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Vaccinating against *Salmonella* in poultry: a fundamental tool still scaling to a global reality

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Non-typhoidal Salmonella remains one of the most persistent threats to global food safety, causing an estimated 93.8 million illnesses and 155,000 deaths worldwide every year, with poultry products among the principal vehicles of transmission (Majowicz et al., 2010). The genus is also taxonomically vast; Salmonella enterica alone comprises 2,659 recognized serovars under the White-Kauffmann-Le Minor scheme, each with distinct epidemiological and ecological characteristics (Monte and Sellera, 2020). This diversity presents a substantial challenge to the global eradication of Salmonella, particularly through vaccination alone. However, global eradication should not be confused with the elimination or effective control of specific serovars within defined poultry populations, which may be achievable through targeted vaccination programs combined with appropriate biosecurity and surveillance measures. The relevant question, therefore, is not whether vaccination can eliminate Salmonella worldwide, but how effectively it can reduce the prevalence, colonization, and transmission of epidemiologically important serovars within specific production systems.

Pre-harvest control has become an industry priority under this more realistic framing, and live-attenuated Salmonella vaccines, engineered bacterial strains carrying targeted deletions that abolish virulence while preserving immunogenicity, have earned their place as a fundamental pillar of that effort, moving from experimental curiosities to commercially deployed tools in broiler and layer production (Uribe-Diaz et al., 2025).

Evidence from a systematic review of 127 studies across different animal hosts supports the potential of Salmonella vaccination, although reported efficacy varies considerably according to vaccine formulation, host species, challenge conditions, and outcome measures. Mutant-attenuated vaccines achieved a pooled efficacy estimate of 82.5% in chickens (95% CI 75.5–93.6), supporting their potential for reducing Salmonella colonization under experimental conditions (Siddique et al., 2024).

Emerging platforms have also shown promising experimental results. The same review reported pooled efficacy estimates of 91.3% for bacterial ghost vaccines and 83.5% for candidates developed through reverse vaccinology across animal hosts (Siddique et al., 2024). However, these estimates should not be interpreted as evidence of superior performance, given differences in experimental models, vaccine formulations, and challenge protocols. Moreover, the limited number of studies evaluating some emerging platforms restricts conclusions regarding their broader applicability. Further standardized studies, particularly under commercial poultry production conditions, are needed to determine whether these experimental findings translate into consistent protection in the field.

Two recent studies involving commercially available live-attenuated Salmonella vaccines illustrate their protective potential and interactions with the poultry gut microbiota. Khan and colleagues evaluated a commercial live-attenuated vaccine (Vaxsafe ST) in broiler chickens challenged with different doses of wild-type Salmonella Typhimurium and demonstrated reduced bacterial loads and shedding in vaccinated birds. The study also identified differences in cecal microbiota composition, with vaccination associated with relatively limited changes in microbial community structure compared with unvaccinated, challenged birds (Khan et al., 2025). Importantly, these microbiota findings represent a distinct outcome and do not establish that microbial community changes directly contributed to vaccine-mediated protection.

Ager and colleagues further investigated the interaction between a live-attenuated Salmonella vaccine (AviPro Megan Vac 1) and dietary iron supplementation, including SQM Iron. Their findings revealed that vaccination and nutritional supplementation, individually and in combination, influenced cecal microbial community composition, with some combined effects differing from those observed with either intervention alone (Ager et al., 2026). However, these microbiota changes should not be interpreted as evidence of enhanced vaccine efficacy, as improved protection against Salmonella was not demonstrated. Rather, the findings highlight the need for further studies integrating microbiome analyses with direct measures of pathogen colonization, shedding, and vaccine-induced protection to determine whether nutritional interventions can improve vaccination outcomes.

The extensive serovar diversity of Salmonella presents a substantial challenge to vaccine development, although multivalent formulations offer a promising strategy for broadening protection. Crouch and colleagues evaluated a trivalent inactivated vaccine containing S. Enteritidis, S. Typhimurium, and S. Infantis and demonstrated significant reductions in intestinal colonization and internal organ invasion following experimental challenges with both homologous and heterologous serovars, including S. Heidelberg, S. Virchow, and S. Hadar (Crouch et al., 2020a). In a complementary study involving 10,229 broiler breeder pullets raised under commercial conditions, the same vaccine induced sustained serovar-specific antibody responses and significantly reduced fecal shedding following experimental challenges with homologous serovars and the heterologous serovar S. Hadar (Crouch et al., 2020b). Although these findings support the potential for cross-protection, they should not be interpreted as evidence of universal protection against antigenically diverse Salmonella serovars. Rather, they demonstrate that appropriately formulated multivalent vaccines can provide protection beyond their constituent serovars, reinforcing their potential contribution to integrated Salmonella control programs.

This context-dependency is not unique to these studies. A recent review of poultry Salmonella vaccine immunology indicates that different live-attenuated vaccine strains may exert distinct effects on the cecal microbiota, whereas other formulations appear to have limited effects on microbial community composition (Uribe-Diaz et al., 2025). This

variability underscores the importance of evaluating vaccine performance under different production conditions, considering factors such as circulating serovars, poultry genetics, nutritional management, and environmental exposure. Consequently, findings obtained under one experimental or production setting may not necessarily translate into equivalent outcomes elsewhere.

Two major challenges remain. First, evidence regarding the interactions among vaccine formulations, dietary interventions, host characteristics, and circulating Salmonella serovars remains limited, highlighting the need for comparative studies across diverse poultry production systems. Second, the implementation of routine Salmonella vaccination remains uneven worldwide, particularly in resource-limited settings. Economic constraints, vaccine availability, storage and distribution requirements, regulatory differences, and limited access to veterinary services can restrict vaccination programs, especially among smallholder and semi-commercial poultry producers (Islam and Rahman, 2023; Grace et al., 2024; Prakasan et al., 2026). Addressing these barriers requires not only continued vaccine development and field validation but also improved delivery strategies, producer education, and locally adapted vaccination programs. Expanding access to effective vaccines should therefore be regarded as an essential component of sustainable Salmonella control rather than an alternative to complementary biosecurity and surveillance measures.

None of this should be read as a case against vaccination. Salmonella vaccines are, and should be regarded as, a fundamental tool for reducing Salmonella burden in poultry, with evidence supporting reductions in intestinal colonization and pathogen shedding under evaluated conditions. Their promise lies not in achieving global eradication through vaccination alone, but in sustainably reducing the burden of epidemiologically important serovars, while recognizing that targeted vaccination programs may contribute to their elimination or effective control within defined poultry populations. Achieving these outcomes requires continued research, broader implementation across diverse production systems, and integration with complementary interventions, including competitive exclusion cultures, targeted feed additives, bacteriophage therapy, and genomic surveillance of circulating Salmonella serovars along the poultry production chain. As an essential component of a long-term, integrated pathogen control strategy rather than a stand-alone eradication tool, Salmonella vaccination deserves continued scientific investment and, equally importantly, expanded access in production systems where its implementation remains limited.

Conflict of interest

The author declares no competing interests.

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