in selective inhibition of PEDV replication.[29] Similarly, Cao, et al. (2022) demonstrated that an aqueous extract of *Moringa oleifera* effectively suppressed PEDV replication by modulating oxidative stress pathways, reducing reactive oxygen species (ROS) levels and inflammatory cytokine expression.[30] While the work is interesting, the lack of understanding around the important active ingredients frequently makes the study outcomes unpredictable.

Lactobacillus species

Probiotic *Lactobacillus* strains have garnered increasing attention as potential antiviral agents against PEDV due to their ability to enhance gut immunity, modulate inflammatory responses, and inhibit viral replication through competitive exclusion and immune modulation. Several studies have explored their efficacy, utilizing different strains and delivery mechanisms, including live bacterial supplementation, recombinant antibody-expressing strains, and bacterial-derived antimicrobial peptides.

One strains, *Lactobacillus rhamnosus* GG (LGG), has been evaluated for its ability to protect the intestinal tract of PEDV-infected piglets. In a controlled feeding trial, 15 piglets were divided into three groups: A control (basal diet), a PEDV-infected group, and a LGG-supplemented group receiving 3×10^9 CFU/day of the bacteria.[31] The study demonstrated that LGG supplementation significantly improved intestinal morphology, enhanced antioxidant capacity, and alleviated jejunal mucosal inflammation. Moreover, LGG was found to modulate lipid metabolism disorders, indicating the bacterium may have broader physiological benefits beyond direct viral inhibition.

Lactobacillus plantarum strains have also been studied for their antiviral effects. A study by Chen, et al. (2022) systematically screened 60 different lactic acid bacterial (LAB) strains isolated from nursing piglet feces.[32] The study identified *Ligilactobacillus agilis* (YM22) and *Ligilactobacillus salivarius* (YM33) as the most effective ones that were evaluated, each showing prophylactic effects against PEDV infection in Vero cells. Notably, these strains did not exhibit direct viral binding activity, suggesting that their protective effects were likely mediated through innate immune stimulation and suppression of pro-inflammatory cytokines such as TNF-α and IL-8.

A study focusing on *Lactobacillus casei* examined its potential to stimulate intestinal cells to produce antimicrobial peptides.[33] The authors found that oral administration of *L. casei* induced the expression of Reg3a, a host-derived antimicrobial peptide, which significantly inhibited PEDV replication and promoted intestinal epithelial cell proliferation and repair.

A novel strategy involves engineering *Lactobacillus* strains to express PEDV-specific neutralizing antibodies. Sun, et al. (2024) developed a recombinant *Lactobacillus* strain (pPG-Fab/J31) that secreted the Fab fragment of a neutralizing antibody against PEDV.[34] In an oral administration trial, piglets receiving pPG-Fab/J31 exhibited significantly reduced viral shedding, less severe intestinal lesions, and an improved survival rate of 100% compared to controls. A complementary approach by Liu, et al. (2020) involved expressing porcine IFN-λ3 on the surface of *Lactobacillus plantarum* as a means of delivering antiviral cytokines directly to the gut.[35] This strategy effectively upregulated antimicrobial molecules and antiviral cytokines, further demonstrating the versatility of *Lactobacillus*-based delivery systems for antiviral applications.

Beyond live bacterial administration, cell-free supernatants (CFS) from *Lactobacillus* strains have shown potential as antiviral agents. Yang, et al. (2023) tested CFS and live cells from seven locally isolated LAB strains against a pandemic strain of PEDV.[36] The study found that CFS from *Lactobacillus plantarum* 25F and *Pediococcus pentosaceus* 77F significantly reduced viral infectivity in Vero cells, suggesting that bacterial metabolites may possess direct antiviral properties. Zhou, et al. (2018) constructed a recombinant *Lactobacillus casei* strain expressing bovine lactoferricin (Lfcin), a broad-spectrum antimicrobial peptide.[37] While primarily developed for use as a feed additive, this approach demonstrated potential for enhancing host immune responses and inhibiting PEDV replication.

Canning, et al. (2017) evaluated the use of *Bacillus subtilis* C-3102 as a dietary supplement in nursery pigs, assessing its impact on PEDV infection.[38] While treated pigs showed no significant differences in fecal virus shedding compared to controls, histological analysis suggested some improvement in intestinal health markers, indicating potential indirect benefits of probiotic supplementation.

The search for effective therapeutics against PEDV has led to diverse strategies, ranging from chemical antivirals and plant-derived compounds to probiotics and immuno-modulatory agents. Studies above highlight only part of the full spectrum of antiviral agents that have been evaluated against PEDV. While more than 90% of the papers reviewed on the topic demonstrated antiviral effects *in vivo* or *in vitro*, few appear to have made their way successfully into a commercial setting. Future research should focus on combining these approaches with vaccine strategies, optimizing formulations, and conducting large-scale field trials to develop effective and sustainable PEDV control measures.

Role of purposeful virus exposure, passive immunity, and cross-protection

Control of PED is complicated by the need to provide cross-protection between different PEDV strains. Controlled purposeful viral exposure (biofeedback), enhancement of colostrum-mediated immunity, and the development and innovative uses of vaccines are being used to help deal with the problem.

A study by Zhang, et al. (2020) sought to determine whether vaccination with one PEDV strain could protect against another.[39] Under the conditions of the experiment, the researchers showed that G2a-based vaccines could provide sterilizing immunity against both homologous (G2a) and heterologous (G1a) challenges, whereas G1a-based vaccines only provided partial protection against G2a strains. This suggests that possibly the more recent and highly virulent G2 strains induce a broader immune response, reinforcing the need for vaccination programs to be updated to match circulating field strains. Taking this concept further, Song, et al. (2024) developed a bivalent vaccine incorporating spike proteins from both G2a and G2b subtypes.[40] The results demonstrated significantly higher neutralizing antibody titers in piglets, confirming that multivalent vaccines could improve cross-protection across PEDV subtypes.

Beyond vaccines, some researchers have explored whether natural infection with less virulent PEDV strains could induce cross-protective immunity. Goede, et al. (2015) found that sows previously exposed to a naturally attenuated PEDV strain passed strong passive immunity to their piglets, leading to significantly reduced mortality upon secondary infection.[41] This study suggests that mild PEDV strains could serve as a natural form of immunization, although the practicality of deliberately exposing sows is a decision that needs to be considered with caution due to unpredictable field conditions. However, not all mild strains offer reliable protection. Annamalai, et al. (2017) and Lin, et al. (2015) tested whether prior infection with an S-INDEL PEDV strain (a naturally attenuated variant) could protect against a highly virulent PEDV challenge.[42,43] While some degree of cross-protection was observed, neutralizing antibody titers were lower, and disease severity was not completely mitigated. This underscores the inconsistency of using mild strains as a natural vaccine, particularly as some strains may induce weaker immune responses.

Given the initial absence of vaccines and the limitations of vaccination and natural cross-protection, some producers have turned to purposeful viral exposure, or biofeedback, as a method of inducing herd immunity. This involves deliberately exposing sows to live PEDV before farrowing, with the goal of stimulating colostral antibody production and reducing piglet susceptibility. However, while biofeedback has shown some immunological benefits, its long-term consequences remain contentious. Srijangwad, et al. (2017) compared the effects of single vs. double biofeedback exposure in gilts.[44] While a single exposure yielded only modest increases in IgG titers, a second exposure shortly before farrowing significantly boosted IgA levels in colostrum, suggesting that repeated viral exposure may be necessary to maximize maternal antibody transfer. Similarly, Clement, et al. (2016) assessed how long biofeedback-induced immunity persisted.[45] Neutralizing antibodies remained detectable for up to 24 weeks post-feedback, with piglets from exposed sows exhibiting partial protection against PEDV challenge. However, these findings were highly farm-dependent, indicating that biofeedback may not be equally effective across different herd management systems.

Despite its potential benefits, biofeedback carries significant risks, particularly in large-scale production systems. Yamagami, et al. (2021) found that on 172 Japanese farms, biofeedback exposure extended the duration of PEDV outbreaks, with affected farms experiencing outbreaks lasting 145 days compared to 66 days on non-feedback farms.[46] This suggests that biofeedback may inadvertently contribute to viral persistence, rather than achieving rapid herd immunity. Also concerning, Nguyen Thi, et al. (2022) detected genetic mutations in PEDV strains from feedback-exposed herds, raising the possibility that repeated viral exposure could accelerate antigenic drift, making existing vaccines less effective.[47] These findings underscore the need for caution when implementing biofeedback strategies, as the potential for viral evolution could undermine long-term disease control.

Since neonatal piglets rely on passive immunity, researchers have explored ways to optimize maternal antibody transfer, including strategic vaccination, dietary supplementation, and improvement of colostrum quality. Langel, et al. (2019) investigated how the timing of maternal infection affects colostrum-derived immunity.[48] The results were clear: Infection during the second trimester (day 38 to 76 of pregnancy) led to the highest colostral IgA and IgG levels, with 100% piglet survival upon PEDV challenge. By contrast, third trimester (day 77 to 114 of pregnancy) infection resulted in weaker antibody responses and higher piglet mortality. These findings emphasize the importance of strategic timing in maternal immunization programs. In addition to vaccination, dietary supplementation has been explored as a method to enhance colostrum quality. Amimo, et al. (2024) demonstrated that Vitamin A supplementation significantly boosted colostral IgA titers, leading to improved piglet survival rates (98% vs. 87% in controls).[49] These results suggest that targeted nutritional strategies may provide an additional layer of passive immunity enhancement.

Although colostrum is essential for neonatal immunity, Yuan, et al. (2022) found that it may also serve as a transmission route for PEDV.[50] The study detected viral RNA within colostrum-derived CD31+ T cells, raising concerns that infected sows could pass PEDV to their piglets through milk. This highlights the need to balance passive immunity benefits with potential transmission risks.

While cross-protection and biofeedback exposure offer potential immunity benefits, they also pose risks of incomplete protection and viral evolution. The most consistently effective strategy remains the optimization of colostrum-derived immunity, which can be enhanced through strategic vaccination, proper gestational timing of vaccination, nutritional supplementation, and likely controlled exposure to the virus. Future efforts should focus on refining these complementary strategies to improve disease resistance in neonatal piglets while minimizing the risks of viral persistence and antigenic drift.

Epidemiological modelling

Porcine epidemic diarrhea virus continues to challenge swine production systems worldwide, with recurring outbreaks, regional transmission, and persistent endemicity occurring in some areas. While vaccination and biosecurity interventions play essential roles in disease control, epidemiological modeling, outbreak forecasting, and risk factor analysis have become increasingly important tools for disease management. Researchers have applied a range of spatio-temporal models, machine learning techniques, and observational studies to understand PEDV dynamics, identifying key risk factors such as animal movement, biosecurity lapses, environmental conditions, and feed contamination.

PEDV's introduction into North America and Asia led to severe epidemics, prompting researchers to investigate how the virus spreads between farms and within regional networks. Several studies have provided key insights into primary transmission routes, outbreak characteristics, and factors influencing farm-level infection risks. One of the most comprehensive epidemiological analyses of PEDV emergence was conducted using data from the 2014 outbreak in Canada. Perri (2019) employed case-control studies, network analysis, and machine learning models to evaluate potential transmission routes.[51] The study identified contaminated feed - specifically, spray-dried porcine plasma from a single supplier - as a primary source of infection. Further analysis revealed that feed supply networks played a central role in disease dissemination, with a high degree of connectivity between affected farms and common feed distributors. Animal movement and semen transport did not appear to be significant transmission factors during this outbreak, highlighting the unique role of feed in PEDV epidemiology. Expanding on these findings, Perri, et al. (2019) used network modeling to map PEDV transmission dynamics in Canadian swine herds.[52] The study demonstrated that highly connected farms, particularly those receiving feed from major suppliers, had an elevated risk of infection, reinforcing the importance of supply chain monitoring in outbreak prevention.

A study in Vietnam identified farm proximity to slaughterhouses (<1 km), farrow-to-wean production type, and the presence of chickens on-site as the three most significant risk factors for PEDV transmission.[53] The identification of poultry as a potential mechanical vector is unique among the published studies and it is unknown whether this putative risk factor is simply related to contaminated fomites or whether a cross-species interaction was occurring and contributing to PEDV persistence in endemic areas.

Several studies have explored how farm size, production type, and regional density influence PEDV spread. Toyomaki, et al. (2018) analyzed the 2013-2014 Japanese epidemic, finding that larger farms and those with higher regional farm densities were significantly more likely to experience outbreaks.[54] The study also highlighted slaughterhouse contamination, shared composting facilities, and pig effluent disposal services as important risk factors, pointing to biosecurity gaps in waste management as a key area for intervention.

As PEDV remains endemic in some regions, forecasting models have become essential for anticipating outbreaks and guiding preventive strategies. Several researchers have developed machine learning models, spatial analysis tools, and network simulations to predict PEDV spread and identify farms at greatest risk. Paploski, et al. (2021) developed a machine learning platform to forecast PEDV outbreaks at the farm level using data from 15% of U.S. sow farms.[55] The model incorporated animal movement, environmental conditions, and disease occurrence patterns to predict outbreaks up to two weeks in advance. While the model achieved high specificity (99.9%) and negative predictive value (99.4%), its sensitivity remained low (19.9%), indicating that while false positives were rare, the model struggled to detect all potential outbreaks. A similar study by Ajayi, et al. (2019) tested various machine learning techniques, including random forests, artificial neural networks, and classification trees, to predict PEDV trends in Ontario, Canada.[56] The results showed that random forests provided the most accurate predictions, reinforcing their suitability for disease trend forecasting in swine production systems.

Recognizing that PEDV transmission is influenced by both farm-level biosecurity and broader environmental conditions, researchers have explored how climate, topography, and land use impact outbreak risks. Machado, et al. (2019) combined spatial analysis with machine learning to investigate the role of pig movement and environmental factors in disease occurrence.[57] The study found that pig density, wind speed, temperature, precipitation, and topographical features such as slope significantly influenced PEDV risk, highlighting the need for region-specific disease control strategies. Makau, et al. (2024) examined seasonal trends in PEDV persistence across the United States, revealing a clear winter clustering effect (January through March) with a 2.2-fold increase in risk during colder months.[58] This aligns with previous findings that PEDV survives longer in cooler temperatures, reinforcing the need for enhanced winter biosecurity measures.

Despite advances in modeling and forecasting, PEDV remains a persistent challenge in some areas due to environmental persistence, biosecurity lapses, and inconsistent elimination efforts. One critical challenge in PEDV control is the virus's ability to survive for extended periods in manure storage systems. Tun, et al. (2016) found that PEDV remained viable in earthen manure storage (EMS) for up to nine months post-infection, with viral loads independent of temperature and pH.[59] Importantly, the study suggested that PEDV may replicate within the EMS environment, potentially finding alternative hosts. This raises concerns about long-term environmental reservoirs and the potential for future reintroductions.

Recognizing the role of environmental contamination in PEDV persistence, Stewart, et al. (2022) implemented environmental swabbing and monitoring as a tool for real-time biosecurity adjustments during an outbreak.[60] The study demonstrated that targeted sampling and response strategies significantly reduced viral contamination on farm surfaces, suggesting that environmental monitoring could play a crucial role in outbreak response efforts.

Beyond environmental factors, human decision-making and risk tolerance have also been identified as critical factors in PEDV transmission. Agent-based modeling has been used to explore how swine producers' risk tolerance influences their investment in biosecurity.[61,62] The results of this work suggested that strong initial biosecurity investment was more effective at preventing outbreaks than delayed interventions, reinforcing the importance of proactive rather than reactive disease control strategies.

Epidemiological modeling and risk factor analysis have provided critical insights into how PEDV spreads, which farms are most at risk, and what interventions are most effective. Key findings from this body of research have identified feed contamination, animal movement, and environmental persistence as significant risk factors for PEDV outbreaks. Predictive models using machine learning and spatial analysis can improve early outbreak detection and responses and environmental monitoring and manure management should be prioritized to reduce long-term PEDV reservoirs. Human behavior plays a crucial role in disease control, with proactive biosecurity investments yielding better outcomes than reactive measures.

Feed risk

Early epidemiological investigations into the global pandemic of PED that started in 2013 struggled to identify a clear route of virus introduction into the U.S., leading to widespread speculation about possible transmission pathways. Unlike traditional disease vectors such as animal movement, fomites, or airborne spread, the hypothesis that contaminated feed played a role in PEDV transmission was initially met with skepticism. However, over time, accumulating evidence - including controlled trials, field studies, and modeling efforts - provided compelling data linking PEDV outbreaks to contaminated feed ingredients.

Through experimental and field-based research, it has been confirmed that PEDV can remain viable in feed ingredients, survive transport over long distances, and initiate infections in naïve pigs. Today, biosecurity measures in feed production, thermal processing, chemical mitigation, and feed ingredient selection are recognized as crucial tools in PED prevention.

The role of feed in PEDV transmission was first suspected following unexplained outbreaks in North America, where traditional risk factors such as infected animal movement or personnel contamination failed to account for disease spread. Initial studies attempted to establish a temporal and spatial link between contaminated feed and PEDV outbreaks. One of the earliest published studies to investigate the role of feed ingredients in PEDV transmission was conducted by Aubry, et al. (2017), who assessed the epidemiological link between Spray Dried Porcine Plasma (SDPP) and PEDV outbreaks in Canadian swine herds.[63] The study found a strong statistical association between PEDV cases and farms that had received SDPP-containing feed, with a relative risk (RR) of 9.0 (95% CI, 1.3–64.0). The attack rate of PEDV increased in direct proportion to the concentration of SDPP in feed, with farms receiving higher SDPP inclusion rates (3–6%) exhibiting a significantly higher risk of infection compared to those receiving lower concentrations (1–1.5%).

Schumacher, et al. (2016) conducted a controlled experimental trial to determine the minimum infectious dose of PEDV in feed.[64] The study found that pigs became infected when exposed to feed containing as little as 5.6×10^3 TCID/g of PEDV (corresponding to a Ct value of 37 in real time PCR assays). Notably, this concentration was above the detection threshold used by many diagnostic laboratories at the time, raising concerns that false-negative PCR results could overlook infectious feed borne PEDV.

As more controlled experiments were conducted, researchers began to understand the mechanisms that allowed PEDV to persist in feed and how different ingredients influenced viral stability. Several studies identified soybean meal as a particularly problematic feed ingredient due to its ability to prolong PEDV viability. Trudeau, et al. (2017) found that soybean meal had the longest PEDV survival time among common feed ingredients, with a delta value (time for 1-log viral reduction) of 7.5 days.[65] This was significantly higher than other feed ingredients, such as corn, distillers dried grains with solubles, or vitamin/mineral premixes, suggesting that soy protein content or processing conditions could contribute to PEDV stabilization.

Confirming these findings, Dee, et al. (2022) conducted a large-scale transport study, showing that PEDV remained viable in soybean meal samples shipped around the continental U.S.[66] In contrast, complete feed samples were negative for PEDV by day 23, despite some piglets developing infection after natural feeding behaviors. This suggested that feed sampling techniques may underestimate PEDV persistence in finished feed, whereas ingredient-based contamination remains a distinct risk.

Another critical finding was the ability of PEDV to persist on equipment in feed mills and contaminate subsequent feed batches. Schumacher, et al. (2018) tested whether batch sequencing could reduce PEDV cross-contamination in feed manufacturing.[67] While later feed batches had higher Ct values (lower viral loads), sequenced feed still resulted in infections in bioassay piglets, demonstrating that even low levels of residual contamination could pose a risk to naïve herds. In a separate but related study, Huss, et al. (2017) found that feed dust was a major contributor to viral spread within manufacturing facilities, with non-feed-contact surfaces testing positive for PEDV RNA even after standard decontamination procedures.[68] This suggested that airborne dust particles could act as secondary transmission vectors.

As evidence of feed borne transmission mounted, research has shifted toward identifying effective mitigation strategies to reduce PEDV risks in feed. Several studies have investigated chemical interventions to neutralize PEDV in feed, with formaldehyde-based products and medium-chain fatty acids (MCFA) emerging as leading candidates. Dee, et al. (2014) demonstrated that Sal CURB® (formaldehyde-based) treatment prevented PEDV transmission to naïve piglets, confirming its efficacy as a feed disinfectant.[69] Cochrane, et al. (2020) compared MCFA blends (caproic, caprylic, and capric acids) to traditional formaldehyde treatments, finding that 1% MCFA inclusion was equally effective in preventing PEDV transmission in feed.[70] Phillips, et al. (2022) tested a

monoglyceride-based alternative, which provided 100% protection against PEDV transmission at lower inclusion rates than MCFAs, highlighting the potential for new antiviral feed additives.[71]

Another mitigation approach has focused on thermal processing and extended storage. Trudeau, et al. (2016) found that heating feed above 130°C for at least 15 minutes or using eBeam irradiation at 50 kGy effectively eliminated 99.9% of PEDV infectivity[72] and Gebhardt, et al. (2024) validated extended storage (58 days at 23.9°C) as a means to inactivate PEDV.[73] This approach completely eliminated PEDV infectivity in stored feed, providing an alternative for high-risk feed ingredients.

The understanding of feed borne PEDV transmission has evolved significantly from early speculation to definitive experimental proof. Over the past decade, research has confirmed that: PEDV remains viable in certain feed ingredients, particularly soybean meal and SDPP, for extended periods; feed mills and contaminated equipment can act as long-term viral reservoirs, with dust and batch sequencing contributing to cross-contamination; and that chemical mitigation strategies (formaldehyde, MCFAs, and monoglycerides) can effectively inactivate PEDV in feed. Thermal processing and extended storage are additional strategies to reduce the risk of feed borne transmission.

Host resistance

Unlike some other swine pathogens, for which genetic resistance has been identified and selectively bred into commercial pigs (e.g., PRRSV-resistant pigs via CD163 knockout), no definitive PEDV-resistant pig breeds have been established. This is largely because the precise host genetic factors governing PEDV susceptibility remain poorly understood. Recent advances in genome editing, transcriptomics, and host-pathogen interaction studies have provided some insight into the molecular determinants of PEDV infection. Research has focused on host receptors, immune evasion strategies employed by PEDV, and gene-editing approaches to generate PEDV-resistant pigs. However, clear breakthroughs in resistance breeding remain elusive, with most studies identifying only partial reductions in viral susceptibility rather than full immunity. Efforts to identify naturally occurring resistance genes have been inconclusive, and while some promising host factors have been identified, no major resistance-associated alleles have been incorporated into breeding programs.

A review by Yuan, et al. (2022) examined the state of genetic resistance research across multiple swine diseases, including PEDV, porcine reproductive and respiratory syndrome (PRRS), classical swine fever (CSF), and transmissible gastroenteritis (TGE).[74] The study emphasized that while CRISPR/Cas9-based gene editing has successfully produced disease-resistant pigs for PRRS virus and CSF virus, no such breakthroughs have been reported for PEDV. This is primarily due to the poor understanding of key host factors involved in PEDV entry and replication.

Several receptor candidates have been explored, particularly aminopeptidase N (APN, also known as CD13), which was once thought to be a major PEDV entry receptor. However, subsequent research has shown contradictory results regarding APN's role in PEDV susceptibility, complicating efforts to engineer resistance through APN modifications. Among the various host factors investigated, APN (aminopeptidase N) has received considerable attention as a potential PEDV receptor. However, research findings have been inconsistent, leading to ongoing debate regarding its true role in viral entry and replication. A controlled trial by Wang, et al. (2021) explored the regulatory role of APN expression in PEDV susceptibility.[75] Using CRISPR/Cas9 gene editing, researchers generated APN-knockout IPEC-J2 cells and assessed their ability to support PEDV replication. The results demonstrated that APN-knockout cells exhibited increased resistance to PEDV, suggesting that APN plays a role in viral entry or replication. Furthermore, the study identified a single nucleotide polymorphism (SNP) in the APN promoter region that influenced APN transcriptional activity, implying that genetic variation in APN could contribute to differences in PEDV susceptibility among pig breeds.

Despite these findings, other studies have challenged APN's role as a critical PEDV receptor. Liu, et al. (2023) generated APN-chimeric gene-edited pigs using CRISPR/Cas9-mediated knock-in strategies to assess their resistance to PEDV.[76] While kidney epithelial cells isolated from these pigs exhibited strong resistance to TGEV (Transmissible Gastroenteritis Virus, another porcine coronavirus), they remained fully susceptible to PEDV. This suggests that APN is not the primary functional receptor for PEDV, or at least that its deletion alone is insufficient to confer resistance.

Given these conflicting findings, APN-based genetic modifications remain controversial. While certain mutations in APN may influence PEDV infection dynamics, they do not appear to be a silver bullet for PEDV resistance. Future studies should explore alternative receptors, co-factors, or intracellular immune pathways that may govern PEDV susceptibility. Since genetic resistance remains largely unresolved, researchers have also focused on how PEDV interacts with the host immune system to evade detection and clearance. A review by Ma, et al. (2024) summarized PEDV's immune evasion mechanisms, highlighting its ability to inhibit the interferon (IFN) response and suppress host antiviral gene expression.[77] The study outlined several key PEDV proteins that actively downregulate host immune defenses, including: Nsp1 and Nsp15, which inhibit IRF3 activation, preventing IFN production; nucleocapsid (N) protein, which interacts with host RNA pathways to suppress antiviral responses; and non-structural proteins (Nsps) that interfere with STAT1 signaling, disrupting IFN-induced antiviral gene transcription.

Although no genetic resistance markers have been confirmed, some studies suggest that modifying the host immune response could improve PEDV resistance. For instance, certain SNPs in interferon regulatory genes (such as IRF7 and IFNLR1) have been associated with stronger innate antiviral responses in pigs, suggesting that genetic selection for stronger IFN-producing phenotypes may offer an alternative route to enhancing PEDV resistance.

While gene editing has been successful for other swine diseases, its application to PEDV remains in its infancy. Yuan, et al. (2022) noted that while APN, CD163, and ANPEP are promising targets for gene-editing, no fully resistant pigs have been produced to date. The pursuit of host resistance to PEDV remains an ongoing challenge. While APN has been investigated as a potential receptor, conflicting results suggest that it is not the sole determinant of susceptibility. Efforts to develop gene-edited pigs resistant to PEDV have so far been unsuccessful, highlighting the need for alternative strategies such as selective breeding for stronger innate immunity.

Viral inactivation

Effective strategies and methods for inactivation of PEDV are crucial to reducing viral transmission and improving biosecurity in swine production systems. Research has explored thermal inactivation, chemical disinfectants, alkaline treatments, and novel decontamination techniques to determine the most effective methods for eliminating PEDV infectivity. While early studies provided limited guidance on practical inactivation measures, more recent research has established clear thresholds for temperature, disinfectant efficacy, and manure treatment strategies.

Heat-based inactivation has been widely investigated as a practical, chemical-free approach for PEDV control in farm environments, manure, and contaminated feed. Studies have assessed time-temperature combinations necessary to eliminate viral infectivity, with findings informing truck and trailer decontamination, manure treatment, and biosecurity protocols. One of the earliest controlled studies on PEDV thermal inactivation was conducted by Thomas, et al. (2015), who examined the efficacy of heat treatments for disinfecting livestock trailers.[78] The study found that PEDV remained infectious on metal surfaces unless exposed to at least 71°C for 10 minutes or 20°C (room temperature) for 7 days. Lower temperature treatments (e.g., 63°C for 10 minutes or 38°C for 12 hours) were not completely effective, indicating that short-duration heating below 71°C is insufficient for full viral inactivation.

More recently, Mil-Homens, et al. (2024) expanded on these findings by testing PEDV survivability across various temperatures and surfaces.[79] The study determined that PEDV persisted for 24 hours at 30°C, 12 hours at 40°C, and 6 hours at 50°C, reinforcing that high temperatures significantly reduce PEDV infectivity. Interestingly, aluminum surfaces took longer to reach inactivation thresholds compared to cardboard, suggesting that surface material properties can influence virus persistence.

PEDV can persist for months in stored manure, making manure treatment a key concern for controlling environmental contamination. Stevens, et al. (2018) demonstrated that alkaline stabilization (pH 10) using hydrated lime effectively inactivated PEDV in manure slurry, providing a practical treatment option for waste management.[80] However, concerns about ammonia volatilization and potential respiratory hazards must be considered when implementing high-pH manure treatments. Similarly, Vitosh-Sillman, et al. (2017) investigated composting as a biosecure disposal method for PEDV-infected pig carcasses.[81] The study found that sustained compost temperatures above 55°C for 4 hours completely degraded PEDV RNA, demonstrating that composting can serve as a viable biosecurity measure in outbreak scenarios.

Chemical disinfection remains one of the most commonly used methods for controlling PEDV contamination in swine production settings. Studies have evaluated different disinfectant classes, their efficacy under field conditions, and optimal application methods. Hydrogen peroxide-based disinfectants have been widely tested for PEDV inactivation. Baker (2020) evaluated accelerated hydrogen peroxide (AHP) and peroxygen-based disinfectants under freezing conditions, demonstrating that while PEDV can be inactivated by chemical disinfection, the combination of washing, disinfecting, and drying was most effective in preventing transmission.[82] A follow-up study by Holtkamp, et al. (2017) confirmed that AHP applied at a 1:16 dilution successfully inactivated PEDV in swine feces on metal surfaces, preventing transmission in a pig bioassay model.[83]

Emerging research has explored alternative disinfectants with enhanced efficacy against PEDV, including: Chitosan, a natural antimicrobial compound, evaluated by Kim, et al. (2021), who found that a 0.01% chitosan solution effectively inactivated PEDV without causing cellular toxicity, making it a potential candidate for environmentally friendly disinfection;[84] peracetic acid (PAA)-based formulations which found that a 0.5% solution of Bioxy (peracetic acid powder) could inactivate PEDV within 15 minutes;[85] and nano-graphene oxide (nanoGO) which was tested by Chung, et al. (2021) and revealed a dose-dependent antiviral activity against PEDV, suggesting its potential for use in new biosecurity products.[86]

Inactivation methods that do not rely on heat or chemicals have gained interest due to their potential for use in feed processing, cold-chain logistics, and biosecure animal plasma treatments.

Several studies have evaluated the effectiveness of ultraviolet-C (UV-C) irradiation in deactivating PEDV. Mendes Peter, et al. (2022) found that UV-C exposure at 360 mJ/cm² reduced PEDV titers by at least 3 log10 on hard surfaces, confirming UV-C as an effective decontamination tool[87] and Blázquez, et al. (2019) demonstrated that UV-C irradiation of liquid animal plasma successfully inactivated PEDV, suggesting its use as a biosafety step in plasma processing.[88]

For decontamination of feed and cold storage materials, Liu, et al. (2022) tested high-energy electron beam (E-beam) irradiation, showing that a 10 kGy dose inactivated more than 98% of PEDV on packaging materials at -20°C.[89] This suggests that E-beam irradiation could be applied in cold-chain logistics or potentially feed ingredient processing to mitigate PEDV transmission risks.

PEDV is known to persist on surfaces and in organic material, requiring specific strategies to mitigate environmental contamination. One of the most significant findings regarding PEDV persistence in manure came from Tun, et al. (2016), who demonstrated that PEDV could remain viable in earthen manure storage (EMS) for up to 9 months.[59] The study suggested that frequent agitation of manure could expose PEDV to UV light, reducing viral loads.

PEDV inactivation research has provided critical insights into effective biosecurity and decontamination practices. Key findings include: Thermal inactivation at ≥71°C for 10 minutes or prolonged exposure at room temperature (≥7 days) effectively eliminates PEDV on surfaces; hydrogen peroxide-based, peracetic acid, and chitosan disinfectants have demonstrated strong efficacy in biosecurity applications; ultraviolet and electron beam irradiation are emerging as promising non-chemical disinfection methods for feed and processing environments; and manure agitation and cold-chain disinfection strategies are critical for reducing environmental PEDV persistence.

Viral shedding

Porcine epidemic diarrhea virus is primarily transmitted through the fecal-oral route, with viral shedding in infected pigs playing a crucial role in outbreak persistence and farm-to-farm transmission. Shedding patterns are influenced by age, immune status, viral strain, and environmental conditions, making it critical to understand the duration and magnitude of viral shedding to inform disease control and biosecurity measures. Studies have demonstrated significant variability in PEDV shedding with neonates shedding high viral loads for extended periods, while older pigs tend to clear the virus more quickly. PEDV shedding is not strictly confined to feces - it has been detected in nasal secretions, oral fluids, and, in rare cases, semen and other tissues. Jung, et al. (2020) has provided a review of a number of previously published findings related to viral shedding[90] and a selection of key studies are included below.

Several studies have confirmed that neonatal pigs shed PEDV for significantly longer periods than older pigs. Madson, et al. (2014) demonstrated that 3-week-old weaned pigs shed PEDV for up to 24 days post-infection (dpi), with viral loads peaking at dpi 2–4.[91] Similarly, Díaz, et al. (2022) found that most pigs stopped shedding within 14 days, but some individuals continued shedding up to 42 dpi, highlighting variability in viral clearance rates among infected animals.[92] A study by Curry (2017) reported that PEDV RNA was detected in feces as early as 1 dpi, with peak shedding occurring at 5 dpi.[93] However, shedding ceased by dpi 6 in all pigs, suggesting that older nursery pigs clear the virus faster than younger animals. These findings are consistent with Gerber, et al. (2016), who observed that 10-day-old piglets shed significantly more virus than 8-week-old pigs, with fecal viral loads declining more gradually in neonates.[94]

In adult pigs, shedding tends to be shorter-lived but still relevant for viral transmission. Brown, et al. (2019) evaluated shedding in replacement gilts, showing that previous PEDV exposure shortened shedding duration, while vaccination had no effect on fecal viral shedding length.[95] Similarly, Schumacher, et al. (2022) confirmed that S INDEL PEDV strains resulted in milder disease and reduced shedding compared to non-S INDEL strains, reinforcing the strain-dependent nature of PEDV shedding.[96]

Although feces are the primary route of PEDV excretion, the virus has also been detected in oral fluids, nasal secretions, semen, and even internal tissues. Oral fluids and nasal secretions may serve as alternative transmission pathways in some settings. Bjustrom-Kraft, et al. (2016) found that oral fluids and rectal swabs remained PCR-positive for PEDV for up to 69 dpi, emphasizing the potential role of indirect transmission via contaminated saliva.[97] Likewise, Niederwerder, et al. (2016) detected PEDV RNA in nasal swabs at 21 and 28 dpi, raising concerns about the possibility of airborne transmission or contamination of shared surfaces.[18] Research has also investigated whether PEDV persists in tissues beyond the intestine. Bhandari (2019) detected PEDV RNA in mesenteric lymph nodes (MLN) at 28 dpi, despite absence in most other tissues.[98] This suggests that the MLN may serve as a reservoir for prolonged PEDV presence, though its role in viral shedding remains unclear. Additionally, Krishna, et al. (2020) demonstrated that PEDV RNA persisted in the intestine even after fecal shedding ceased at 28 dpi, reinforcing the idea that subclinical infections may contribute to intermittent viral excretion.[99]

While fecal shedding remains the dominant mechanism of PEDV spread, some studies suggest additional, less common shedding routes. Several studies have investigated the potential for PEDV shedding in semen, particularly in artificial insemination boar studs. McCarty, et al. (2015) reported no PEDV RNA detection in semen samples from infected boars, despite virus presence in the

reproductive organs.[100] However, Gallien, et al. (2019) found low-level PEDV RNA in the sperm-rich fraction of semen at 7 dpi, raising concerns about the potential for venereal transmission.[101] Despite these findings, the significance of PEDV transmission via semen is unclear.

PEDV was historically believed to be exclusively transmitted via the fecal-oral route, but Ryu, et al. (2022) provided the first direct evidence of transplacental transmission. In this study, PEDV RNA was detected in umbilical cords and testicles from piglets born to PEDV-positive sows, confirming that in utero infection is possible.[102] This finding has major implications for breeding herds and neonatal piglet management, suggesting that PEDV may establish infection before birth in certain conditions.

Several factors have been identified that affect the duration and magnitude of PEDV shedding, including age, immune status, and infectious dose. Multiple studies have demonstrated that neonatal pigs have a significantly lower infectious dose threshold and shed virus for longer durations than older pigs.[94,103] Older pigs clear the virus faster, likely due to more developed immune responses and greater resilience to enteric infections.

Both Krishna, et al. (2020) and Brown, et al. (2019) found that prior PEDV infection reduced but did not eliminate fecal shedding upon re-exposure, while killed vaccines had no effect on shedding duration. These findings underscore the challenge of achieving full protection against PEDV shedding through vaccination alone.[95,99]

PEDV shedding patterns play a crucial role in disease transmission, farm biosecurity, and outbreak control strategies. Key findings from this body of research include: Neonatal pigs shed higher viral loads for longer periods than older pigs; PEDV RNA can be detected in oral fluids, nasal secretions, and mesenteric lymph nodes, raising concerns about alternative transmission routes; semen can contain PEDV RNA, but its infectivity remains uncertain; transplacental transmission has been documented, suggesting that infection can occur before birth; prior infection reduces but does not eliminate PEDV shedding; and killed vaccines have no effect on shedding duration.

Transportation risks

The role of contaminated trucks, trailers, and transport equipment in spreading PEDV has been well-documented, particularly in outbreak scenarios where biosecurity failures at key points such as slaughterhouses and lairages contribute to viral dissemination. PEDV is a highly contagious enteric virus, and once introduced into a transport network, it can persist on surfaces, cross-contaminate clean animals, and spread between farms over long distances.

Transport vehicles, particularly livestock trailers, slaughterhouse holding pens, and feed trucks, are high-risk fomites that can introduce and maintain PEDV circulation. Several studies have quantified the prevalence of PEDV contamination in swine transport vehicles, highlighting both the risk of exposure and the limitations of standard cleaning protocols. One of the most comprehensive early studies was conducted by Lowe, et al. (2014), who assessed PEDV contamination rates in livestock trailers before and after unloading at six U.S. slaughter facilities.[104] The study found that 6.6% of trailers were contaminated upon arrival and an additional 5.2% became contaminated after unloading, likely due to exposure to infected pigs or environmental contamination from lairages.These findings suggest that even if a trailer arrives at a facility clean, it can quickly become contaminated during unloading, reinforcing the need for thorough disinfection between transport cycles. A similar study conducted in Italy by Boniotti, et al. (2018) evaluated PEDV contamination in trucks arriving at slaughterhouses and farm loading docks.[105] The results showed that PEDV was still detectable in 46% of trucks post-cleaning, particularly in winter months when viral loads in feces were high ($Ct < 25$) and that disinfection procedures, though reducing contamination, did not entirely eliminate PEDV, raising concerns about incomplete viral inactivation under commercial cleaning conditions.

The ability of PEDV to persist on contaminated trailers and transport equipment is a key driver of between-farm transmission, necessitating strict decontamination protocols. Several studies have evaluated the use of heat treatments for disinfecting swine transport trailers, given that PEDV is highly susceptible to high temperatures. van Kessel, et al. (2020) conducted a controlled trial to determine the minimum heat exposure required to inactivate PEDV and other swine pathogens.[106] The study found that 75°C for 20 minutes was sufficient to inactivate PEDV in cell culture. However, the authors speculated that in real-world conditions with fecal contamination, dried feces had the potential to insulate the virus, preventing effective inactivation. In the study, within fist-sized pieces of dried fecal matter the internal temperatures never exceeded 65°C, allowing the virus to survive. These findings emphasize that heat treatment alone is not sufficient unless trailers are properly washed beforehand. Without effective removal of organic material, PEDV can and will survive despite high-temperature disinfection protocols.

While washing and disinfection are expected to be part of standard practices in commercial trailer sanitation, studies have questioned their effectiveness in eliminating PEDV. Krishna K. Thakur, et al. (2017) developed a Bayesian model to assess the probability of trailer contamination after different cleaning protocols.[107] The model predicted that washing alone would have a negligible impact on reducing contamination but that washing plus disinfection plus drying could result in a >99% reduction in contamination risk, reinforcing that drying is a critical step in inactivation. These findings suggest that trailers that are only washed,

but not disinfected and dried remain significant transmission risks. Proper biosecurity protocols should include all three steps (washing, disinfecting, and drying) to minimize PEDV persistence.

Given that manual trailer inspections are time-consuming and subjective, researchers have explored rapid cleanliness assessments using ATP bioluminescence. Letsch, et al. (2024) evaluated ATP bioluminescence as a tool for assessing trailer cleanliness post-wash.[108] The study found that ATP readings correlated well with residual organic contamination and that the method provided real-time feedback on sanitation effectiveness. However, they recommended that baseline cleanliness standards need to be established for practical implementation of ATP bioluminescence monitoring.

PEDV can spread not only through direct pig-to-pig contact, but also through contaminated transport networks, enabling long-distance transmission between regions. A network-based epidemiological model by VanderWaal, et al. (2018) examined the role of animal movement and transport-associated fomites in PEDV spread.[109] The study analyzed data from 400 farms and 10,709 pig shipments, revealing that while direct animal movement was the dominant transmission route, contaminated trailers and feed trucks played a significant role in long-distance jumps between regions. This reinforces the idea that biosecurity measures must extend beyond the farm to include transport sanitation, feed delivery trucks, and slaughterhouse vehicle management.

Contaminated transport vehicles are a well-established but persistent risk factor in PEDV transmission. Studies have confirmed that trailer contamination is common at slaughterhouses, and even properly cleaned trailers can still harbor PEDV. Heat treatment (75°C for 20 minutes) effectively inactivates PEDV, but only if trailers are properly washed first; washing alone is ineffective - disinfection and drying must be included in biosecurity protocols. ATP bioluminescence may serve as a real-time cleanliness assessment tool, though standardized protocols are needed; and that transport-associated fomites play a key role in long-distance PEDV transmission, reinforcing the need for strict biosecurity in animal movement and feed transport.

Vaccine development and use

The control of PEDV has been a persistent challenge in global pig production. Given the virus's high mutation rate and diverse strains, vaccine development has focused on several platforms, including recombinant subunit vaccines, plant-based antigen production, live-attenuated vaccines, virus-like particle (VLP) vaccines, and nanoparticle-based immunization strategies. Recent research has sought to enhance immunogenicity, optimize delivery methods, and improve passive immunity transfer to protect neonatal piglets. In theory, these approaches offer improved safety, stability, and targeted immune responses. Advances in molecular engineering have facilitated the development of vaccines capable of differentiating infected from vaccinated animals, an essential tool for disease eradication. Despite these innovations, challenges remain in achieving broad-spectrum protection against evolving PEDV strains, emphasizing the need for continued research and vaccine refinement. Early vaccine development efforts relied on vaccines developed against classical PEDV strains, particularly the GI-a subtype, such as the CV777 strain. These vaccines initially helped reduce disease prevalence, but their effectiveness diminished with the emergence of highly pathogenic GII variants in 2010. Current conventional vaccines, including inactivated and live-attenuated formulations, provide only partial protection due to the virus's genetic variability and rapid evolution. The emergence of COVID likely contributed to the large amount of recently published research on PEDV vaccines and its potential translational application to human disease. At least six comprehensive reviews of PEDV vaccines have been published since 2020.[9,110-114] As of January 30, 2025 in the U.S., there is one commercially available inactivated vaccine and one prescription vaccine based on an RNA particle platform (https://www.aphis.usda.gov/product-summaries-animal-species-swine, accessed February 28, 2025) against PED. The information presented below therefore only highlights some representative work on the spectrum of research being done in the area.

Recombinant subunit vaccines leverage genetically engineered viral proteins, particularly the spike (S) protein, which mediates viral entry and contains critical neutralizing epitopes. Several studies have explored the immunogenic potential of these vaccines using different antigen presentation systems. A recent study by Murtaza, et al. (2024) evaluated a novel chimeric recombinant vaccine, fusing a modified core neutralizing epitope (COE) of PEDV with the N-terminal fragment of flagellin (FliC99), a potent Toll-like receptor 5 (TLR-5) ligand.[115] This fusion aimed to enhance immune recognition and antigen presentation. Following computational modeling and molecular docking analyses, the vaccine was tested in a murine model. Results demonstrated strong immunogenicity, with robust TLR-5 affinity and significant antigen-specific immune responses comparable to those elicited by inactivated whole-virus vaccines. These findings suggest that integrating innate immune stimulators with subunit vaccines could improve protection against PEDV. Makadiya, et al. (2016) created recombinant S1 domain of the spike protein expressed in three eukaryotic systems (yeast, insect, and mammalian cells) in an effort to create high quality glycosylated antigen.[116] The vaccine was administered intramuscularly to pregnant sows, and the resulting colostrum and milk contained high titers of virus-neutralizing IgG and IgA antibodies, which were transferred passively to piglets. Although vaccinated sows' piglets exhibited higher survival rates and reduced clinical severity, viral shedding and diarrhea remained unaffected, indicating that while the subunit vaccine conferred partial protection, it did not completely prevent PEDV transmission.

Building on these advancements, Zhang, et al. (2024) developed a chimeric PEDV strain (YN-S2DR13) by replacing the S2 subunit of a genotype 2 (G2) strain with that of a genotype 1 (G1) strain.[117] This modification significantly enhanced viral

proliferation in vitro, and broadened cross-neutralization capacity against both G1 and G2 PEDV strains. When tested in pigs, the chimeric virus exhibited reduced pathogenicity while maintaining strong immunogenicity, suggesting a promising strategy for broad-spectrum PEDV vaccines.

As cost-effective alternatives to traditional vaccines, plant-based antigen production has been explored for PEDV immunization, leveraging transgenic plants as bioreactors for recombinant viral proteins.

A study by Ho, et al. (2022) investigated a plant-expressed COE epitope (COE/G2a-pII), targeting a highly virulent Vietnamese PEDV genotype 2a strain.[118] Pregnant sows were vaccinated with the plant-derived antigen, resulting in high titers of PEDV-specific IgG and IgA antibodies in milk and colostrum. After being challenged with virulent PEDV, piglets born to vaccinated sows exhibited complete survival, normal clinical health, and no fecal shedding.[118] Similarly, Maj, et al. (2021) explored a maize-based vaccine strategy, where pregnant sows were fed transgenic maize grains expressing PEDV S protein. This novel approach induced strong maternal antibody responses, with higher neutralizing antibody titers in colostrum correlating with increased piglet survival. Importantly, piglets from low-dose maize-fed sows exhibited the best outcomes, indicating that dose optimization may be critical for efficacy.[119] Kim, et al. (2005) successfully incorporated PEDV neutralizing epitopes into transgenic potato plants, while Kang, et al. (2004) employed a tobacco mosaic virus (TMV)-based vector to produce PEDV antigens in tobacco plants. These approaches demonstrated high antigen yield, although further studies are required to validate immunogenicity in pigs.[120,121] The field of plant-based antigen vaccines for PEDV using a variety of plant species remains active with many other avenues of research being explored.[122-128]

Live-attenuated vaccines (LAVs) remain one of the most promising strategies for inducing strong and durable immune responses against PEDV. However, the challenge lies in achieving effective attenuation without the risk of reversion to pathogenicity.

One of the primary methods for attenuation is serial passaging in non-natural host cells, which drives adaptive mutations that reduce viral pathogenicity. Building on this, Ge, et al. (2022) conducted a serial passage experiment on a G2c PEDV strain (SHXX1902) in Vero cells, demonstrating that the attenuated virus retained high immunogenicity.[129] Pigs immunized with SHXX1902 produced IgG responses comparable to those elicited by commercial vaccines, though their IgA titers were lower, underscoring the need for booster strategies to reinforce mucosal immunity. Similarly, Kim, et al. (2023) focused on Korean PEDV G2b strains, developing a live-attenuated PEDV candidate.[130] This strain significantly increased piglet survival rates and reduced diarrhea incidence, demonstrating protective efficacy. The study suggested that protease-mediated viral attenuation, which selectively weakens viral entry and replication mechanisms, could further enhance LAV safety and immunogenicity, providing a pathway for future refinement.

Beyond traditional serial passaging, researchers have explored genetic engineering approaches to fine-tune virulence attenuation. Zhang, et al. (2024) investigated a chimeric PEDV strain in which the S2 subunit of a G2 strain was replaced with that of a G1 strain.[131] This modification not only reduced virulence but also increased viral proliferation, leading to broader cross-neutralization against both G1 and G2 PEDV variants. The chimeric strain was found to be safe and highly immunogenic in piglets, highlighting the potential of targeted genetic modifications to develop broadly protective LAVs.

Overall, live-attenuated vaccines offer a highly effective means of PEDV control, particularly in fostering both humoral and mucosal immunity.

Virus-like particles (VLPs) are structurally similar to native viruses, eliciting strong immune responses without containing genetic material. Du, et al. (2023) designed a VLPs, incorporating PEDV and TGEV spike epitopes, which elicited potent neutralizing antibodies and robust cytokine responses in piglets, marking them as promising candidates for rapid vaccine deployment.[132] Others have published similar promising results though the work appears to yet be tested in a field setting.[133-136]

Nanoparticle-based vaccines have also emerged as next-generation strategies. Deng, et al. (2024) developed a mucoadhesive chitosan-catechol system, enabling intranasal delivery of inactivated PEDV.[137] This approach enhanced antigen retention in nasal mucosa, improved dendritic cell activation, and induced strong immune responses, positioning intranasal vaccines as viable alternatives for PEDV control. Novel application of nanoparticles technology in inducing protective immunity appears to be attracting attention with diverse use in both pigs and pregnant sows,[138,139] intraperitoneal dosing,[140] coupling with novel adjuvant systems (Poly (d,l-lactide-co-glycolide) nanoparticle),[141] and others.

The landscape of PEDV vaccine research has significantly evolved, with diverse immunization platforms demonstrating varying degrees of success. Recombinant subunit and plant-based vaccines offer scalable, cost-effective solutions, while VLPs and nanoparticle formulations provide highly immunogenic responses. Live-attenuated vaccines remain promising but require fine-tuning to balance attenuation and efficacy. Mucosal immunization approaches, including oral and nasal vaccines, have shown potential, particularly in maternal antibody transfer for piglet protection.

Role of wildlife

Porcine epidemic diarrhea virus is widely recognized as a swine-specific enteric coronavirus, primarily transmitted via the fecal-oral route among domestic pig populations. However, concerns about wildlife acting as reservoirs, spillover hosts, or mechanical vectors have persisted, particularly in regions where feral pig populations interact with domestic herds or where wild mammals share agricultural landscapes. Despite early speculation that wild boars, rodents, birds, and other wildlife species could harbor PEDV and contribute to its spread, extensive surveillance has largely indicated that wildlife plays a minor role in PEDV epidemiology. While some studies have detected low levels of PEDV antibodies in wild pigs or environmental carriers such as houseflies, the majority of investigations have failed to find active viral shedding or significant transmission risks from wildlife species.

Feral pigs and wild boars have been extensively tested for PEDV, given their close genetic relationship to domestic pigs and their frequent interaction with livestock production systems in certain regions. Multiple studies have tested wild boar populations across different continents for evidence of PEDV infection or antibody presence. Ferrara, et al. (2022) conducted a retrospective serosurvey in the Campania region of Italy, testing 444 wild boar serum samples for PEDV antibodies.[142] The study found a seropositivity rate of 3.83%, suggesting low-level exposure but no significant role as a reservoir. Similarly, Antas, et al. (2021) investigated 157 wild boars in Poland and found only 3.2% of animals seropositive for PEDV antibodies, while RT-PCR testing on fecal samples found no active infections.[143] These results reinforce the conclusion that wild boars may occasionally encounter PEDV but do not appear to sustain the virus or contribute to ongoing outbreaks.

In contrast, Lee, et al. (2016) reported a higher PEDV seropositivity rate of 9.75% (28/287) in wild boars in South Korea, raising concerns that localized wildlife populations could serve as intermittent spillover hosts.[144] However, the study did not confirm active infection or shedding, leaving the epidemiological relevance unclear.

Several studies have specifically examined feral pig populations in North America, given their rapid expansion and increasing overlap with domestic pig farms. Tirado, et al. (2023) tested 38 feral pigs in Mexico (Chihuahua and Durango) for PEDV via rectal swabs, reporting 100% negative results, suggesting little to no circulation in wild swine.[145] Ghimire (2017) conducted a molecular screening of 44 feral pigs in California and found no evidence of PEDV RNA, reinforcing that feral swine in the U.S. do not appear to be involved in PEDV transmission as yet.[146] Bevins, et al. (2018) tested 7,997 serum samples from wild pigs across multiple U.S. states, detecting low-level PEDV seropositivity in just 0.1% of cases (8 confirmed positives).[147] These findings suggest that exposure events occur but do not lead to widespread transmission within feral pig populations. Taken together, these results indicate that while wild boars and feral pigs can occasionally be exposed to PEDV, they do not serve as major reservoirs or amplify the virus in natural settings.

Beyond wild swine, researchers have explored whether other wildlife species, such as rodents, birds, and insects, may contribute to PEDV transmission. Rodents and stray animals frequently live in and around pig farms, raising concerns that they could mechanically transport PEDV or serve as subclinical hosts. Truong, et al. (2013) screened 102 rodents and 24 stray cats captured around pig farms in South Korea. While the study found several swine bacterial pathogens in these animals, only 4.2% of stray cats tested PCR-positive for PEDV.[148] However, the study did not assess whether the detected PEDV was viable or capable of transmission. Makovska, et al. (2023) conducted a systematic review of wildlife-associated pathogen risks and concluded that rodents, while potential carriers of bacterial pathogens, do not appear to play a significant role in PEDV transmission.[149]

Concerns about waterfowl spreading PEDV via contaminated water sources led to targeted surveillance in North America. Nelson, et al. (2019) tested 538 cloacal swabs from ducks in the Mississippi Flyway and found zero positive cases for PEDV or porcine deltacoronavirus (PDCoV).[150] This suggests that waterfowl are unlikely to be involved in PEDV epidemiology.

While wildlife reservoirs appear to play a minor role, mechanical transmission via insects has been documented. Masiuk, et al. (2018) conducted an experimental study in Ukraine, exposing newborn piglets to PEDV-contaminated houseflies (*Musca domestica vicina*).[151] The study confirmed that flies carrying PEDV on their bodies could contaminate the environment and potentially initiate infections in susceptible piglets. However, the virus did not replicate within the flies, confirming a mechanical (not biological) role in transmission.

While domestic pigs remain the primary host for PEDV, researchers have detected related coronaviruses in non-swine wildlife species. Sanchez-Chicana, et al. (2024) analyzed samples from 90 wild mammals rescued by the National Forest and Wildlife Service of Peru, detecting sequences closely related to PEDV in multiple species.[152] This raises concerns that wild mammals may harbor coronaviruses capable of recombining with swine enteric viruses, but their role in PEDV transmission remains speculative.

Despite early concerns, wildlife does not appear to be a significant reservoir or driver of PEDV transmission. Studies confirm that wild boars and feral pigs show occasional seropositivity but do not sustain active infections; rodents, stray cats, and waterfowl do

not appear to contribute meaningfully to PEDV epidemiology; houseflies can mechanically transport PEDV but do not serve as biological hosts; and related coronaviruses have been detected in wild mammals, but their role in PEDV evolution remains unclear.

Discussion:

The feasibility of a regional or national eradication program for PEDV depends on the interaction between transmission dynamics, intervention strategies, and the practical constraints of implementation at an industry-wide level. The findings of this systematic review highlight critical transmission risks, the effectiveness (or ineffectiveness) of control measures, and existing gaps in knowledge, all of which must be considered in evaluating eradication potential.

The complexity of transmission and control measures

One of the major challenges to PEDV eradication is the combination of multiple transmission pathways that contribute to viral persistence. Unlike eradication efforts for viruses such as pseudorabies which relied on coordinated surveillance, regulatory oversight, controlling movement of animals, and highly effective DIVA (differentiation-of-infected-from-vaccinated-animals) vaccines, a PED eradication effort in the U.S. is currently not supported by any of these tools. The issues created by the lack of regulatory oversight are important in any debate around national eradication of PEDV[153] and it is well worthwhile reviewing the extensive experiences learned from the Aujeszky's eradication program before another such program is considered.[154] Porcine epidemic diarrhea virus's ability to persist in environmental reservoirs, contaminated transport networks, and asymptomatic shedding animals, furthers the complexity of a national elimination program.

Although feed contamination was initially seen as a major barrier, research has provided clear and effective mitigation strategies to reduce this risk. Studies have demonstrated that feed additives such as medium-chain fatty acids (MCFAs), formaldehyde-based treatments, and monoglycerides significantly reduce PEDV viability, while improvements in quality assurance within feed mills and supply chains further mitigate introduction risks. While feed remains a potential source of reintroduction, the industry has developed effective tools to manage this risk, making it a controllable factor rather than a fundamental obstacle to eradication.

In contrast, transport networks remain a major, ongoing challenge. Studies indicate that even after standard cleaning and disinfection protocols, a significant proportion of trailers remain contaminated, particularly in cold weather. Thermal inactivation (≥71°C for 10 minutes) is effective, but in practice, organic material (e.g., dried feces) insulates the virus, reducing the efficacy of heat treatment. Without standardized trailer sanitation protocols across the industry, transport-related viral spread will remain a major limitation to PEDV eradication efforts.

Vaccination and virus shedding: Key factors influencing eradication

While vaccines are a critical component of disease management strategies, their role in PEDV eradication is inherently limited by the apparent inability of coronavirus vaccines to induce sterilizing immunity. Studies on PEDV, TGEV, and even SARS-CoV-2 confirm that while vaccines can reduce the severity of clinical disease, lower viral shedding, and require a higher exposure dose for infection, they do not fully prevent infection or transmission. As a result, even well-vaccinated herds remain potential reservoirs of virus, complicating eradication efforts.

Additionally, cross-protection between PEDV strains remains inconsistent, similar to challenges seen with human coronaviruses. Variability in vaccine efficacy across different PEDV genotypes suggests that new variant emergence could undermine long-term control, requiring continuous vaccine updates and reformulation efforts. This is particularly relevant given the demonstrated antigenic drift in PEDV spike proteins, mirroring the challenges faced in human coronavirus vaccine development.

Despite extensive research into novel antiviral and vaccine candidates, the translation of laboratory-based efficacy into commercially available products has been largely unsuccessful. While many studies report highly effective experimental vaccines and antiviral compounds, only two commercial vaccines exist in the U.S. and their efficacy is a matter of some debate.[9,155-157] This gap between academic research and commercial implementation suggests that regulatory, economic, or industry adoption barriers continue to hinder new product development. While existing vaccines likely have a role as part of a national control strategy, their role in an eradication program is not imperative.

Environmental persistence and long-distance transmission

PEDV's ability to persist in manure, fomites, and contaminated transport vehicles makes environmental decontamination a persistent challenge. Unlike viruses with limited survival outside the host, PEDV has been found to remain viable in manure pits for months and to persist on metal and plastic surfaces in cold temperatures. Further, the propensity of the virus to be shed from infected pigs well after the point of clinical recovery (at least in post-weaning age pigs) contributes the problem of fomite transmission.

Transport-related spread is one of the most critical challenges for PEDV control. Even with extensive cleaning protocols, livestock trailers, slaughterhouse holding pens, and feed trucks remain high-risk fomites. Studies confirm that even after thorough washing, disinfection, and drying, some surfaces still test positive for PEDV RNA, indicating incomplete decontamination. These findings suggest that current industry biosecurity practices may not be stringent enough to support complete eradication. Lessons from pseudorabies virus eradication indicate that strict biosecurity, combined with movement restrictions, was key to success, but PEDV's resilience in transport networks makes similar control measures more difficult to enforce.

Epidemiological modeling: Managing, not eliminating PEDV

Epidemiological models provide valuable insights into transmission patterns and control strategies, helping to evaluate whether PEDV eradication is feasible. Machine learning models indicate that farms receiving feed from common suppliers have a significantly higher risk of PEDV introduction, while regional disease clustering suggests that transport-associated spread is a dominant risk factor. Models also confirm seasonal peaks in PEDV outbreaks, with colder months posing the highest risk due to extended viral persistence. There is at least some evidence that airborne spread of up to at least a few kilometers may occur and thus can't be ignored, though its contribution to perpetuation of an outbreak in the face of a control or eradication program is unknown.

These findings suggest that while PEDV eradication may be achievable in localized regions with strong biosecurity and closed herd systems, the potential for reintroduction from external sources - whether through transport, contaminated facilities, or new variant emergence - poses a persistent risk at the national level. Unlike pseudorabies eradication, which was achieved through coordinated, surveillance, depopulation, and vaccination, PEDV's ability to persist in the environment and spread via multiple vectors makes elimination far more challenging. A more realistic goal may be regional suppression rather than complete eradication.

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