Multidrug-resistant *Salmonella* in poultry: A one health perspective on epidemiology, antimicrobial resistance mechanisms, and mitigation strategies

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Abstract

The emergence of multidrug-resistant (MDR) *Salmonella* in poultry has become a major One Health challenge, threatening global food safety, poultry production, international trade, and public health. Intensive poultry production systems, combined with inappropriate and excessive antimicrobial use, have accelerated the selection and dissemination of antimicrobial resistance determinants, primarily through mobile genetic elements such as plasmids, integrons, and transposons. Zoonotic non-typhoidal *Salmonella* (NTS) serovars, including *S. Enteritidis*, *S. Typhimurium*, *S. Infantis*, and *S. Kentucky*, are among the leading causes of foodborne infections worldwide, frequently contaminating poultry meat and eggs. In contrast, poultry-adapted serovars such as *S. Gallinarum* and *S. Pullorum* are rarely zoonotic but remain responsible for substantial economic losses in the poultry industry. The emergence of MDR strains, particularly those resistant to critically important antimicrobials such as fluoroquinolones and extended-spectrum cephalosporins, has further complicated disease treatment and control. This review synthesizes current knowledge on the epidemiology, antimicrobial resistance mechanisms, diagnostic approaches, and control strategies for both zoonotic and poultry-adapted *Salmonella*, while highlighting critical gaps in global surveillance and resistance monitoring. Preventive measures, including strengthened farm biosecurity, antimicrobial stewardship, vaccination, routine surveillance, and integrated occupational health and hygiene programs, are essential to reduce pathogen transmission across the food chain. A coordinated One Health approach, supported by genomic surveillance and evidence-based policy interventions, is crucial for controlling MDR *Salmonella*, protecting public health, and ensuring sustainable poultry production.

Keywords: Multidrug-resistant *Salmonella*, Poultry, One Health, Antimicrobial resistance, Food safety, Genomic surveillance

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Introduction

The relentless emergence and global dissemination of multidrug-resistant (MDR) *Salmonella* serovars within poultry production systems epitomize a quintessential One Health crisis, where the health of humans, animals, and ecosystems is inextricably linked (WHO, 2024). This convergence of threats directly undermines food safety, jeopardizes international trade, and poses an escalating challenge to public health systems worldwide (Lajmorak *et al*., 2025). Poultry, as a primary and affordable source of animal protein globally, sits at the heart of this complex dynamic (FAO, 2023). Intensive farming practices, designed to meet soaring global demand, have inadvertently created optimal conditions for pathogen evolution and spread by housing large numbers of genetically similar hosts in close proximity, facilitating transmission (Menconi *et al*., 2020). The widespread, and often unregulated or indiscriminate, use of antimicrobials—spanning therapy, prophylaxis, and historical growth promotion—has exerted an unprecedented selective pressure, serving as the principal engine driving the selection and amplification of resistance determinants (Van Boeckel *et al*., 2015; Ventola *et al*., 2015).

The crisis extends beyond the mere selection of resistance. The remarkable genetic plasticity of *Salmonella*, facilitated by a vast repertoire of mobile genetic elements (MGEs) such as conjugative plasmids, integrons, and transposons, allows for the rapid horizontal transfer of resistance genes not only among *Salmonella* populations but also across genera within the complex microbial ecosystem of the poultry gut and environment (Siguier *et al*., 2006; Cambray *et al*., 2013; Carattoli *et al*., 2013). This "mobile resistome" effectively turns poultry farms into bioreactors for the development and dissemination of MDR strains (Partridge *et al*., 2018). While host-adapted serovars like *S. Gallinarum* and S. Pullorum continue to cause severe economic losses through flock mortality and control costs (Barrow *et al*., 2011, 2012), the primary public health menace stems from zoonotic non-typhoidal *Salmonella* (NTS) serovars, most notably *S. Enteritidis, S. Typhimurium,* and the increasingly problematic *S. Infantis* and *S. Kentucky*. These serovars frequently contaminate poultry meat and eggs, leading to an estimated 93.8 million annual human cases of gastroenteritis (Adley *et al*., 2025). Alarmingly, the rising prevalence of strains exhibiting resistance to critically important antimicrobials (CIAs) like fluoroquinolones and third-generation cephalosporins severely compromises treatment efficacy, leading to prolonged illness, increased risk of invasive disease, and higher mortality (Folster *et al*., 2022; Papic *et al*., 2022).

Addressing this multifaceted threat demands a paradigm shift from siloed interventions to an integrated, holistic approach. The One Health framework provides the essential blueprint for effective action, recognizing that sustainable solutions require

coordinated efforts across human medicine, veterinary science, and environmental management. This narrative review synthesizes and critically appraises the current evidence, moving beyond mere description to analyze the interconnected drivers of the MDR *Salmonella* pandemic in poultry. We delve into the global epidemiological shifts and the impact of control programs, unpack the sophisticated molecular machinery of resistance and virulence, evaluate the strengths and limitations of modern diagnostic arsenals, and advocate for a synergistic suite of mitigation strategies. By identifying persistent knowledge gaps and future priorities, this review aims to inform policy, guide research, and galvanize the coordinated, cross-sectoral efforts required to safeguard both poultry production and global public health (Table 1).

Table 1: Structure, features, and biology of non-typhoidal *Salmonella* (NTS).

Section	Key Points	References
1. Classification & General Features	Rod-shaped bacteria,2-5µm long,0.7-1.5 µm wide. Genus: *Salmonella*; Family: *Enterobacteriaceae*; Gram-negative, facultative anaerobe, non-spore forming; Motile (peritrichous flagella, except *S. Gallinarum*, *S. Pullorum*).	(Fang *et al*., 2016)
2. Structure (Microscopic & Molecular)	Cell wall: LPS (Lipid A, core polysaccharide, O-antigen); Flagella: H-antigen; Capsule: rare in NTS (Vi antigen in *S. Typhi* only); Virulence plasmids present.	(Hendriksen *et al*., 2019)
3. Cultural & Biochemical Features	Lactose-negative on MacConkey; Red colonies with black centers on XLD agar (H_2S); Catalase +, oxidase –; Ferment glucose & mannitol, gas production; Citrate utilization often +.	(Rozwandowicz *et al*., 2018)
4. Genetic & Molecular Biology	Genome size: 4.5–5 Mbp; Pathogenicity Islands (SPIs): SPI-1 (T3SS-1, invasion), SPI-2 (T3SS-2, survival in macrophages), others for siderophores & stress adaptation.	(Jaffee *et al*. 2019)
5. Pathogenesis	Oral entry → acid tolerance → epithelial invasion (T3SS-1) → inflammation & diarrhea → survival in macrophages (T3SS-2) → systemic spread (severe cases). Diseases: gastroenteritis, septicemia (immunocompromised), focal infections.	(Hendriksen *et al*., 2019)

Table 1 (continued):

Section	Key Points	References
6. Immunology	Immune response: humoral + cell-mediated; Major antigens: O-antigen, H-antigen, fimbriae; Reinfections common (no long-term immunity).	(Uche *et al*., 2017)
7. Differences: NTS vs. Typhoidal	NTS: broad host range, gastroenteritis, no Vi antigen, self-limiting. Typhoidal (*S. Typhi, S. Paratyphi*): human-specific, systemic disease, Vi antigen present, severe.	(Galan *et al*., 2021)
8. Antibiotic Resistance	Many serovars show multidrug resistance, including Resistance to fluoroquinolones, cephalosporins, ampicillin; Presence of ESBLs & AmpC β-lactamases; Major concern in public health & veterinary medicine.	(Andrews *et al*., 2020)
9. Epidemiology	Human infections: mainly *S. Enteritidis* & *S. Typhimurium*; Poultry: *S. Pullorum* & *S. Gallinarum*; Sources: contaminated food (eggs, poultry, meat, milk) & exotic pets.	(Andrews *et al*., 2020)

Global epidemiology and the evolution of high-Risk clones

Geographical disparities and the impact of control programs

The global landscape of poultry-associated salmonellosis is markedly heterogeneous, shaped by varying production intensities, regulatory frameworks, surveillance capacities, and socioeconomic factors (Jaffee *et al*., 2019). In regions with stringent, risk-based control programs, significant progress has been demonstrated. The European Union's comprehensive approach, targeting key serovars across the production chain—from grandparent flocks to final products—has led to a notable decline in human cases linked to poultry (EFSA, 2019). Success hinges on a combination of mandatory flock monitoring, vaccination (particularly for layers), strict biosecurity, and slaughterhouse process hygiene controls, as outlined in EU regulation 2160/2003 (Desin *et al*., 2013; EFSA, 2019). Similarly, in the United States, the implementation of the USDA-FSIS *Salmonella* Performance Standards has pushed processors to adopt enhanced sanitary measures and process controls, contributing to variable but documented reductions in contamination rates for certain product categories, although challenges persist with specific serovars and product types like ground poultry (USDA, 2024).

In stark contrast, many low- and middle-income countries (LMICs) in Asia, Africa, and the Middle East face a more daunting scenario characterized by

higher reported prevalence rates (Stanaway *et al*., 2019). For instance, studies indicate *Salmonella* contamination in 20-50% of fresh chicken meat in parts of Southeast Asia and 15-40% in the Middle East (Yang *et al*., 2020). These figures frequently reflect underlying systemic challenges: fragmented farming structures with a predominance of small-scale operations, limited veterinary oversight and diagnostic capacity, suboptimal feed hygiene with contamination rates in feed ingredients reaching 30-40% in some African nations, and widespread, often unregulated, antimicrobial use (Rodrigues *et al*., 2011, Li *et al*., 2012). A critical, amplifying vulnerability is the heavy dependence on imported feed ingredients (e.g., soybean meal, corn). Global trade in these commodities can inadvertently introduce novel, resistant *Salmonella* strains into naive poultry populations, as evidenced by molecular studies linking feed imports to specific clones in recipient countries (Roussan *et al*., 2024). This interplay between local practices and globalized trade networks complicates containment efforts and underscores the need for international cooperation on biosecurity standards.

The ascendancy of multidrug-resistant "super-clones"

Beyond general prevalence, the specific identity and genetic makeup of circulating serovars determine the level of threat. Recent years have witnessed the alarming rise of specific MDR clones that combine virulence, persistence, and extensive resistance, often facilitated by specific genetic platforms (Kim *et al*., 2024).

Salmonella Infantis (pESI-positive clone), This represents perhaps the most formidable contemporary challenge. The global dissemination of strains carrying the pESI-like megaplasmid is a paradigm shift in the epidemiology of poultry salmonellosis (Aviv *et al*., 2017). This large, conjugative plasmid is a veritable "resistance and virulence arsenal." It typically harbors genes conferring resistance to at least seven antimicrobial classes (including blaCTX-M-65 ESBL, tetA, sul1, dfrA14, aadA1), heavy metals (mercury, arsenic), and disinfectants (quaternary ammonium compounds) [16, 33]. Furthermore, it carries virulence genes (e.g., ycfR, siiE) enhancing biofilm formation, cell adhesion, and host colonization (Aviv *et al*., 2017). This genetic package confers a remarkable fitness advantage, allowing *S. Infantis* to persistently colonize flocks, survive in farm environments, and withstand routine cleaning, while rendering clinical treatment in both poultry and humans exceedingly difficult (Franco *et al*., 2022).

Salmonella Kentucky ST198: This sequence type has emerged as a global pandemic clone strongly associated with poultry, particularly in parts of Africa, the Middle East, and Europe. Its hallmark is high-level resistance to ciprofloxacin, primarily due to accumulated chromosomal mutations in the gyrA (Ser83Phe, Asp87Asn/Gly) and parC genes (Wong *et al*., 2014; Folster *et al*., 2022). Fluoroquinolones

are CIAs for human medicine; the establishment and spread of such a resistant clone in the food animal reservoir represent a direct and significant erosion of therapeutic options for severe human salmonellosis (WHO, 2019).

Monophasic *S. Typhimurium* (1,4,[5],12:i:-), This variant, which lacks the second-phase flagellar antigen, has become a major cause of human infections and foodborne outbreaks in many regions. Often displaying a characteristic MDR pattern (ampicillin, streptomycin, sulfonamides, tetracycline - ASSuT), it is frequently linked to pork but is also persistently isolated from poultry, indicating potential cross-contamination in processing environments or shared sources on farms, and highlighting the interconnectedness of livestock reservoirs (ECDC, 2026).

The substantial and multifaceted burden

The consequences of this epidemiological landscape are profound and multidimensional. The human health burden remains staggering; beyond the millions of gastroenteritis cases, invasive NTS (iNTS) infections are estimated to cause over 500,000 cases and approximately 77,000 deaths annually, disproportionately affecting young children and immunocompromised adults in sub-Saharan Africa (Adley *et al*., 2025). Economically, the costs are systemic and felt at multiple levels. For the poultry industry, direct losses stem from mortality (ranging from 2-12% during acute outbreaks), reduced feed efficiency and weight gain, decreased egg production and quality, coupled with costs of treatment, diagnostics, and enhanced biosecurity measures (Rushton *et al*., 2015). At a macro level, trade disruptions are a potent economic weapon; detection of MDR *Salmonella* can lead to immediate embargoes or costly rejections of poultry exports, devastating national industries reliant on foreign markets (WOAH, 2022). Furthermore, loss of consumer confidence following high-profile outbreaks can have long-term market impacts. In LMICs, these economic shocks disproportionately affect smallholder farmers, threatening livelihoods and local food security (Grace *et al*., 2016). The projected escalation of AMR-related deaths to 10 million annually by 2050, with resistant infections from all pathogens potentially costing the global economy up to $100 trillion, underscores the catastrophic trajectory if current trends persist, with foodborne pathogens like *Salmonella* contributing significantly to this burden (Jones *et al*., 2019).

Recent surveillance studies from diverse geographical regions further illustrate the high prevalence and concerning MDR profiles of *Salmonella* in retail chicken products, underscoring its role as a major vehicle for human exposure (Stanaway *et al*., 2019; Kim *et al*., 2024) (Table 2).

Table 2: The contribution MDR strains of *Salmonella* in chicken products, in different countries.

Study (Author, Year)	Country / Region	Sample type / Source	No. of samples / isolates	Prevalence (%)	Dominant serovar	Antibiotic resistance / MDR (%)	Key findings
Retail Chicken Carcasses … Qatar (Microbial Drug Resistance, 2021–2018)	Qatar	Retail chicken carcasses	270 carcasses	11.11%	—	High resistance to tetracycline (73.7%), nitrofurantoin (53.3%), ampicillin; MDR ≈ 43.3%	Differences between local and imported poultry; some ESBL producers
Saudi Arabia, Retail Chickens (MDPI, 2025)	Saudi Arabia	Retail chicken meat (small/medium/large farms)	212 samples	9.3%	*S. Enteritidis*	High resistance to nalidixic acid (~90%), amoxicillin-clavulanate, tetracycline (~70%); MDR ≈ 70%	Problematic resistance in small producers; limited serovar diversity
Egypt, Poultry meat & Patients (Gut Pathogens, 2015)	Egypt	Poultry meat and fecal samples from diarrheic patients	150 poultry + 50 patients	~10% poultry; ~4% patients	*S. Typhimurium*, Derby, Kiel, Rubislaw	Complete resistance to erythromycin/tetracycline; high to amoxicillin-clavulanate; MDR multiple isolates	Shows virulence gene diversity; cross-host comparison
UAE (chilled broiler carcasses, 2024)	UAE	Chilled broiler carcasses from multiple companies	315 carcasses; 105 tested; 60 WGS	41.2%	*S. Infantis* / ST32; S. Minnesota / ST458	Very high resistance (97.1% tetracycline, ciprofloxacin, ceftriaxone); MDR ≈ 99%	WGS confirmed high-level MDR threat
Iran, Broiler chickens / *S. Enteritidis* (Frontiers Vet Sci, 2025)	Iran	Broiler chickens from farms	1,274 samples; 114 isolates (97 S. Enteritidis)	8.94%	*S. Enteritidis*	100% resistant to nalidixic acid; high ampicillin & amoxiclav; some sensitive to carbapenems	MAR index high; still sensitive to limited antibiotics
Iraq, Wasit Province (Vet World, 2023)	Iraq	Raw and frozen chicken meat (retail)	150 samples; 19 positives	12.7% overall	*S. Enteritidis* (63.2%), *S. Typhimurium* (36.8%)	High resistance to nalidixic acid (73.7%), tetracycline; MDR ≈ 63.2%	Resistance differs between raw/frozen samples
Iran, Poultry meat Shahrekord (BMC Microbiology, 2023)	Iran	Poultry meat from retail markets	440 samples	~9%	*S. Typhimurium*	High resistance to tetracycline, sulfamethoxazole-trimethoprim, nalidixic acid; MDR high	Includes analysis of virulence and resistance genes

Molecular pathogenesis and the engine of resistance

The dialogue of infection: Virulence mechanisms and host adaptation

Salmonella's success as a pathogen lies in its sophisticated, biphasic interaction with the host, masterfully regulated by an array of virulence factors (Fabrega *et al*., 2013). The initial dialogue is mediated by *Salmonella* Pathogenicity Island 1 (SPI-1). The encoded Type III Secretion System (T3SS-1) acts as a molecular syringe, injecting effector proteins (e.g., SipA, SipC, SopE) into intestinal epithelial cells. These effectors trigger profound actin cytoskeletal rearrangements, leading to membrane ruffling and active bacterial engulfment—a process of "triggered uptake" that is distinct from phagocytosis (Galan *et al*., 2021). Once intracellular, the pathogen's strategy shifts dramatically.

SPI-2, induced within the unique environment of the *Salmonella*-containing vacuole (SCV), deploys a second set of effectors via T3SS-2 (e.g., SifA, SseF). These proteins remodel the SCV, preventing its fusion with lysosomes, recruiting host cell organelles like the Golgi apparatus for nutrient acquisition, and enabling bacterial replication. This intracellular niche is key for systemic spread to deeper organs like the spleen and liver, particularly in systemic infections (Farhat *et al*., 2023).

This core pathogenic toolkit, however, is differentially deployed and complemented by serovar-specific adaptations. Host-adapted avian serovars (*S. Gallinarum, S. Pullorum*) are highly invasive, causing acute systemic typhoid-like diseases in poultry but rarely infecting humans, likely due to genome degradation, host-specific metabolic adaptations, and a distinct repertoire of surface structures (Zhao *et al*., 2024). In contrast, generalist zoonotic serovars (*S. Enteritidis, S. Typhimurium*) have evolved a more nuanced relationship with their avian hosts. They often cause subclinical or mild intestinal infections in chickens, allowing for persistent cecal colonization and fecal shedding without debilitating the host—a perfect strategy for silent dissemination through flocks and into the food chain (Mc Ewen *et al*., 2018). This dichotomy is central to the One Health challenge: the very trait (low host pathogenicity) that makes a serovar successful and persistent in poultry production makes it a stealthy and prolific contaminant of human food.

The mobile resistome: Plasmids, integrons, and the acceleration of AMR

The MDR phenotype in contemporary poultry *Salmonella* is predominantly a consequence of horizontal gene transfer (HGT), a process turbocharged in the microbial-dense environment of the poultry gut under constant antibiotic selection pressure (Li *et al*., 2022).

Plasmids are the primary vectors of resistance spread. Specific plasmid incompatibility groups have become notorious in poultry isolates. Narrow-host-range IncI1 and IncFIB plasmids are prolific carriers of ESBL genes (blaCTX-M-1, -55, -65) (Roswandowicz

et al., 2018). Broad-host-range plasmids like IncA/C2, IncHI2, and the recently recognized IncX1 and IncX4 are of particular concern as they can transfer between diverse Gram-negative bacteria. These plasmids often carry an astonishing array of resistance determinants to virtually all major antibiotic classes (beta-lactams, quinolones, aminoglycosides, tetracyclines, sulfonamides, phenicols), frequently organized within complex transposon and integron structures [8, 54]. The co-localization of multiple resistance genes on a single, transmissible plasmid means that the use of any one antibiotic can select for and maintain resistance to many others, a phenomenon known as co-selection (Gillieatt *et al*., 2024).

Class 1 Integrons are highly efficient gene-capturing and expression systems central to the assembly of MDR profiles. They consist of an integrase gene (intI1), a primary recombination site (attI1), and a promoter (Pc) driving expression of captured gene cassettes (Cambray *et al*., 2010). In poultry *Salmonella*, these cassettes most commonly encode resistance to aminoglycosides (aadA variants), trimethoprim (dfrA variants), and beta-lactams (blaOXA, blaGES). Integrons are frequently embedded within transposons (like Tn21) and located on conjugative plasmids, creating powerful, nested mobile genetic units that facilitate the rapid evolution, consolidation, and global spread of complex resistance patterns (Gharieb *et al*., 2015).

The Fitness Cost Paradigm and Compensatory Evolution: Traditional models suggested that carriage of large MGEs imposed a metabolic fitness cost on bacteria, potentially limiting their spread in the absence of antibiotic selection. However, emerging high-risk clones like MDR *S. Infantis* challenge this view. The pESI plasmid, for example, appears to carry beneficial genes beyond resistance (e.g., for heavy metal detoxification, disinfectant tolerance, enhanced virulence) that likely enhance bacterial fitness in the specific niche of the modern poultry farm environment (Aviv *et al*., 2016). This compensatory evolution ensures the plasmid's stability and the clone's success even in the absence of direct antibiotic pressure, making eradication more difficult.

Persistence in the environment: Biofilms and stress responses

Controlling *Salmonella* is not just about treating infected birds; it is about eradicating it from the production environment, where it proves remarkably resilient through adaptive mechanisms (Hald *et al*., 2004). Many strains form robust, multi-layered biofilms on abiotic surfaces—water pipes, feed troughs, cage materials, and conveyor belts in processing plants. Biofilm formation, primarily regulated by the csgD-controlled production of curli fimbriae and cellulose, encases bacterial communities in a protective extracellular polymeric substance (EPS) matrix (Steenackers *et al*, 2012). This EPS matrix acts as a formidable barrier,

significantly reducing the penetration and efficacy of disinfectants and desiccants, and shielding embedded bacteria from host immune responses upon ingestion (Vestby *et al*., 2020). Furthermore, *Salmonella* employs a suite of overlapping global regulatory systems to survive transient harsh conditions. The RpoS (σS) regulon governs the general stress response to starvation, osmotic, and oxidative stress. The PhoP/PhoQ two-component system is crucial for survival within macrophages and adaptation to magnesium limitation and acidic pH, such as that encountered in organic acid-treated feed or the host stomach (Groisman *et al*., 2001). This combination of biofilm-mediated protection and robust stress response machinery turns farm infrastructure and equipment into persistent environmental reservoirs, enabling the reinfection of successive flocks even after depopulation and standard cleaning procedures—a major hurdle for effective biosecurity.

Diagnostic frontiers: Informing precision control

Effective intervention is predicated on accurate, timely, and informative diagnosis. The diagnostic paradigm has evolved decisively from mere detection towards detailed characterization for actionable intelligence and surveillance.

Culture-based and serological methods: Foundational tools

Despite the advent of rapid methods, traditional culture following internationally recognized protocols like ISO 6579-1 remains the indispensable gold standard (ISO, 2017). Its strengths are irreplaceable: it confirms the presence of viable, cultivable organisms, provides pure isolates essential for all downstream phenotypic analyses (serotyping, antimicrobial susceptibility testing - AST), and serves as the definitive benchmark for validating novel diagnostic techniques. The multi-step process—non-selective pre-enrichment (e.g., Buffered Peptone Water) to recover stressed cells, selective enrichment (e.g., Modified Rappaport-Vassiliadis broth), plating on differential and selective agars (XLD, Brilliant Green), followed by biochemical confirmation—is robust but time-consuming, typically requiring 4-7 days for a confirmed result (Andrews *et al*., 2020). Serological assays, particularly enzyme-linked immunosorbent assays (ELISA), play a different but valuable role in flock-level health monitoring. By detecting anti-*Salmonella* antibodies in serum or egg yolk, they can indicate past exposure and assess the effectiveness of vaccination programs or the historical infection pressure within a flock, though they cannot distinguish between serovars or confirm active, ongoing infection (Van Kessel *et al*., 2008).

The molecular and genomic revolution: Speed, specificity, and surveillance

Molecular techniques have dramatically accelerated and refined *Salmonella* diagnostics, enabling a shift from reactive to proactive management.

Real-time PCR (qPCR), This technology allows for the highly sensitive, specific, and quantitative detection of *Salmonella* DNA (often targeting the invA gene) and discrimination of key serovars (e.g., *S. Enteritidis, S. Typhimurium*) directly from complex sample matrices within a few hours (Malorney *et al*., 2004). This enables rapid screening of feed, environmental swabs, or cloacal samples, facilitating prompt on-farm decisions regarding flock status and the need for interventions before contamination spreads.

Whole-Genome Sequencing (WGS), WGS represents a transformative leap forward, becoming the ultimate tool for modern, high-resolution public health and veterinary surveillance (Tyson *et al*., 2015). It delivers a comprehensive digital genetic blueprint of an isolate. Subsequent bioinformatic analysis pipelines can simultaneously and accurately predict: Serovar (via in silico serotyping), the complete Antimicrobial Resistance Gene (ARG) profile (resistance), the presence of Virulence Factors and plasmid replicons (pathogenic potential), and provide high-resolution Phylogenetic clustering (relatedness). This allows investigators to link isolates from farms, feed mills, processing plants, and human clinical cases with unprecedented precision, distinguishing between sporadic cases and true outbreaks, and tracing transmission pathways back to their source (Ashton *et al*., 2016). The integration of WGS into routine surveillance transforms it from a reactive, descriptive activity into a predictive, intelligence-driven system capable of tracking the emergence and spread of high-risk clones like pESI-positive *S. Infantis* in near real-time (Nadon *et al*., 2017).

Integrated mitigation: A synergistic one health framework

No single intervention can solve the MDR *Salmonella* crisis. Success lies in the simultaneous, synergistic, and sustained application of multiple strategies across the entire production chain, underpinned by the One Health principle.

Foundational pillar: Antimicrobial stewardship and regulatory action

Prudent and responsible use of antimicrobials in poultry production is the non-negotiable first step to reduce the selection pressure that fuels resistance (WHO, 2019). This requires a multi-faceted approach:

Eliminating all use of antibiotics for growth promotion, a practice already banned in the European Union, many other countries, and advocated globally by the WHO (EMA, 2016).

Restricting prophylactic (preventive) use to very high-risk, time-limited situations under strict veterinary prescription, moving away from routine, metaphylactic administration in feed or water.

Ensuring therapeutic use is based on clinical signs and, whenever possible, guided by antimicrobial susceptibility testing (AST) results to promote targeted

rather than empirical broad-spectrum treatment.

Strict adherence to legally mandated withdrawal periods to prevent violative antibiotic residues in meat and eggs, which also pose a direct consumer health risk (PHAC, 2023).

National regulatory frameworks must enact, enforce, and regularly update policies aligned with international standards set by the WHO, OIE (WOAH), and Codex Alimentarius (CAC, 2021). Importantly, reducing antibiotic use must be proactively paired with investments in improved animal husbandry, nutrition, and health management to prevent disease outbreaks, avoiding a vacuum that could lead to increased morbidity and welfare issues.

Breaking the chain: Biosecurity, hygiene, and feed safety

Robust, multi-level biosecurity forms the primary physical barrier to prevent pathogen introduction and on-farm spread (Altekruse *et al*., 1997). Effective measures include: secured perimeter fencing, controlled access points with sanitation protocols (footbaths, changing clothing/ footwear), comprehensive vermin (rodents, insects) and wild bird control programs, and operational practices like strict all-in/all-out production with thorough cleaning and disinfection between flocks. Feed hygiene is particularly critical, as contaminated feed is a major introduction route. Heat treatment (pelleting) at temperatures exceeding 85°C is effective in reducing *Salmonella* load, but meticulous attention must be paid to preventing re-contamination during cooling, transportation, and on-farm storage (Zhuang *et al*., 2024). Water sanitation, through continuous chlorination, UV treatment, or acidification, is equally vital. Disinfection protocols must be scientifically validated against prevalent local strains and biofilm forms; oxidizing agents like peracetic acid/hydrogen peroxide blends and chlorine dioxide have shown efficacy against *Salmonella* biofilms when applied with sufficient contact time and in conjunction with mechanical cleaning to remove organic debris that inactivates many disinfectants (Van Kessel *et al*., 2008; de Oliveira *et al*., 2021)).

Vaccination: A targeted immunological shield

Vaccination remains one of the most powerful and direct tools for controlling specific *Salmonella* serovars within flocks [20]. Both live attenuated (e.g., S. Typhimurium and S. Enteritidis mutants) and killed/inactivated vaccines are commercially available. Vaccination of layer and breeder flocks has been a cornerstone of successful national control programs in the EU and US, significantly reducing egg-borne transmission of *S. Enteritidis* by decreasing ovarian colonization and fecal shedding (Gast *et al*., 2024). The ideal vaccine induces robust mucosal and systemic immunity, reducing intestinal colonization and subsequent environmental contamination. Current challenges include the economic and

practical hurdles of developing and deploying multivalent vaccines effective against emerging serovars like *S. Infantis* and *S. Kentucky*, and ensuring long-term vaccine efficacy does not wane under the high bacterial challenge pressures present in endemic settings.

The unifying system: Genomic surveillance and data integration

Integrated, genomics-powered surveillance acts as the "central nervous system" of a modern One Health response to AMR (Elrashedy *et al.*, 2025). It involves the systematic collection, WGS analysis, and shared interpretation of *Salmonella* isolates from across the continuum: poultry (farm, slaughterhouse), retail meat, feed, and human clinical cases. Shared, accessible databases and platforms (e.g., PulseNet, ENTEROBASE) allow public health officials, veterinarians, and food safety agencies to:

- Identify and confirm if human salmonellosis cases are linked to a particular poultry source, product, or clone.
- Monitor in near real-time the evolution, geographic spread, and antimicrobial resistance patterns of high-risk MDR clones.
- Detect diffuse clusters of infections that may signal an emerging outbreak long before traditional epidemiological methods would connect them.
- Objectively evaluate the impact of on-farm or processing interventions by tracking changes in the prevalence and genetic makeup of circulating strains over time.

This intelligence-driven, precision-public-health approach allows for targeted, cost-effective interventions—such as focusing enhanced controls on farms harboring specific high-risk clones—rather than relying on broad, indiscriminate, and often less effective blanket measures [80].

Conclusion and future imperatives

The battle against multidrug-resistant *Salmonella* in poultry is a defining One Health challenge of our time, a complex battle being fought simultaneously in the microbiological arena, within agricultural and economic systems, and at the local and global policy table. This review affirms that while the pathogenic mechanisms, genetic drivers of resistance, and principles of control are increasingly well-understood, the translation of this knowledge into effective, equitable, and sustainable action remains inconsistent and geographically fragmented.

The emergence of "super-clones" like pESI-positive *S. Infantis* signals a new, more concerning phase in the AMR crisis, where resistance, virulence, and environmental persistence are co-opted and packaged together on highly transmissible genetic platforms, conferring a formidable fitness advantage in modern production settings. This evolution demands an equally sophisticated, agile, and globally coordinated response. The path forward must be built on several key, interdependent imperatives:

1. Closing the Surveillance and Capacity Gap: A major global inequity exists in AMR and genomic surveillance capacity. Strengthening laboratory infrastructure, promoting standardized methodologies, and fostering "train-the-trainer" partnerships with and within LMICs are critical to generate a true, representative global picture, direct resources effectively, and ensure no region becomes a blind spot for emerging threats.
2. From Prudent Use to a Post-Antibiotic Toolkit: Stewardship must evolve beyond simply reducing antibiotic use to actively promoting, validating, and facilitating the adoption of effective alternatives. This requires increased investment in research and commercialization of next-generation vaccines (e.g., subunit, mRNA), pre- and probiotics, bacteriophages, enzymes (e.g., bacteriocins), phytogenics, and optimized nutrition strategies that enhance gut health and provide robust competitive exclusion against *Salmonella* colonization.
3. Implementing Economic and Social Levers: For farmers, especially smallholders in LMICs, control measures must be economically viable and socially acceptable. This may involve innovative financing models, subsidies for vaccines or biosecurity infrastructure, insurance schemes linked to good practices, and market-based incentives (premiums, certification schemes) that reward producers for adhering to higher standards of biosecurity and stewardship.
4. Adopting Holistic Farm Ecosystem Management: Future strategies must view the farm as an interconnected ecological unit. This includes advanced manure and litter management to reduce environmental loading, wastewater treatment, and understanding/managing wildlife-livestock interfaces to break environmental transmission cycles. Furthermore, genetic selection for poultry breeds with enhanced innate disease resilience and robustness could provide a sustainable long-term foundation for health.
5. Ensuring Sustained Political Will and Deepened International Collaboration: *Salmonella* and AMR genes respect no borders. Sustained high-level political commitment, enshrined in funded national action plans aligned with the Global Action Plan on AMR, is essential. International bodies (WHO, FAO, WOAH, Codex) must strengthen their roles in facilitating norm-setting, standard development, and cooperative frameworks for joint outbreak response and information sharing.

In conclusion, curbing the pandemic of MDR *Salmonella* from poultry is an immense but achievable goal. It requires a decisive move from a reactive, pathogen-centric model to a proactive, system-based One Health approach. By integrating cutting-edge science with smart economics, equitable policies, and unwavering international cooperation,

we can protect the efficacy of our life-saving antimicrobials, ensure the safety and sustainability of our food supply, and safeguard public health for generations to come. The time for fragmented action has passed; the era of integrated, intelligent, and collective defense must begin.

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