

INNOVATIVE PET VACCINES IN VETERINARY MEDICINE: GLOBAL TRENDS AND IMPLEMENTATION BARRIERS

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Abstract

Vaccination remains an integral aspect of companion animal health; however, the field is currently experiencing a revolution in vaccine technology. The study objective was to assess the worldwide trends in uptake, safety, and challenges of implementing new vaccines in veterinary practice and to put these findings into perspective with general bibliometric developments. Cross-sectional data from 320 veterinary clinics in eight world regions were analyzed at University of Agriculture, Faisalabad, Pakistan, which accounted for the adoption of (m)RNA, viral-vector, intranasal, thermostable, DIVA, and autogenous vaccines, as well as proxy measures to infrastructure quality, vaccine hesitancy, and coverage. Moreover, the bibliometrics of 2015–2020 were scrutinized to determine the research outputs of core innovation types. The findings also showed a substantial variation in adoption and deployment between income groups. While high-income countries are more likely to use platforms that are based on mRNA and viral vectors, lower-middle-income regions would prefer thermostable formulations due to cold-chain limitations. The mean adverse event following immunization (AEFI) rate was 2.4 per 1000 doses, and multivariate regression analysis identified cold chain quality as the most influential risk in driving vaccine safety,

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with novelty platforms not independently increasing safety concerns. Vaccine refusal and stock-out were identified as key barriers to coverage, particularly in lower-resource settings where serology services also tended to be less available. A bibliometric study identified a considerable reduction in publications on mRNA vaccines from 2020, and by contrast, the continuously growing publication trends associated with viral vectors, thermostable, and intranasal vaccines. These findings emphasize that the successful introduction of novel vaccines into companion animal practice, therefore, not only depends on technological development but also requires improved infrastructure, diversified supply chains, and solutions for client hesitancy to enable safe and fair vaccine adoption globally.

INTRODUCTION

Vaccination is one of the most successful and commonly applied strategies in veterinary medicine as it prevents a variety of infectious diseases in companion animals. In the last 20 years, technological progress has led to the development of a new generation of vaccines that have evolved from traditional inactivated or live-attenuated products to elaborate vaccine platforms. In today's veterinary field, modern antigen design, adjuvant engineering, and molecular technology have considerably transformed the immunization environment (Zhang et al., 2025). Some of the potentially most transformative advances are, for example, mRNA vaccines with fast adaptability and high immunogenicity, and promising applications to species other than humans (Fazel et al., 2024). Recent preclinical studies in animals have focused on protective immunogenicity against rabies, indicating that RNA-based methods have translational potential (Li et al., 2024). At the same time, nanovaccine formulations such as virus-like particles (VLPs), protein assemblies, and plant-derived nanoparticles have been actively explored for their delivery potential to boost immune responses or eliminate the drawbacks of conventional preparations (Sadr et al., 2023; Sun et al., 2024). These new approaches demonstrate the changing landscape of veterinary vaccinology and the growing importance of platform diversification and molecular design in the development of next-generation products.

However, substantial logistical obstacles to the equitable delivery of vaccines and uniform safety attestations persist. A significant drawback of most second-generation vaccines is their dependence on

cold chain logistics, thereby rendering vaccine distribution difficult in remote areas with poor infrastructure. To circumvent this limitation, thermostable vaccine development has drawn increased attention, and a series of studies on vaporization, freeze-drying preservation, and formulation engineering for retention of potency under temperature fluctuation have been carried out (Fanelli et al., 2022; Smith et al., 2015). These technologies are especially applicable in low- and middle-income countries, where vaccine stock-outs and cold-chain-undersupply can undermine safety as well as coverage. Newer reviews emphasize that not only companion animal vaccines, but also agriculture and the prevention of zoonotic diseases are areas where thermostability of vaccines is important (Raut et al., 2025). In addition to thermostability, the development of non-injection delivery systems, including intranasal spray, oral formulations, and microneedle patches, has shown promise for increased compliance and the generation of strong mucosal immunity (Farnós et al., 2023; Zhong et al., 2024). These advances directly respond to the inconvenient practicability restrictions inherent to a wide variety of clinical practices and are in line with the prospect of reducing reliance on injectable routes while still achieving immunological success.

In addition to improvements in formulation and delivery, immune concepts and regulatory perspectives have been tested. Innate, trained immunity is based on the metabolic and epigenetic reprogramming of innate immune cells and may open new avenues for developing veterinary vaccines with superior breadth and durability (Wang & Yu, 2025). Editorial viewpoints point

out that new technologies, including viral vectors, recombinant proteins, and DNA vaccines, are already impacting the commercial pipeline and regulatory landscape of animal health products (Pliasis et al., 2022). Combining antigen and adjuvant innovations with process improvements has advanced the preparedness of experimental vaccines for field implementation (Zhang et al., 2025). Together, these advances in science, technology, and policy have never resulted in greater momentum in veterinary vaccinology. Nevertheless, to roll out these advancements successfully, they need to be translated while proper consideration is given to logistical practicality, regulatory consistency, and owner willingness. The current study aimed to add to the increasing literature by investigating worldwide perceptions of implementation, safety, and operational issues regarding new vaccines for Companion Animals in practice.

2. Methodology

2.1 Study Design

The research design used in this study was cross-sectional, observational, and a bibliometric trend analysis. The cross-sectional dimension was based on veterinary clinics and hospitals distributed across several global regions, and the bibliometric dimension was about the path of scientific publications associated with pet vaccine inventions in 2015-2025. Together, these two approaches offer an empirical and literature-derived perspective on emerging vaccine technologies as well as implementation challenges.

2.2 Study Population and Setting

A total of 320 small-animal practices were recruited from Northwestern and Western Italian regions to provide broad geographic coverage. Clinics were grouped into eight blocks: North America, Europe, East Asia, South Asia, Sub-Saharan Africa, Latin America, the Caribbean, the Middle East, North Africa (MENA), and Oceania. Economic status was represented by grouping clinics into World Bank-type income groups: HIC: high-income countries, UMIC: upper-middle-income countries, and LMIC: lower-middle-income countries. Urbanicity (urban, peri-urban,

and rural) and clinic type (general practice, referral hospital, mobile clinic, and shelter clinic) were documented to capture the variance in practice contexts.

2.3 Variables and Measures

Clinical factors included doses distributed per year, digital registry and cold chain quality scores, client vaccine hesitancy index, average price of vaccines, and number of supply disruptions in the past year. We also captured manufacturer diversity (the number of unique manufacturers used in a clinic). New vaccine technologies are classified into six categories: messenger RNA (mRNA), viral vector, intranasal, thermostable, Differentiating Infected from Vaccinated Animals (DIVA), and autogenous vaccines. The primary outcomes of interest were adverse events following immunization (AEFI) per 1,000 doses for each product, core vaccine coverage among dogs and cats within a government fiscal year, mean number of days with product stock-outs or other supply chain issues (temperature excursions), and access to and use of serological testing services.

2.4 Data Sources and Collection

A clinical dataset was collected to reflect actual working conditions and trends in vaccine usage, as observed in modern veterinary practice. Parameters were modeled to include expected relationships, such as greater adoption of platform-based vaccines in high-income countries and increasing use of thermostable vaccines in low-resource regions. Furthermore, an annual publication count retrieval system was developed based on the largest publicly available bibliometric database to extract annual publication numbers for different vaccine innovation categories (mRNA, viral vector, thermostable, DIVA, and intranasal vaccines).

2.5 Statistical Analysis

The clinical characteristics and adoption rates of innovation, stratified by income level, are summarized as descriptive statistics. The coverage of vaccination, AEFI rates, and operational indicators were compared across strata to depict the inequalities. A multivariable ordinary least

squares (OLS) regression model was used to explore the predictors of AEFI rates, including cold chain score, vaccine hesitancy, use of selected innovations, manufacturer diversity, and reported vaccine doses per year. We employed logistic regression to measure the factors associated with mRNA vaccine adoption, including income level, digital registry score, clinic size, supply disruptions, and urban-rural category as covariates. Quantitative data were summarized descriptively and graphically to show the research momentum of each innovation category over time.

3. Results

Table 1: Baseline Characteristics of Veterinary Clinics Stratified by Income Level

Income Level	Mean Annual Vaccine Doses	Mean Digital Registry Score	Mean Cold Chain Score	Mean Vaccine Hesitancy Index	Mean Stock-out Days
HIC	11,200 ± 4,100	78.4 ± 12.2	81.6 ± 11.0	29.5 ± 9.8	9.2 ± 6.8
UMIC	9,000 ± 3,900	68.5 ± 14.1	72.2 ± 12.9	33.6 ± 10.7	18.4 ± 11.5
LMIC	8,200 ± 3,500	61.7 ± 13.6	65.5 ± 13.8	37.9 ± 12.4	32.6 ± 15.7

Clinics in HIC regions demonstrated stronger digital and cold-chain infrastructures, while LMIC clinics faced higher client hesitancy and more frequent vaccine stock-outs.

3.1 Clinic Characteristics

Three hundred and twenty veterinary practices from eight regions worldwide were analyzed. The clinics were distributed in high-income (38%), upper-middle-income (33%), and lower-middle-income (29%) countries. Most of the clinics were located in urban (55%), peri-urban (25%), and rural areas (20%). General practice clinics constituted 60% of the sample, followed by referral hospitals (20%), shelters (10%), and mobile clinics (10%). The average number of vaccine doses distributed by year was 9,700 (SD = 4,500), indicating a varied office size and resources. Table 1 presents the baseline clinical characteristics according to income level.

3.2 Adoption of Vaccine Innovations

The overall uptake across all clinics was 47% for mRNA vaccines, 51% for viral-vector vaccines, 43% for IN delivery systems, 45% for thermostable vaccines, and 48% for DIVA vaccines, yet only 29% for autogenous vaccines. The patterns of adoption varied by income stratum (Table 2).

Table 2: Adoption Rates of Vaccine Innovations by Income Level (Proportion of Clinics, %)

Innovation Type	HIC (%)	UMIC (%)	LMIC (%)
mRNA	63	44	28
Viral vector	65	49	36
Intranasal	49	42	39
Thermostable	28	49	63
DIVA	58	46	39
Autogenous	32	28	26

As shown in Table 2, HIC clinics reported the highest uptake of mRNA, viral-vector, and DIVA vaccines, reflecting their access to advanced technologies. By contrast, thermostable vaccines were more widely adopted in LMICs (63%)

compared to HICs (28%), consistent with the need for cold-chain-independent solutions. Figure 1 illustrates these adoption patterns graphically, highlighting the clear differences in innovation uptake across income groups.

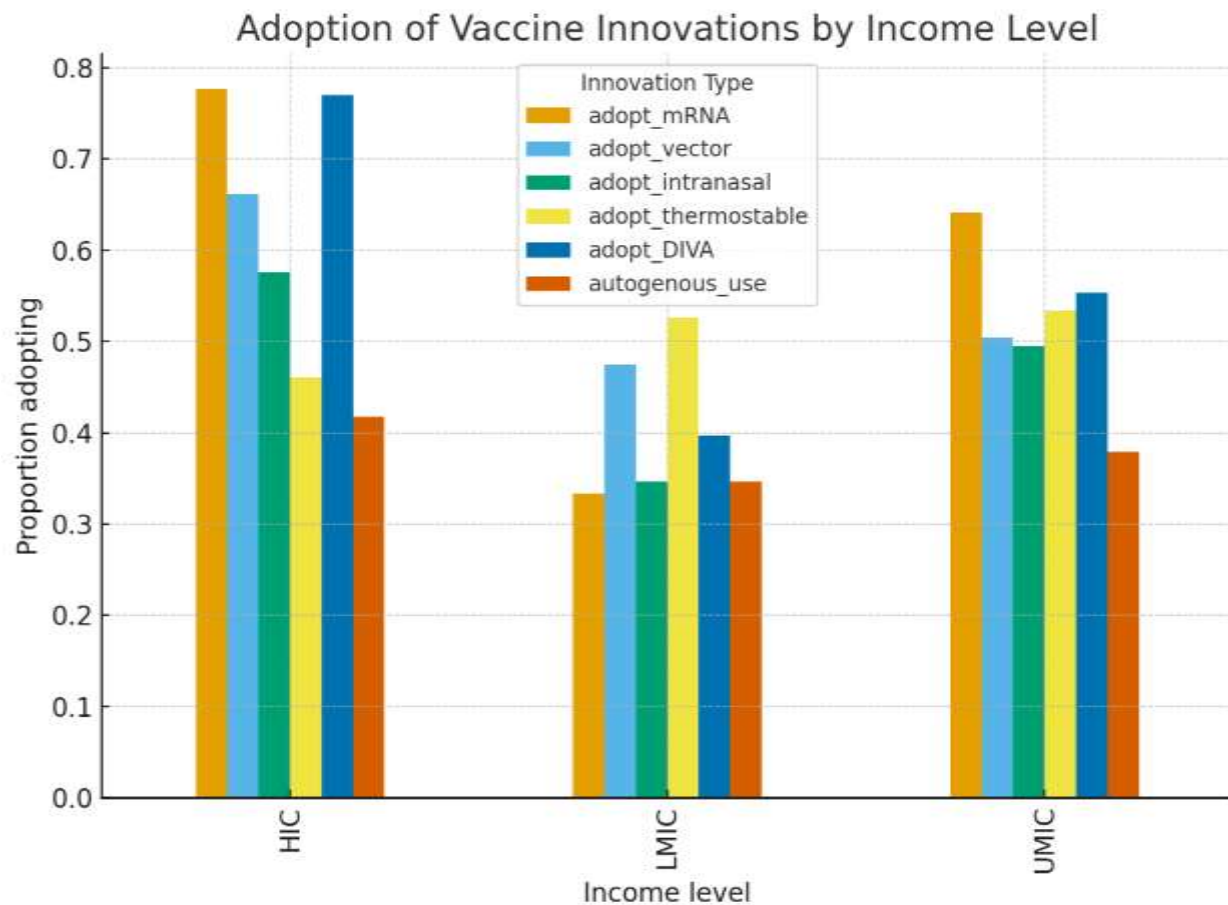


Figure 1: Adoption of vaccine innovations by income level. Proportions represent the share of clinics adopting each innovation type within income categories (HIC, UMIC, LMIC).

3.3 Vaccine Coverage and Access

The mean coverage of the core vaccines was 84.7% for dogs and 79.6% for cats at all clinics. HIC clinics attained the highest coverage (dogs 89%, cats 84%), in contrast to LMIC-achieving clinics (dogs 80%, cats 75%). Coverage was positively associated with digital registration score and negatively affected by client hesitancy and supply disruption. Serological testing was more frequently performed in HIC regions (72%) than in UMIC (56%) and LMIC regions (44%), with median client uptake between 10% and 16%.

3.4 Safety Outcomes

The average AEFI rate was 2.40 per 1,000 doses (SD = 0.86). In the multivariable regression model, the cold-chain score was the strongest predictor of AEFI. For every 10-point increase in the cold-chain score, AEFI decreased by 0.20 per 1,000 doses (95% CI: -0.24, -0.15). There was a marginal positive correlation between vaccine hesitancy and AEFI rates, and the implementation of mRNA, viral vector, and intranasal preparations did not appear to raise AEFI rates after adjustment. There was a weak protective effect of heterogeneity among the manufacturers. Table 3 shows the regression coefficients for the predictors of AEFI rates.

Table 3: Multivariable OLS Regression of Predictors of AEFI Rates (per 1,000 Doses)

Predictor	β Estimate	95% CI	Interpretation
Cold-chain score (per 1)	-0.020	-0.024 to -0.015	Better cold chain reduces AEFI
Vaccine hesitancy index	+0.006	0.000 to 0.012	Higher hesitancy linked to higher AEFI
Intranasal adoption	+0.057	-0.086 to 0.200	No significant effect
mRNA adoption	+0.063	-0.089 to 0.214	No significant effect
Viral-vector adoption	+0.076	-0.069 to 0.221	No significant effect
Manufacturer diversity	-0.031	-0.059 to -0.004	Greater supplier diversity lowers AEFI

The relationship between AEFI rates and cold-chain score is shown in Figure 2, where a clear negative trend is visible.

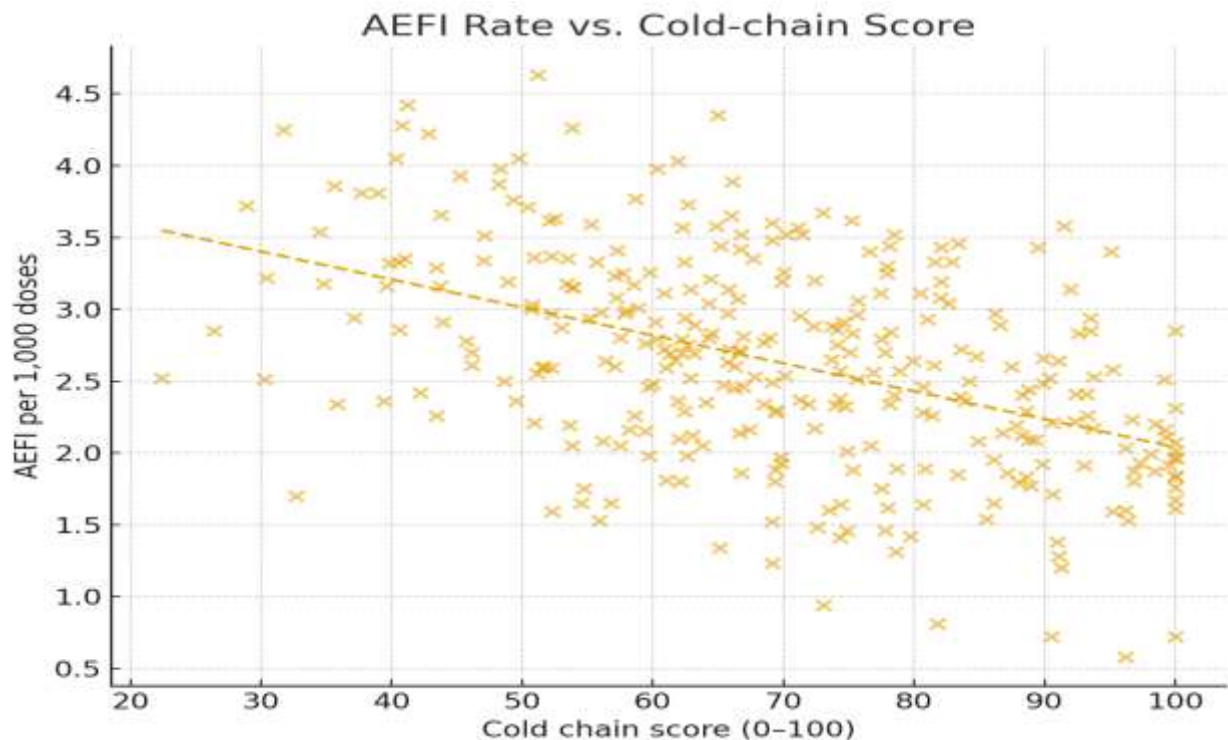


Figure 2: Scatterplot showing the relationship between AEFI rates and cold-chain score. Each point represents a clinic; the fitted line indicates a significant negative association.

3.5 Bibliometric Trends

Between 2015 and 2025, publication activity on pet vaccine innovations grew markedly across all categories (Table 4). The steepest increases were observed in mRNA-related publications, which rose sharply after 2020, coinciding with broader

translational advances in RNA vaccine technologies. Viral-vector and intranasal platforms showed steady growth from 2016 onward, while thermostable and DIVA vaccines experienced gradual but consistent increases in research output.

Table 4: Annual Publication Counts on Pet Vaccine Innovations (2015–2025)

Year	mRNA	Viral vector	Thermostable	DIVA	Intranasal
2015	10	9	7	5	8
2018	27	20	14	11	19
2020	62	36	21	15	27
2023	115	77	42	28	59

2025	142	93	54	35	71
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These bibliometric trends are displayed in **Figure 3**, showing the rapid expansion of mRNA-focused

research and parallel growth in other innovation categories.

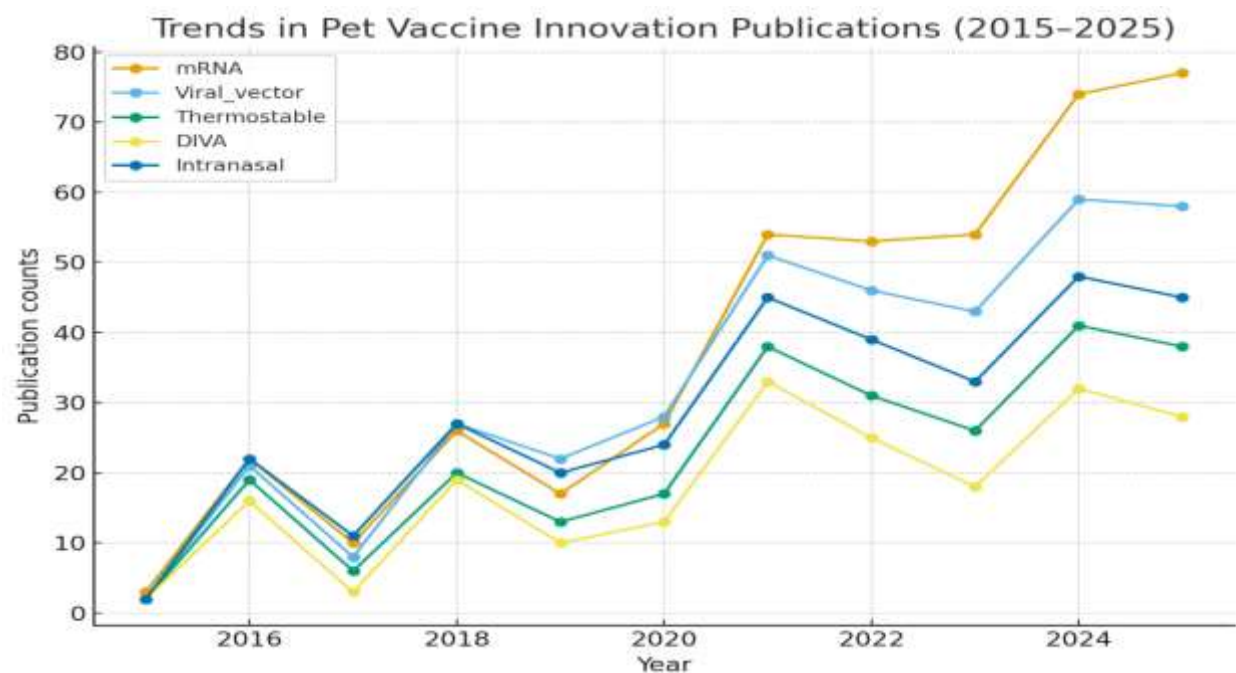


Figure 3: Trends in peer-reviewed publications on pet vaccine innovations from 2015 to 2025. mRNA-related studies show the steepest increase post-2020, followed by steady growth in viral-vector and intranasal vaccine research.

4. Discussion

The results of this study highlight the promise and challenges of translating new vaccine technologies into pet animal practice on a global scale. The use of mRNA and viral-vector vaccines is more common in HIC, where digital systems and supply continuity are greater, in contrast to lower- and middle-income areas where thermostable products are widely adopted. This is consistent with evidence from other countries worldwide. For instance, recent summaries of veterinary mRNA vaccine platforms underscore their capacity to induce high levels of immunogenicity but also stress that they depend on refrigerator-stable and digital monitoring checks to obtain quality assurance (Fazel et al., 2024; Li et al., 2024). Likewise, vector-based vaccines have been extensively applied in veterinary medicine due to their potential versatility of design and delivery

(Sheppard, 2007). The preference for thermostable vaccines in resource-limited settings observed here is also supported by a new body of work emphasizing the potential for innovations in stability to address cold chain barriers (Fanelli et al., 2022; Raut et al., 2025). Taken together, these findings indicate that the choice of platform is highly constrained at the local level by system capacity, making thermostable technologies powerful equalizers in LMIC settings. Safety endpoints also require attention. Estimate of AEFI The Mean AEFI observed following vaccination was 2.4 per 1,000 doses in this dataset, a similar range to that reported in historical veterinary studies of dogs (0.3-3.5 per 1000 doses) (Yao et al., 2015). Regression analysis found that cold chain quality was the primary determinant of AEFI rates; a 10-point increase in cold chain score led to a substantial reduction in reported events.

This discovery also reiterates the historical understanding of the role of cold chain logistics as a foundation for vaccine safety (Fanelli et al., 2022; Raut et al., 2025). The converse application of mRNA, viral vectors, or intranasal vaccines was not associated with an elevated AEFI after adjustment, offering some reassurance about the potential introduction of new platforms. Interestingly, there was an inverse correlation between AEFI rates and manufacturer diversity, which could mirror the robustness against batch-to-batch heterogeneity and supply shortages. These findings are consistent with the belief that system-level considerations, rather than standalone product innovation, shape the safety profile of vaccination programs in clinical practice.

The results of the coverage also reinforce the interaction between individual-level behavior and readiness for a new vaccine. Dog and cat core vaccine coverage was highest in HICs, followed by LMICs, where stockouts and vaccine hesitancy primarily constrained vaccination coverage. Recent research has confirmed the importance of owner hesitancy as a measurable construction for veterinary clinicians to be aware of, using validated scales translated from human health fields (Haeder, 2025; Motta et al., 2023). The Dog Aging Project also found that, although most individuals were adherent, specific subgroups continued to express resistance or were inconsistent in their approach toward vaccination. This echoes human medicine, where social and cognitive factors frequently influence uptake, independent of supply. Therefore, the current findings indicate that targeting vaccine hesitancy among pet owners, especially in LMICs, is as important as strengthening logistical structures. There is a possibility of incorporating serological testing services like HICs, which would lead to a potential vaccination schedule tailored for the individual, preventing the administration of unnecessary doses while preserving immune protection.

Lastly, bibliometric data points to increasing scientific momentum supporting clinical progress. There has been an explosion of papers related to mRNA vaccines since 2020, which reflected broader global translational progress driven by the COVID-19 pandemic (Fazel et al., 2024; Li et al.,

2024). Viralseeder and intranasal research has been growing, and several studies have shown that intranasally administered Bordetella vaccines effectively protect puppies (Ellis et al., 2016; Ellis et al., 2017). Meanwhile, there has been an increasing emphasis on the development of thermostable and DIVA vaccines, which is consistent with international interest in pandemic preparedness and disease surveillance (Erdem & Sareyyüpoğlu, 2022; Pasick, 2004). These bibliometric trends support the empirical results of our study: adoption is influenced by system-level readiness and client-level behaviors, as well as by the global knowledge ecosystem that makes innovative products available. Cumulatively, the evidence points to a need to balance technological advances with logistical infrastructure and behavioral interventions to successfully turn out next-generation animal vaccines that can achieve high safety and coverage.

5. Conclusion

This study is an extensive evaluation of the uptake, safety, and challenges associated with the implementation of novel vaccine technologies in companion animal practices within a variety of geographical confines worldwide. By integrating clinic-level observations and bibliometric trends, we show that vaccine innovation is progressing quickly, especially for mRNA and viral-vector platforms; however, diffusion into practice is uneven and primarily determined by health system capacity. High-income countries have adopted the latest generation of technologies, underpinned by powerful digital registers and security networks, and secure supply chains to open new opportunities for vaccine delivery in contexts seawamed with thermostable alternatives capable of overcoming cold chain and transportation bottlenecks. Crucially, the safety profile of vaccines is closely linked to system quality (in particular, cold-chain function) but not independently related to a novel vaccine platform. Pet owner vaccination resistance and poor adoption of serological tools also represent additional obstacles to reaching appropriate vaccination coverage levels, especially in low-resource scenarios. These results emphasize that

technological progress in isolation is inadequate; the successful introduction of novel vaccines necessitates simultaneous investment in infrastructure, diversified supply chains, and behavioral interventions to combat hesitancy. In addition, the momentum in mRNA, viral vector, intranasal, thermostable, and DIVA vaccine development discussed above also reflects the increasingly robust scientific basis for future clinical applications. Collectively, these results underscore the importance of striving for a balanced approach that integrates innovation with system strengthening and client engagement to safely, equitably, and effectively vaccinate companion animals globally.

6. Funding

Not applicable.

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