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Porcine circovirus type 2 (PCV-2) and its economic implications: A brief review

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Abstract
Porcine Circovirus Type 2 (PCV-2) is a viral pathogen that affects pigs worldwide, leading to significant economic losses in the swine industry. PCV-2 is associated with various clinical manifestations, including post-weaning multisystemic wasting syndrome (PMWS), porcine dermatitis and nephropathy syndrome (PDNS), respiratory disease, and reproductive disorders. These conditions can result in decreased growth rates, increased mortality rates, impaired reproductive performance, and reduced meat quality. Consequently, PCV-2 infections have a direct negative impact on pig health and welfare. The economic implications of PCV-2 are substantial. The disease imposes significant costs on pig producers, including expenses associated with increased mortality, reduced growth rates, vaccination programs, diagnostic tests, and treatment regimens. Additionally, PCV-2-related conditions can result in decreased market value of affected animals and trade restrictions imposed by importing countries, further impacting the profitability of the swine industry. Various control measures have been implemented to mitigate PCV-2 infections, including vaccination programs, improved biosecurity measures, and management practices aimed at minimizing the transmission of the virus. Although these interventions have shown some success in reducing the prevalence and severity of PCV-2-associated diseases, challenges remain in their widespread adoption and effectiveness. Understanding the economic implications of PCV-2 is essential for policymakers, veterinarians, and swine producers to make informed decisions regarding disease prevention, control strategies, and resource allocation. This review article highlights the economic burden of PCV-2 and the importance of continued research and investment in disease management strategies.

Keywords: Porcine circovirus type 2, PCV-2, economic implications, swine industry, disease control, vaccination, biosecurity measures

1. Introduction
PCV-2 belongs to the Circoviridae family, which is a small, non-enveloped DNA virus. PCV-2 is characterized by circular, single-stranded DNA genome that is approximately 1.7 kilobases in length (Gillespie J *et al* 2009) [5]. The genome encodes a limited number of proteins, including the replicase protein (Rep) and the capsid protein (Cap). There are also several accessory proteins encoded by the viral genome. PCV-2 virions are non-enveloped, icosahedral particles with a diameter of around 17-20 nanometers (Bian H *et al* 2021) [4]. The capsid protein forms the outer shell of the virion and encapsulates the viral genome. PCV-2 exhibits genetic diversity, and different genotypes and subtypes have been identified. (Franzo G, Segalés J. 2020) [10]. The genetic diversity of PCV-2 is associated with variations in pathogenicity and geographic distribution. PCV-2 is highly prevalent in pig populations worldwide. Nearly all pig herds are exposed to the virus, and it can be found in various tissues and body fluids of infected animals. The primary mode of PCV-2 transmission is through direct contact between infected and susceptible pigs. Indirect transmission through contaminated fomites and vertical transmission from sows to piglets also contribute to the spread of the virus (López-Lorenzo G *et al* 2019) [14].
PCV-2 infection leads to a range of clinical conditions collectively known as Porcine Circovirus-Associated Diseases (PCVAD) (Gillespie J *et al* 2009) [5]. These diseases have substantial economic implications, affecting pig health, productivity, and overall profitability for swine producers. PCV-2 was first identified in the late 1990s as the causative agent of post-weaning multisystemic wasting syndrome (PMWS), a condition characterized by weight loss, respiratory distress, and lymphoid tissue lesions (Jiang H, *et al* 2019) [12]. Since its discovery, PCV-2 has been associated with various other clinical manifestations, including respiratory

diseases, enteritis, reproductive disorders, and porcine dermatitis and nephropathy syndrome (PDNS) (Palinski R *et al* 2016) [2]. The prevalence and impact of PCV-2 have led to extensive research efforts to understand its pathogenesis, clinical manifestations, and the economic consequences associated with the disease. The virus primarily targets lymphoid tissues, leading to immunosuppression and increased susceptibility to secondary infections. The mechanisms of PCV-2 pathogenesis involve viral replication, modulation of the host immune response, and induction of apoptosis. The economic implications of PCV-2 are multifaceted and affect various aspects of the swine industry. Increased mortality rates among infected pigs directly contribute to economic losses for producers. Additionally, PCV-2-infected pigs may experience growth retardation and reduced feed efficiency, resulting in decreased productivity and profitability. Reproductive disorders caused by PCV-2, such as infertility, abortion, and stillbirths, further impact the economic viability of breeding programs and the replacement of breeding stock. Moreover, the costs associated with diagnosing, treating, and preventing PCV-2 infections add to the economic burden on swine producers. Efforts to control the spread of PCV-2 require investments in biosecurity measures, hygiene practices, and vaccination programs. Trade restrictions imposed by some countries on PCV-2-infected regions further limit market access and decrease export opportunities for affected countries. Given the economic significance of PCV-2, effective management and control strategies are essential for mitigating the disease's impact on the swine industry. Vaccination has shown promise in reducing the clinical signs and economic consequences of PCVAD. Additionally, strict biosecurity measures, proper hygiene practices, and early detection of infections play crucial roles in preventing the spread of PCV-2 within swine populations (Guo J *et al* 2022) [6].

2. Clinical Manifestations of PCV-2

2.1 Porcine Circovirus-Associated Disease (PCVAD): PCVAD is a complex syndrome characterized by a range of clinical manifestations. It encompasses multiple conditions such as porcine dermatitis and nephropathy syndrome (PDNS), porcine respiratory disease complex (PRDC), reproductive disorders, and systemic disease. PCVAD can occur in both subclinical and clinical forms (Opriessnig, T *et al* 2007) [19].

2.2 Postweaning Multisystemic Wasting Syndrome (PMWS): PMWS is one of the most significant diseases associated with PCV-2. It primarily affects piglets after weaning, typically between 5 and 12 weeks of age. PMWS is characterized by progressive weight loss, failure to thrive, enlarged lymph nodes, respiratory distress, and increased mortality rates. The disease affects the immune system, leading to immunosuppression and increased susceptibility to secondary infections (Tucker, A. W., & Donadeu, M. 2006) [28].

2.3 Porcine Respiratory Disease Complex (PRDC): PRDC refers to a multifactorial respiratory disease in pigs, involving various viral and bacterial pathogens, with PCV-2 being one of the contributing factors. PCV-2 can exacerbate the severity of respiratory infections and complicate the clinical picture of PRDC. Affected pigs may exhibit coughing, dyspnea, nasal discharge, reduced growth rates, and increased mortality (Assavacheep P, Thanawongnuwech R. 2022) [3].

2.4 Porcine Dermatitis and Nephropathy Syndrome (PDNS): PDNS is a condition associated with PCV-2 infection, characterized by skin lesions and kidney abnormalities. Pigs with PDNS often develop red, raised, and blotchy skin lesions, mainly on the hind limbs, abdomen, and ears. Additionally, they may show signs of renal dysfunction, such as increased water consumption, weight loss, and reduced urine production (Helke, K. L *et al* 2015) [7].

2.5 Reproductive Disorders: PCV-2 has been linked to reproductive disorders in pigs, including infertility, abortion, mummification, stillbirths, and weak-born piglets. Infections during gestation can lead to embryonic death or fetal development abnormalities, resulting in reproductive failures (Saikumar G, Das T. *et al* 2019) [25].

2.6 Lymphoid System Disorders: PCV-2 primarily targets lymphoid tissues, leading to lymphoid system disorders. These may include lymphadenopathy (enlarged lymph nodes), lymphoid depletion, and lymphoid organ atrophy (Toyama K, *et al* 2022) [27].

2.7 Skin Lesions: Pigs infected with PCV-2 may develop skin lesions such as dermatitis, erythema (redness), or crusty lesions. These skin lesions are often associated with secondary infections (Robbins RC *et al* 2014) [24].

2.8 Jaundice: In some cases, PCV-2 infection can cause liver damage, resulting in jaundice, which is characterized by a yellowing of the skin, mucous membranes, and sclera (the whites of the eyes).

It is important to note that the severity and clinical presentation of PCV-2-associated diseases can vary depending on various factors, including the strain of PCV-2, coinfections with other pathogens, management practices, and host susceptibility.

Fig 1: PWMS affected pig (Duran, C. O., & Render, J. A. 1997) [8]

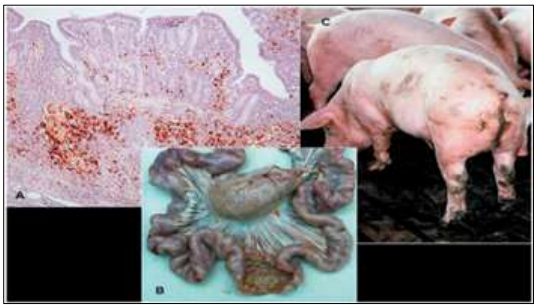

Fig 2: PCV2-associated enteritis. A, PCV2 antigen (brown staining) within lymphocytes and macrophage-like cells in the lamina propria and Peyers patches of the ileum. Immunohistochemistry. Streptavidin-biotin peroxidase complex method, hematoxylin counterstain. B, Thickened intestinal mucosa and a markedly enlarged mesenteric lymph node. C, Grow-finish pig with mild diarrhea (Opriessnig T *et al* 2007) [19].

Fig 3: Litter from a sow experimentally infected with PCV2 at the time of insemination. Note the small litter size and the presence of two mummified fetuses

3. Pathogenesis

It involves several key steps

3.1 Entry and Replication: PCV-2 primarily infects and replicates in cells of the monocyte/macrophage lineage. The virus enters the host's body through the respiratory tract, gastrointestinal tract, or breaks in the skin. It then targets cells of the lymphoid tissues, such as tonsils and lymph nodes, where it replicates.

3.2 Immune Response: PCV-2 infection triggers both innate and adaptive immune responses in the host. However, the virus has developed various mechanisms to evade the immune system, allowing it to establish persistent infections. PCV-2 can modulate immune responses by suppressing immune cell function and interfering with cytokine signaling.

3.3 Viral Spread: PCV-2 can spread systemically through the bloodstream and infect various organs, including the liver, spleen, lungs, and kidneys. The virus can also disseminate to secondary lymphoid tissues, leading to lymphoid depletion and immunosuppression.

3.4 Induction of Pathogenic Processes: PCV-2 infection can lead to the development of PCVAD. The mechanisms underlying PCVAD are not fully understood, but it is believed to be multifactorial. PCV-2 induces direct cytopathic effects on infected cells, leading to cell death and tissue damage. It can also disrupt the normal functioning of the immune system, impairing the host's ability to mount an effective immune response against other pathogens. Additionally, PCV-2 infection can trigger an exaggerated and dysregulated immune response, leading to inflammation and tissue damage. It is important to note that the severity of PCV-2-associated disease can vary widely. While some infected pigs may remain asymptomatic or only develop mild clinical signs, others may experience severe illness, including wasting, respiratory distress, diarrhea, and increased mortality (Gillespie J, *et al* 2009) [5].

4. Diagnosis of PCV-2

The diagnosis of PCV-2 infection involves a combination of clinical evaluation, laboratory testing, and histopathological examination. Here are some common methods used for the diagnosis of PCV-2:

4.1 Clinical Signs and History: PCVAD is characterized by a range of clinical signs, including weight loss, respiratory distress, diarrhea, jaundice, and reproductive problems in sows. A thorough examination of clinical signs and history can provide initial indications of PCV-2 infection.

4.2 Polymerase Chain Reaction (PCR): PCR is a molecular technique used to detect and amplify specific DNA sequences. In the case of PCV-2, PCR can detect and amplify the viral DNA present in clinical samples. Various samples, such as blood, serum, lymph nodes, or tissue samples, can be used for PCR testing. PCR can provide rapid and sensitive detection of PCV-2.

4.3 Immunohistochemistry (IHC): IHC involves the detection of viral antigens in tissue samples using specific antibodies. It can be useful in confirming PCV-2 infection and identifying the distribution of the virus in affected tissues. IHC can be performed on formalin-fixed tissues, such as lymph nodes or other organs.

4.4 Serological Testing: Serological tests detect antibodies produced by the pig's immune system in response to PCV-2 infection. Enzyme-linked immunosorbent assay (ELISA) is commonly used to detect PCV-2-specific antibodies in blood or serum samples. Rising antibody titers or the presence of specific antibodies can indicate PCV-2 infection.

4.5 Viral Isolation: Viral isolation involves the growth and identification of the virus in cell cultures. However, PCV-2 is difficult to grow in cell culture alone, and it requires co-infection with certain helper viruses. Therefore, viral isolation is not commonly used for routine PCV-2 diagnosis.

4.6 Necropsy and Histopathology: Necropsy examination of affected pigs and histopathological analysis of tissues can provide valuable information on PCV-2-associated lesions, such as lymphoid depletion, granulomatous inflammation, and inclusion bodies. While these findings are not specific to PCV-2, they can support the diagnosis when combined with other diagnostic methods (Segalés, J. 2012) [26].

5. Economic Implications

It has significant economic implications for the swine industry. Here are some key economic implications of PCV-2:

5.1 Mortality and reduced growth: PCV-2 can lead to increased mortality rates among piglets, especially in cases where co-infections occur. Infected pigs may also experience reduced growth rates, leading to lower weights at market age. These factors can result in financial losses for pig farmers due to the reduced number of marketable pigs and decreased overall productivity.

5.2 Increased production costs: To prevent and manage PCV-2, farmers often incur additional costs. These include investing in vaccines, diagnostic tests, biosecurity measures, and veterinary care. These increased production costs can have a negative impact on the profitability of pig farming operations.

5.3 Decreased reproductive performance: PCV-2 can also impact the reproductive performance of sows and boars, leading to reduced fertility, increased abortions, and smaller litter sizes. This can result in reduced piglet production and lower revenues for farmers who rely on breeding and selling piglets.

5.4 Market volatility and price fluctuations: PCV-2 outbreaks can cause market volatility and price fluctuations in the swine industry. When significant numbers of pigs are affected by the disease, the supply of pork can decrease, leading to potential price increases for consumers. Conversely, if farmers decide to reduce their pig populations in response to PCV-2 outbreaks, there may be a temporary oversupply of pork, causing prices to decline.

5.5 Trade restrictions: PCV-2 can also have implications for international trade in pork products. Some countries impose trade restrictions on pork imports from regions affected by PCV-2 or require additional testing and certifications to ensure disease-free status. These trade restrictions can limit market access for pig farmers and potentially impact export revenues.

Overall, PCV-2 can have significant economic implications for the swine industry, including reduced productivity, increased production costs, market volatility, and trade restrictions. Efforts to prevent, control, and manage PCV-2 through vaccination, biosecurity measures, and good husbandry practices are crucial to mitigate its economic impact on pig farming operations (Afolabi, K. O. *et al* 2017) [1].

6. Treatment, Management and Control

The treatment of PCV-2 and PCVAD involves various management strategies and supportive care, as there is currently no specific antiviral treatment available. Here are some approaches used in the treatment and control of PCV-2:

6.1 Vaccination: Vaccines against PCV-2 are available and are an essential part of PCVAD prevention and control. Vaccination can help reduce the severity of the disease and decrease viral shedding. These vaccines typically contain inactivated or subunit PCV-2 antigens and are administered to pigs to stimulate an immune response.

Some commonly used PCV-2 vaccines included

1. **Ingelvac CircoFLEX® (Boehringer Ingelheim):** This vaccine contains inactivated PCV-2 antigens and has been widely used to prevent PCVAD in pigs. It can be administered to piglets as early as 3 weeks of age (O'Neill KC *et al* 2011) [17].
2. **Porcilis® PCV (MSD Animal Health):** This vaccine is a subunit vaccine that contains PCV-2 antigens. It can be used in piglets from 3 weeks of age and provides protection against PCVAD (Park C, *et al* 2014) [21].
3. **Suvaxyn® Circo+MH RTU (Zoetis):** This vaccine is a combination vaccine that provides protection against both PCV-2 and Mycoplasma hyopneumoniae (MH). It contains inactivated PCV-2 antigens and can be used in pigs from 3 weeks of age (Mancera Gracia, J. C. *et al* 2021) [16].
4. **Circumvent® PCV (Merck Animal Health):** This vaccine is a subunit vaccine that contains PCV-2 antigens. It can be administered to pigs from 3 weeks of age and helps in the prevention of PCVAD (Karuppannan AK, Opriessnig T. 2017) [13].
5. **Circovac®:** Ceva's vaccine, Circovac®, targets porcine circovirus type 2 and is authorized for administration in piglets and sows. It is an inactivated vaccine effectively stimulating immunity against both ORF-1 and ORF-2. It has been proven to provide protection against PCV2a, PCV2b, and PCV2d strains of the virus (Opriessnig, T *et al* 2021) [18].

6.2 Biosecurity measures: Implementing strict biosecurity measures is crucial in preventing the introduction and spread of PCV-2 within a pig herd. This includes controlling and monitoring pig movement, limiting contact between pigs from different sources, and disinfecting equipment and facilities (López-Lorenzo G, *et al* 2019) [14].

6.3 Segregation and isolation: Implement strict segregation and isolation protocols to prevent contact between infected and susceptible pigs. Keep newly purchased pigs separate from the main herd for a quarantine period to observe any signs of disease.

6.4 Facility design and management: Design pig facilities to minimize the risk of disease transmission. Implement separate zones for different age groups or production stages. Ensure proper ventilation, drainage, and waste management systems to reduce pathogen load.

6.5 Animal sourcing: Source pigs from reputable and disease-free suppliers. Ensure that the pigs are free from PCV-2 and other relevant diseases through proper testing and certification procedures.

6.6 Personnel hygiene: Establish strict hygiene practices for personnel working with pigs. Provide hand washing facilities, proper protective clothing (e.g., boots, coveralls), and ensure regular training on biosecurity protocols.

6.7 Traffic control: Restrict the movement of people, vehicles, and equipment to minimize the risk of introducing or spreading PCV-2. Implement controlled entry points, disinfection stations, and vehicle washing procedures.

6.8 Cleaning and disinfection: Establish rigorous cleaning and disinfection protocols for pig premises, equipment, and vehicles. Use effective disinfectants known to be effective against PCV-2, following manufacturer instructions.

6.9 Pest and vector control: Implement measures to control pests and vectors that can transmit PCV-2. This may include proper waste management, rodent control, and measures to prevent the entry of birds or other wildlife into pig facilities.

6.10 Health monitoring and surveillance: Implement regular monitoring and surveillance programs to detect PCV-2 or PCVAD cases early. This allows for prompt intervention and appropriate management strategies (Patterson, A. R., *et al* 2011) [22].

6.11 Education and training: Provide ongoing education and training to all personnel involved in pig production about PCV-2, its transmission, and the importance of biosecurity measures. This helps ensure everyone understands their role in preventing and controlling the disease (Alarcón, L.V. *et al* 2021) [2].

6.12 Good management practices: Maintaining optimal herd management practices can help reduce stress and enhance the

pig's immune response, which is crucial in minimizing the impact of PCV-2. This includes providing a clean and comfortable environment, appropriate nutrition, and timely health monitoring.

6.13 Supportive care: There is no specific treatment for PCV-2 infection, but supportive care is important to manage the clinical signs and reduce secondary complications. This may involve providing fluids and electrolytes to maintain hydration, administering medications to control secondary bacterial infections, and ensuring proper nutrition.

6.14 Herd monitoring and surveillance: Regular monitoring and surveillance of the pig herd for PCV-2 infection can help detect the virus early and implement appropriate control measures. This may involve routine diagnostic testing and analysis of clinical signs and production data (Patterson, A. R. *et al* 2011) [22].

6.15 Sanitation and hygiene: Maintaining a clean and hygienic environment is essential to control PCV-2. Regular cleaning and disinfection of pig housing, equipment, and transportation vehicles can help reduce the virus's survival and transmission.

6.16 Breeding and selection: Selecting breeding stock that is free from PCV-2 or has a low viral load can help reduce the risk of transmission to offspring. Regular testing and culling of infected animals from the breeding herd can aid in PCV-2 control (Eddicks, M. *et al* 2022) [9].

7. Impact on Reproduction

It is known to cause a disease called Porcine Circovirus-Associated Disease (PCVAD) or Porcine Circovirus Disease (PCVD). PCV-2 primarily affects the immune system and can have various impacts on reproduction in pigs. PCV-2 infection can lead to reproductive disorders in sows and boars, which can result in reduced fertility and increased mortality of piglets. PCV-2 infection in sows can lead to smaller litter sizes, which means fewer piglets are born in each litter. This can have economic implications for pig farmers as they rely on larger litters for profitability. PCV-2 can cause increased rates of stillbirths and mortality in piglets before they reach the weaning age. Infected piglets may be born weak or with congenital defects, making them more susceptible to early death. PCV-2 infection in gilts (young female pigs that haven't given birth) can delay the onset of puberty. This delay can affect the reproductive efficiency of the herd by prolonging the time it takes for gilts to become sexually mature and produce their first litter. PCV-2 can also impact boars' reproductive performance by reducing semen quality. Infected boars may produce lower-quality semen, resulting in reduced fertility rates and lower conception rates in sows (Madson, D., & Opriessnig, T. 2011) [15].

8. Conclusion

In conclusion, PCV-2 infections have significant economic implications for the swine industry. The virus causes decreased growth rates, increased mortality, and reduced reproductive performance in pigs, resulting in substantial economic losses for producers. The additional costs associated with veterinary interventions and treatments further contribute to the financial burden. Additionally, trade restrictions imposed to control the spread of PCV-2 can disrupt international trade and have long-term economic consequences. Understanding the economic impact of PCV-2 is crucial for developing effective prevention and control strategies to mitigate the losses and maintain the sustainability of the swine industry.

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