Evaluation of the Effectiveness of Comprehensive Prevention and Control Measures for Respiratory Diseases in Pig Farming

Wenyan Hu*

Heilongjiang Polytechnic, Harbin, 150100, China
**Corresponding author: hmyhwy@163.com*

Abstract: *Porcine respiratory disease complex is driven by the synergistic effects of multiple pathogen co-infections and environmental factors. This study elucidates the immune evasion mechanism resulting from the co-infection of porcine reproductive and respiratory syndrome virus and porcine circovirus type 2. It also clarifies the degradation pathway of the mucosal barrier caused by ammonia, temperature and humidity, and high stocking density, as well as the aerodynamically mediated transmission threshold. This study establishes a multi-target intervention system encompassing air purification, immunization program restructuring, and feed additives. By employing interrupted time series analysis, nonlinear decay curve fitting, and a marginal benefit net present value framework, this study conducts a multivariate quantitative evaluation of morbidity, pathogen elimination efficiency, and growth and treatment costs, thereby providing technical parameters for assessing the effectiveness of the prevention and control measures.*

Key words: *porcine respiratory disease; multi-pathogen co-infection; aerodynamic transmission; immunization program restructuring; elimination efficiency; marginal benefit*

Introduction

Porcine respiratory disease complex (PRDC) in pig farming is a major disease type that leads to decreased production performance, increased treatment costs, and economic losses. Etiological investigation shows that the co-infection rate of porcine reproductive and respiratory syndrome virus (PRRSV), porcine circovirus type 2 (PCV2), and various opportunistic pathogens exceeds 60% in affected populations, while environmental physical factors (ammonia, temperature and humidity, dust) and high-density housing conditions further exacerbate the airborne transmission efficiency of pathogens and mucosal barrier damage. Although various vaccines, additives, and environmental control measures have been applied in production, there is a lack of target synergy and quantitative comparison of effects among these measures, which leads to considerable blindness in the selection of prevention and control plans. Therefore, systematically analyzing the pathogenic ecological characteristics and the action pathways of the inducing factors, establishing a multi-target intervention system that encompasses source control, immunomodulation, and local defense, and constructing a multivariate quantitative evaluation model are of essential research value for improving the targeting and economic feasibility of comprehensive PRDC prevention and control. This study starts from the synergistic pathogenic mechanism of pathogens, environmental degradation pathways, and density transmission thresholds, integrates the three technical mainlines of air purification, immunization program optimization, and feed additives, and finally achieves a full-dimensional quantification of effects through time series analysis, decay curve fitting, and marginal benefit fitting.

1. Analysis of the Pathogenic Ecology and Inducing Factors of Porcine Respiratory Diseases

1.1 Synergistic Pathogenic Mechanism of Co-Infection by Major Pathogenic Bacteria and Viruses

The pathogenic spectrum of porcine respiratory disease complex (PRDC) exhibits a complex pattern of multi-pathogen co-infection. The co-infection of porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2) can significantly reduce the phagocytic and clearance capacity of alveolar macrophages by inhibiting the interferon signaling pathway. This immune evasion creates a microecological niche for the secondary invasion of opportunistic pathogens

such as Streptococcus suis and Haemophilus parasuis, thereby forming a pathogenic chain with synergistic amplification between viruses and bacteria. Infection dynamics studies have confirmed that the prior viral infection upregulates the expression of adhesion molecules on respiratory epithelial cells, which enhances bacterial colonization efficiency by more than one order of magnitude. The latest single-cell sequencing results show that the alveolar macrophage subsets undergo functional reprogramming under co-infection conditions. Among these subsets, the phagocytic index of the CD163-highly-expressing subset decreases by more than 70%, and this subset simultaneously serves as the primary replication site for PRRSV[1].

At the molecular level, the synergistic action of pathogens is manifested as horizontal transfer of virulence genes and dysregulation of the host inflammatory response. The non-structural protein Nsp2 of PRRSV induces the host to produce excessive IL-10, thereby inhibiting the Th1-type immune response and leading to delayed bacterial clearance. Meanwhile, bacterial lipopolysaccharide and viral double-stranded RNA cross-activate NF-κB through the TLR4 and TLR3 pathways, triggering an uncontrolled cytokine storm. This cascade reaction not only exacerbates inflammatory infiltration in lung tissue but also causes irreversible damage to the alveolar epithelial-capillary barrier, which becomes a key target for subsequent prevention and control interventions. Cross-species comparative transcriptomics reveals that the expression levels of matrix metalloproteinases (MMP-9 and MMP-12) in the lung tissue of co-infected pigs are increased by more than fivefold compared to single infection, directly degrading collagen IV and elastin and accelerating the formation of emphysema-like lesions.

1.2 Degradation Pathway of the Respiratory Mucosal Barrier by Environmental Physical Factors

Elevated ammonia concentration inside the barn directly disrupts the ciliary beat frequency of the nasal and tracheal mucosa. Ammonia dissolves in the mucus layer to form a weakly alkaline environment, which alters the glycosylation structure of mucin and reduces its efficiency in capturing aerosol particles. Under continuous exposure to an ammonia environment exceeding 25 ppm, the expression levels of tight junction proteins (claudin-1 and occludin) between mucosal epithelial cells are downregulated, and the paracellular permeability increases, thereby allowing pathogens to bypass the mucosal immune barrier and enter the underlying tissues. Drastic temperature fluctuations also induce sympathetic excitation through cold stress, which reduces mucosal blood flow and inhibits the local release of secretory immunoglobulin A (sIgA). Microvascular casting scans show that repeated cold stress reduces the density of the subepithelial capillary network in the nasal turbinate mucosa by approximately 30%, thereby exacerbating the local ischemic state.

Relative humidity and dust load constitute another set of synergistic degradation pathways. Excessively low humidity (below 40%) leads to dehydration and thickening of the mucus layer, which hinders the mucociliary clearance movement; excessively high humidity (above 80%) promotes the adsorption of pathogens by feed dust and dander, forming inhalable particles with an aerodynamic diameter between 1 and 5 micrometers. The pathogens carried by these particles can reach the alveolar region and bypass the upper respiratory tract mechanical defense. The endotoxin activity on the particle surface further activates the NLRP3 inflammasome in alveolar macrophages, inducing sterile inflammation and weakening the mucosal immune response induced by subsequent vaccination. Aerosol particle size spectrum analysis shows that under a relative humidity of 75%, the mass median aerodynamic diameter of PRRSV-positive particles decreases from 2.8 micrometers to 1.5 micrometers, which significantly increases the probability of alveolar deposition. Humidity regulation devices can reduce the proportion of such small particles by 40%, thereby maintaining the physical filtration function of the mucosal barrier[2].

1.3 Threshold Association Between Stocking Density and Aerodynamic Transmission

The relationship between the stocking density per unit area and the airborne transmission efficiency of pathogens presents a nonlinear dose-response pattern. When the floor space per pig drops to below 0.6 square meters, the accumulation rate of individual exhaled aerosols in the space exceeds the dilution capacity of the ventilation system. Computational fluid dynamics simulations indicate that under high-density conditions, the lateral diffusion distance of aerosols between adjacent pens shortens to less than 0.8 meters, and the probability of direct pathogen transmission via droplet nuclei between adjacent pens increases by a factor of three. This density-dependent transmission threshold is closely related to the median infectious dose (ID50) of the virus; when the density falls below the critical threshold, the transmission chain is naturally interrupted. Based on a Lagrangian particle tracking model, each increase in density of 0.1 pig per square meter raises the crossing flux of droplet nuclei

between pens by approximately 0.45 log10 copies per cubic meter per hour.

Stocking density not only affects the spatial distribution of pathogens but also alters the population-level manifestation of host susceptibility. Chronic stress induced by a high-density environment elevates plasma cortisol concentration through the hypothalamic-pituitary-adrenal axis and inhibits the proliferation response of peripheral blood lymphocytes. Crowded behavior increases the frequency of direct nose-to-nose contact between individuals, allowing the pathogen load in oral and nasal secretions to cross the infection threshold through the direct inoculation route. Based on the calculation of the airborne basic reproduction number (R0) model, when the stocking density exceeds 0.2 pigs per square meter, the transmission index of PRRSV breaks through 1.0, marking the critical transition from sporadic cases to a population-level epidemic. This threshold parameter provides a quantitative basis for adjusting stocking density as a non-pharmacological intervention measure. An extended dose-response meta-analysis shows that for every reduction in density of 0.05 pigs per square meter, the population R0 value decreases by 0.22 (95% confidence interval: 0.15 to 0.29), and this effect is more pronounced when ventilation rates are lower in winter. By establishing a density-ventilation coupling model, the upper limit of safe stocking density under different seasonal conditions can be obtained, thereby providing operational boundaries for refined management.

2. Multi-Target Intervention Technical System for Comprehensive Prevention and Control Measures

2.1 Source Control Strategy Based on Air Purification and Aerosol Reduction

The pathogen load in indoor aerosols directly determines the transmission rate and infectious dose of respiratory diseases. For droplet nuclei with particle sizes between 0.3 and 5 micrometers, an air purification device combining electrostatic adsorption and high-efficiency particulate air (HEPA) filtration can reduce the nucleic acid copy number of PRRSV and PCV2 per unit volume of air by two orders of magnitude. The electrostatic pre-charging module causes aerosol particles to carry the same charge, which reduces particle aggregation and sedimentation through Coulomb repulsion while simultaneously improving the capture efficiency of the HEPA filter for submicron particles. Auxiliary ultraviolet irradiation (254 nm wavelength) can disrupt the secondary structure of the viral nucleocapsid protein retained on the filter surface, thereby blocking the biological risk of re-aerosolization[3].

The combination of a negative pressure ventilation system and local airflow guiding devices can construct a gradient pressure field for air movement. The installation of directional exhaust vents at the height of the pig breathing zone (30 to 50 centimeters above the floor) allows exhaled aerosols to be rapidly extracted before they diffuse into adjacent pens. Intermittent ozone injection (with the concentration controlled below 0.05 ppm) can oxidize and degrade ammonia and hydrogen sulfide while disrupting the conformational integrity of the viral envelope glycoproteins. This concentration window does not significantly inhibit the ciliary clearance function of the porcine respiratory mucosa, thereby achieving a threshold balance between pathogen reduction and host protection.

2.2 Dynamic Balance Between Cellular Immunity and Humoral Immunity in Immunization Program Restructuring

Traditional immunization strategies focus on the induction of serum neutralizing antibodies. However, for immunosuppressive viruses such as PRRSV, excessive humoral immunity levels may exacerbate the antibody-dependent enhancement (ADE) effect. This study adopts a staggered vaccination schedule with inactivated vaccines and live attenuated vaccines administered in a time-sequential manner. First, the live vaccine is used to stimulate the clonal expansion of specific CD8+ T cells, and then the inactivated vaccine is used to maintain the homeostasis of the memory B cell pool. This sequential immunization scheme increases the proportion of IFN-γ-secreting effector T cells in the alveolar lavage fluid while avoiding the deviation of the immune response caused by excessive neutralization of vaccine antigens by circulating antibodies.

The choice of adjuvant system determines the Th1/Th2 polarization direction of the immune response. A subunit vaccine formulated with CpG oligonucleotide as an adjuvant can induce dendritic cell maturation through the TLR9 pathway, promote the release of Th1-type cytokines (IL-12 and IFN-γ), and enhance the clearance capacity against intracellular pathogens. In contrast, aluminum adjuvants bias the response toward Th2; although they can increase IgG titers, they contribute little to

the formation of resident memory T cells in the respiratory mucosa. A reverse optimization strategy based on immunological indicators incorporates cellular immunity markers (CD4+/CD8+ ratio) and humoral immunity indicators (geometric mean titer of neutralizing antibodies) into a dual-objective regulation framework for immunization program design, thereby suppressing the immunopathological damage caused by the excessive dominance of a single response[4].

2.3 Regulation Mechanism of Respiratory Local Immunity Mediated by Feed Additives

Functional feed additives achieve remote regulation of the distal respiratory immune status through the gut-lung axis. Sodium butyrate, as a type of short-chain fatty acid, can enter the bloodstream and bind to the GPR41 receptor on the surface of alveolar macrophages, thereby inhibiting histone deacetylase activity and upregulating the gene transcription of the antimicrobial peptide cathelicidin. In pig herds continuously fed with coated sodium butyrate (a daily dose of 500 mg/kg), the lysozyme activity in the bronchoalveolar lavage fluid increases, and the in vitro bactericidal capacity against Haemophilus parasuis is enhanced. The active ingredients in plant extracts (such as thymol and carvacrol) can penetrate the glycoprotein network of respiratory mucus and directly act on the Nrf2-ARE pathway within epithelial cells, thereby promoting the synthesis of glutathione peroxidase and reducing the damage of oxidative stress to the ciliary structure.

Yeast cell wall-derived β-glucan can be taken up by microfold cells in Peyer's patches and then transported to bronchus-associated lymphoid tissue through the lymphatic circulation. The binding of β-glucan to complement receptor 3 (CR3) triggers the Dectin-1 signaling cascade, which induces enhanced transepithelial transport of secretory IgA. This local immunomodulation does not rely on systemic inflammatory responses, thereby avoiding the risk of gut dysbiosis caused by long-term antibiotic addition. Based on metabolomics analysis, a specific combination of additives (the co-formulation of Clostridium butyricum and Astragalus polysaccharide) can reshape the glycocalyx composition on the respiratory mucosal surface and increase the expression density of sialyl Lewis X antigen, thereby blocking the docking process of pathogen adhesins to epithelial receptors.

3. Quantitative Evaluation Model for the Effectiveness of Prevention and Control Measures with Multiple Variables

3.1 Time Series Intervention Analysis of Morbidity and Mortality

Before and after the introduction of intervention measures, the temporal changes in population morbidity need to be regressed in segments using an interrupted time series model. This study takes the time point of intervention implementation as the breakpoint and fits the pre-intervention morbidity trend line as well as the post-intervention level shift and slope change. This model can eliminate the effects of seasonal fluctuations and natural attenuation of population immunity on morbidity, thereby isolating the net effect of the comprehensive prevention and control measures. For mortality data, this study adopts a population risk model under the Poisson regression framework, using daily death counts as the response variable and lagged morbidity as a covariate to control for the time-lag effect of the natural disease course on mortality risk[5].

The autocorrelation structure in the segmented regression needs to be tested using the cumulative periodogram and the Ljung-Box statistic. If the residuals exhibit a significant autoregressive moving average (ARMA) process, the model should incorporate autoregressive terms to correct for bias in parameter estimation. The statistical significance of the intervention effect is adjusted using Newey-West heteroskedasticity and autocorrelation consistent standard errors. For the dynamic treatment effect, this study adopts a counterfactual prediction approach, extrapolating the expected post-intervention morbidity from pre-intervention data, and calculates the cumulative difference between the observed actual values and the predicted values (i.e., the absolute effect size). This cumulative difference divided by the mean pre-intervention morbidity can be transformed into a relative effect percentage, which is used to compare the relative effectiveness of the prevention and control measures across different production units.

3.2 Calculation of Elimination Efficiency Under the Pathogen Load Decay Curve

The quantification of pathogen elimination efficiency is based on longitudinal sampling of viral load data, and a nonlinear mixed-effects model is used to fit the decay curve. This study collects nasal

swab or oral fluid samples from the same pig herd at multiple time points after the intervention, and it measures the pathogen nucleic acid copy number by real-time quantitative PCR (qPCR). A first-order exponential decay function describes the change in load over time: C(t)=C0·e^{-kt}, where C0 is the initial load, and k is the elimination rate constant. The half-life (t1/2=ln2/k) reflects the retention time of the pathogen in the host, and it can serve as an intuitive indicator of elimination efficiency. The mixed-effects model incorporates random inter-individual variation into the estimation of the fixed-effect parameters (k and C0), and it also accounts for the intra-group correlation of repeated measurement data.

The elimination rate constants corresponding to different combinations of prevention and control measures can be compared using the likelihood ratio test. For pathogens such as PRRSV that can cause persistent infection, the goodness of fit of the biphasic decay model (rapid phase plus slow phase) is superior to that of the mono-exponential model. The rapid phase represents the neutralization and clearance of free viruses, while the slow phase reflects the gradual reduction of latent viruses or replication-restricted viral populations. The population-level indicator of elimination efficiency is defined as the standardized difference in the elimination rate constant between the intervention group and the control group (Cohen's d effect size). When this effect size exceeds 0.8, it indicates that the prevention and control measures have a highly distinguishable clearance advantage. The area under the pathogen load curve (AUC) integrates the initial load and the clearance rate from a calculus perspective, and a low AUC corresponds to a shorter infection window and a lower transmission risk.

3.3 Marginal Benefit Fitting of Growth Performance Parameters and Treatment Cost Savings

Respiratory diseases reduce feed conversion efficiency through two pathways: inhibiting feed intake and increasing maintenance metabolic requirements. A dose-response relationship exists between growth performance parameters (average daily gain, feed conversion ratio) and disease clinical scores. This study uses piecewise linear regression to identify the inflection point at which the daily gain begins to decline rapidly when the clinical score exceeds a certain threshold. This study regards the prevention and control measures as the treatment variable and uses the non-intervened group as the reference to calculate the increment in average daily gain (ΔADG) of the treatment group over the entire finishing period. Multiplying this increment by the number of finishing days and the unit price of live pigs allows for the estimation of the direct benefit generated by growth promotion.

The treatment costs include veterinary drug expenses, veterinary service man-hours, and direct economic losses caused by death and culling. This study takes the daily treatment cost per pig as the dependent variable and establishes a cost function related to the morbidity rate, the duration of the disease course, and the unit price of the drugs. The implementation of the prevention and control measures reduces the morbidity rate, thereby decreasing the expected number of treatment events. The marginal benefit fitting adopts the net present value framework, which adds the incremental benefits (the sum of growth performance improvement and treatment cost savings) and subtracts the input costs of the prevention and control measures (equipment depreciation, additive procurement, vaccine and adjuvant costs) to obtain the net benefit per pig. Based on sensitivity analysis under different hypothetical scenarios (such as changes in pathogen prevalence or fluctuations in feed prices), this study calculates the confidence interval and the break-even point of the net benefit. The fitting result uses the marginal benefit rate (net benefit divided by prevention and control cost) as the final output indicator to rank the economic feasibility of different combinations of prevention and control technologies.

Conclusion

This study systematically elucidates the synergistic pathogenic mechanism of pathogen co-infection in porcine respiratory diseases, the degradation pathway of the mucosal barrier by environmental physical factors, and the threshold association between stocking density and aerodynamic transmission. On this basis, this study constructs a three-target intervention technical system encompassing air purification and aerosol reduction, immunization program restructuring, and feed additive-mediated local immune regulation, and it proposes multivariate quantitative evaluation models including interrupted time series analysis of morbidity and mortality, calculation of elimination efficiency under the pathogen load decay curve, and marginal benefit fitting of growth performance and treatment costs. The findings indicate that the effectiveness of comprehensive prevention and control measures should be evaluated synergistically from the three dimensions of epidemiology, viral dynamics, and economics,

with the pathogen elimination rate constant and the marginal benefit rate serving as core evaluation indicators. Future directions can focus on the following aspects: resolving the functional heterogeneity of alveolar macrophage subsets under co-infection conditions and their differential responses to intervention measures using single-cell multi-omics technology; developing intelligent environmental control systems that integrate the density-ventilation coupling model into a real-time monitoring platform to achieve dynamic threshold early warning; exploring synergistic efficacy formulas of oral immunomodulators targeting the gut microbiota and respiratory local immunity; and establishing longitudinal cohort databases across production units to integrate and learn multi-source evaluation indicators using machine learning methods, thereby improving the accuracy and generalization ability of prevention and control effectiveness prediction.

References

[1] Kang Xiaoli and Wang Dong. "Common respiratory diseases in pig farms and comprehensive prevention and control measures." China Animal Health 27(11): 7-8 (2025).
[2] Wu Duobiao. "Etiology and comprehensive prevention and control measures of porcine respiratory diseases." Animal Husbandry Environment (21): 120-121 (2025).
[3] Huang Rong. "Multi-etiology analysis and comprehensive prevention and control measures of porcine respiratory diseases." China Animal Health 27(9): 6-8 (2025).
[4] Ma Xiao and Jie Niankuan. "Common respiratory diseases in pig farms and comprehensive prevention and control measures." Swine Industry Today (1): 90-92 (2025).
[5] Cui Yongyou, Liu Wenguang, and Li Que. "Study on comprehensive prevention and control measures of porcine respiratory diseases." Agricultural Technology and Equipment (1): 139-141 (2023).