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## Trends in a Persistent Strain of Multidrug-Resistant *Salmonella* Infantis (REPJFX01) in Humans and Chickens — United States, 2010–2023

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### Abstract

Chicken is a major source of foodborne salmonellosis in the United States. The number of human illnesses and the prevalence in chicken of a multidrug-resistant strain of *Salmonella enterica* serotype Infantis called REPJFX01 have increased during the last decade. REPJFX01 isolates are often resistant to antibiotics used for treatment including ampicillin, ceftriaxone, ciprofloxacin, and trimethoprim-sulfamethoxazole. Using data from the U.S. Centers for Disease Control and Prevention's PulseNet system and the U.S. Department of Agriculture's Food Safety and Inspection Service during 2003–2023, we examined trends in REPJFX01 isolation from humans and chicken carcasses to assess whether they coincide. We used penalized B-spline generalized additive models to quantify trends in human infection burden and REPJFX01 prevalence on chicken carcasses. We used a time-lagged rank-order cross-correlation to characterize the association between the two time series. A significant, increasing annual trend in the incidence of human infections and chicken carcass prevalence began in 2016. A 0-year lag on chicken carcass REPJFX01 prevalence maximized rank-order cross-correlation with REPJFX01 infection burden in humans. REPJFX01 trends in humans and chickens appear coincident (both occurring during the same time period), suggesting that chickens may be an important reservoir for REPJFX01.

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**Disclaimer:** The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

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Efforts to prevent *Salmonella* contamination of chicken and strengthen safe handling and cooking of chicken should be prioritized.

## Keywords

foodborne diseases; *Salmonella* enterica; incidence; chicken; serovar Infantis; REP strain

## Introduction

Nontyphoidal *Salmonella* (referred to as *Salmonella* hereafter) is a leading cause of foodborne bacterial enteric disease in the United States, affecting an estimated 1.3 million people each year (Scallan Walter et al., 2025). Chicken is a major source of foodborne salmonellosis; in 2022, 20% of domestically acquired foodborne salmonellosis was attributed to chicken based on outbreak data (IFSAC, 2024). *Salmonella enterica* serotype Infantis (Infantis) is the sixth most frequently reported serotype among cases monitored by the Centers for Disease Control and Prevention's (CDC) Foodborne Diseases Active Surveillance Network (FoodNet) (Shah et al., 2024). Although most Infantis infections are sporadic (not associated with outbreaks), Infantis outbreaks linked to chicken during 2012–2021 had a high burden of illness with an increased outbreak trajectory in terms of outbreak associated illnesses (Marshall et al., 2024); as of 2023, Infantis outbreaks linked to chicken had a low burden with decreasing trajectory (CDC, 2025). A study comparing trends in the incidence of human Infantis infection with Infantis prevalence in chicken at processing suggested that the increase in human Infantis infection was likely due to non-chicken transmission pathways (Powell and Williams, 2024).

A multidrug-resistant (MDR) strain of Infantis was first detected in a U.S. resident in 2012; this resident reported traveling to Peru prior to illness onset. Since then, reports of illness from this strain have increased to approximately 500 culture-confirmed illnesses annually during 2018–2024. Although Infantis is only the 6<sup>th</sup> most common serotype causing human illness (Shah et al., 2024), interest in this serotype is high due to the frequency of MDR. The persisting strain, identified as REPJFX01, is monitored by the CDC as a reoccurring, emerging, or persisting (REP) strain and varies in genetic diversity beyond the typical outbreak strain (CDC, 2024d). Most REPJFX01 isolates have a chromosomal mutation in the *gyrA* gene and a pESI-like megaplasmid that carries resistance to multiple antimicrobials, including several that are recommended for first-line or alternative treatment (CDC, 2024d, Tate et al., 2017). Although most people with salmonellosis recover without antibiotics, resistance is concerning because, if treatment is needed, infections resulting from REPJFX01 may not be treatable with antibiotics commonly recommended for *Salmonella*. Additionally, resistance genes and mutations on mobile plasmids such as pESI can more easily spread to other bacteria, including human and animal pathogens.

REPJFX01 illnesses have historically been linked to international travel and chicken. Local, state, federal health, and regulatory partners investigated 11 outbreaks of REPJFX01 illness during 2016–2023 and identified chicken products as the suspected or confirmed source in three of six outbreaks with a known source. A chicken-associated outbreak of REPJFX01

has not been identified since 2019. (CDC, 2024d, Hutchinson et al., 2018). REPJFX01 has been isolated from the primary U.S. meat and poultry commodities (beef, pork, turkey, chicken), but it is most often isolated from chicken products (CDC, 2024d). Other potential reservoirs of REPJFX01 (i.e., other food, animal, and environmental samples) are not as routinely sampled and reported to PulseNet. Consequently, more than 93% of the >7000 non-clinical REPJFX01 isolates submitted to CDC were from poultry or poultry products (CDC, 2024d), most of which were collected by the USDA due to the Agency's extensive poultry sampling programs (USDA-FSIS, 2021a).

Because there may be different transmission pathways for different strains of *Infantis*, we aimed to examine the emergence and trends of REPJFX01 in humans and chickens to assess whether these trends coincide.

## Material and methods

### Data sources.

To assess trends in human infections, we used data from PulseNet, a national laboratory network that gathers isolate data to identify the *Salmonella* strains making people sick and detect potential outbreaks. We queried all *Infantis* isolates submitted to PulseNet during 2003–2023. To meet the current molecular definition for REPJFX01, *Infantis* isolates must undergo whole genome sequencing (WGS) and fall within an overall range of 0 to 82 allele differences by core genome multilocus sequence typing (cgMLST) (CDC, 2024d). Isolates meeting this definition were included in the analysis; we excluded isolates known to be collected from the same patient and the same episode of illness.

Many human isolates collected before 2019 did not undergo WGS. In this analysis, we wanted to capture non-sequenced isolates that would fit the REPJFX01 definition if they underwent WGS. We linked PulseNet data with antimicrobial resistance data from the CDC's National Antimicrobial Resistance Monitoring System (NARMS). CDC NARMS is a U.S. public health surveillance system that tracks antimicrobial resistance in enteric bacteria from humans by conducting antimicrobial susceptibility testing on clinical isolates received at CDC from public health laboratories (including 5% of *Salmonella*), and by screening sequenced isolates submitted to PulseNet for resistance genes and mutations (as previously described (CDC, 2018, CDC, 2024b)). Nearly all REPJFX01 isolates are nonsusceptible to fluoroquinolones due to a chromosomal mutation in the *gyrA* gene (CDC, 2024d). This mutation typically confers resistance to the quinolone nalidixic acid and nonsusceptibility to ciprofloxacin (MIC  $\geq 0.12$   $\mu\text{g/ml}$ ). We used the strain's unique antibiotic resistance and pulsed-field gel electrophoresis (PFGE) results to identify non-sequenced REPJFX01 isolates. A non-sequenced isolate was defined as REPJFX01 if it had resistance to nalidixic acid and a PFGE pattern found among sequenced REPJFX01 isolates (Supplementary Data 1).

To assess trends in REPJFX01 prevalence in chicken, we used data from routine sampling of young chicken carcasses for Hazard Analysis and Critical Control Points (HACCP) verification by the United States Department of Agriculture's (USDA) Food Safety and Inspection Service (FSIS). HACCP plans identify controls at points in a food production

process where hazards can be prevented, controlled, eliminated, or reduced. Verification sampling provides an opportunity to verify that a HACCP plan is preventing microbial contamination and/or growth (USDA-FSIS, 2021b). The methods used by USDA-FSIS for detecting *Salmonella* in young chicken carcasses for HACCP verification have been described previously (Gamble et al., 2016, Powell and Williams, 2024). To determine the number of young chicken carcass samples tested annually during 2003–2023, we used data available from the USDA-FSIS website (FDA, 2024, USDA-FSIS, 2016, USDA-FSIS, 2024). Sequenced isolates from chicken carcass samples that met the cgMLST definition for REPJFX01 were provided by USDA-FSIS. To identify chicken carcass REPJFX01 isolates during 2003–2014 that did not undergo WGS, we used antimicrobial susceptibility and PFGE data from HACCP samples submitted to NARMS, as described above (FDA, 2024).

### Trends analysis.

All analyses were conducted in R version 4.4.0. Similar to Powell and Williams' analysis of Infantis incidence in humans and prevalence on chicken carcasses, we used generalized additive models with cubic penalized B-spline regression to separately examine the trends for burden of REPJFX01 human infections (number of REPJFX01 isolates submitted to PulseNet) and chicken carcass prevalence (Powell and Williams, 2024). To assess change in the burden of human REPJFX01 infections over time, we implemented separate Poisson and negative binomial regressions and then determined which had the best fit. We used a log offset of population in the negative binomial model using U.S. Census Bureau population data (U.S. Census Bureau, 2024).

We implemented separate generalized logistic and negative binomial regressions to assess the change in chicken carcass REPJFX01 prevalence over time. A log offset of the total samples tested was used as an offset in the negative binomial regression. Although there was a change in chicken carcass testing during 2016–2019 with the adoption of the use of neutralizing Buffered Peptone Water, we did not include an indicator variable for these changes based on the previous analysis (Powell and Williams, 2024).

Similar to Powell and Williams (Powell and Williams, 2024), we used a second-order difference penalty and an unconstrained basis of dimension  $k = 10$  in the human and chicken models, performed a diagnostic test for whether the basis dimension for a smooth function was adequate, and used the Ljung-Box test to test for first-order autoregressive [AR(1)] serial correlation. We compared model fit using the Akaike information criterion (AIC). The results from the models with the lowest AIC were reported.

### Rank-order cross-correlation analysis.

We performed a time-lagged rank-order cross-correlation analysis to measure the association between the human and chicken time series, similar to Powell and Williams (Powell and Williams, 2024). We implemented this analysis in R using the ccf function in the tseries package, transforming the human burden and chicken prevalence into respective rank-order data by year (Trapletti et al., 2024).

### Sensitivity analyses.

We performed a sensitivity analysis that excluded travel-associated cases from the human data set because exposures may differ between domestically acquired infections and infections associated with international travel (Brown et al., 2018, CDC, 2024d). Also, we conducted a sensitivity analysis using data from chicken product sampling because the type of chicken product tested may affect the observed trends. Chicken product data include routine microbiological sampling of raw chicken parts and comminuted chicken (excluding carcasses) collected at federally inspected slaughter establishments under USDA-FSIS jurisdiction.

### Ethics.

This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and policy.<sup>1</sup>

## Results

During 2003–2023, there were 3,307 reported REPJFX01 human infections; 3,297 human isolates underwent WGS and 10 were not sequenced but met the REPJFX01 definition based on resistance and PFGE pattern Supplementary Data 1. The first identified human REPJFX01 infection occurred in 2012, and by 2019, REPJFX01 accounted for approximately 30% of all human clinical *Infantis* isolates (Figure 1). There were 516 REPJFX01 chicken carcass isolates; all underwent WGS. REPJFX01 was first isolated from a chicken carcass sample in 2016, and by 2019, REPJFX01 accounted for >90% of all *Infantis* isolated from chicken carcass samples (Figure 1).

### Trends analysis.

Since REPJFX01 was first identified in humans and chicken carcasses after 2010, we limited our analyses to 2010–2023. The Poisson regression provided the best fit for the human data and the negative binomial model provided the best fit for the chicken data (Figure 2). Both models demonstrated a significant annual increasing trend ( $p < 0.001$ ); REPJFX01 illnesses in humans and prevalence on chicken carcasses both began to increase in 2016. Using the diagnostic test for basis dimension and the Ljung-Box test, we confirmed that the default unconstrained basis dimension ( $k = 10$ ) was sufficient and that there was no evidence of AR(1) serial correlation, respectively.

### Rank-order cross-correlation analysis.

The rank-order cross-correlation showed that the increase in REPJFX01 human illness and prevalence on chicken carcasses also began in 2016, supporting the regression results. Specifically, a 0-year lag on chicken carcass REPJFX01 prevalence maximized rank-order cross-correlation with human REPJFX01 infections (estimated cross-correlation value 0.88).

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<sup>1</sup>See 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq

### Sensitivity analyses.

Results of the sensitivity analyses were consistent with the main results and are reported in Supplementary Data 2.

### Discussion

We found that the increase in U.S. illnesses due to REPJFX01 coincided with the emergence of REPJFX01 in U.S. chicken carcasses in 2016, and both REPJFX01 illnesses and carcasses have increased since 2016. Combined with findings from surveillance, outbreak investigations, and evidence that REPJFX01 emerged as a leading strain in retail chicken since 2016 (Brown et al., 2018, CDC, 2024d, McMillan et al., 2022, Tyson et al., 2021), our analysis suggests that chicken is likely an important reservoir.

MDR Infantis strains with a pESI-like plasmid, such as REPJFX01, are not unique to the United States. These MDR Infantis strains likely originated in South America and have been isolated from humans, animals, and the environment around the world (Alvarez et al., 2023, Georganas et al., 2024, Guzinski et al., 2023, Li et al., 2024, Mattock et al., 2024). Although there are several reservoirs for MDR Infantis (CDC, 2024d), it has spread rapidly among chickens globally (Alvarez et al., 2023, Kim et al., 2024, Tate et al., 2017, Tyson et al., 2021). In a systematic review, broilers and chicken meat were found to be the primary sources for MDR Infantis strains (Alvarez et al., 2023). The pESI plasmid has multiple characteristics that contribute to the selection and persistence of this strain in chickens, including fimbria and siderophores, resistance genes, and a higher tolerance to hydrogen peroxide (McMillan et al., 2024, McMillan et al., 2020, Tate et al., 2017).

Illness due to MDR Infantis with a pESI-like plasmid is a public health concern. Globally, these infections have been associated with increased virulence (Alvarez et al., 2023, Fenske et al., 2023, Tyson et al., 2021). In the United States, a recent study did not classify Infantis as a higher virulence serotype (Fenske et al., 2023), and serotypes other than Infantis (e.g., Enteritidis and Typhimurium) have a much higher overall burden (~1% of *Salmonella* uploads to PulseNet are REPJFX01). However, public health surveillance data show that the hospitalization rate for REPJFX01 infection is comparable to that of other serotypes classified as having higher virulence, like *S. Enteritidis* and *S. Typhimurium* (all ~30%) (CDC, 2024d, CDC, 2024e). Additionally, MDR Infantis is more likely to result in extraintestinal infections compared with non-MDR Infantis (CDC, 2024d, Fenske et al., 2023). Also, the antibiotic resistance carried by these isolates is concerning because it can complicate treatment when treatment is needed (Shane et al., 2017), and the plasmid and resistance genes can spread to other *Salmonella* serotypes and pathogens (FDA, 2022, Li et al., 2024, Tate et al., 2017, Tyson et al., 2021).

Poultry is a leading source of *Salmonella* foodborne illness in the United States. People can become infected with *Salmonella* when handling raw chicken, eating undercooked chicken, or eating other foods and beverages that are contaminated by raw chicken or its juices (CDC, 2024c). There is evidence from US outbreak investigations and the international literature that chicken consumption is a transmission pathway for (sometimes severe) human MDR Infantis illness (Alvarez et al., 2023, CDC, 2024d). Also, REPJFX01 has spread rapidly in

chickens in the United States (Tyson et al., 2021). Most REPJFX01 isolates from non-human sources reported to PulseNet were from chicken product samples (CDC, 2024d), and in our study, REPJFX01 accounted for 21% of all *Salmonella* and 97% of all *Infantis* isolated from chicken carcasses in 2023. However, not all potential reservoirs for REPJFX01 are as robustly sampled (e.g., water, wildlife and other environmental sources). REPJFX01 illnesses have not been linked to contact with live animals, such as backyard chickens, but two *Infantis* isolates with *gyrA* mutations were isolated from backyard poultry compost during a study of backyard and commercial broiler production systems in the Southeastern United States (Parzygnat et al., 2025).

*Salmonella* prevention measures are important to prevent salmonellosis in humans. However, *Salmonella* strains carrying a pESI plasmid may be harder to prevent in chicken environments; their characteristics (e.g., oxidizer tolerance, fimbriae that increase epithelial attachment, increased biofilm production) can make standard cleaning and disinfection protocols less effective (McMillan et al., 2024, Newton et al., 2020). Disinfecting feeder lines and external areas and applying bacteriophages after cleaning and before disinfection were shown to effectively reduce MDR *Infantis* in commercial broiler facilities (Newton et al., 2020, Sevilla-Navarro et al., 2024). Furthermore, consumers can prevent REPJFX01 and other *Salmonella* infections by keeping raw meat and poultry separate from ready-to-eat food, by washing hands and food contact surfaces after handling raw poultry, and by using a food thermometer to ensure poultry is cooked to an internal temperature of 165°F (CDC, 2024a).

This study has several limitations. First, our analysis of human REPJFX01 infections was limited to culture-positive infections reported to PulseNet. Ill persons with REPJFX01 who did not seek medical care or did not have their diagnosis culture-confirmed do not appear in the PulseNet database. We also may have missed some REPJFX01 infections because not all *Salmonella* isolates underwent WGS, particularly before 2019. We calculated a sensitivity of 99.9% and specificity of 98.7% of resistance to nalidixic acid for REPJFX01 isolates compared with other *Infantis* isolates (Table A.2), and few isolates that did not undergo sequencing had nalidixic acid resistance and a PFGE that mapped to REPJFX01, suggesting that such cases were likely rare. Second, travel history was not routinely reported to CDC, so we were unable to exclude all international travelers from our analyses; the sensitivity analysis excluding patients with known international travel found similar results to the main analysis. Third, our analysis focused only on REPJFX01 isolated from chicken, although other non-human sources have been reported to PulseNet. Furthermore, we limited our analysis of REPJFX01 prevalence to chicken carcass isolates because chicken carcass sampling methods were more consistent throughout the study period, isolates were routinely submitted to PulseNet, and our sensitivity analysis found similar results when using chicken product data. Lastly, our analysis only establishes a correlation between trends in human infections and chicken carcass prevalence and consequently does not show causation and should not be used to infer attribution. Further research to attribute REPJFX01 illnesses to food sources and more robust sampling and inclusion of non-chicken isolates in PulseNet would be useful to assess chicken consumption as a potential transmission pathway and contextualize it alongside other sources potentially contributing to the overall burden of REPJFX01 human illness.

## Conclusions

Although there are likely multiple sources for REPJFX01 infection, the increase in REPJFX01 burden in human illness is highly correlated and concurrent with the increase in prevalence on chicken carcasses. This important MDR strain should be considered in *Salmonella* prevention strategies. Consumers can prevent REPJFX01 by practicing safe food handling and cooking practices.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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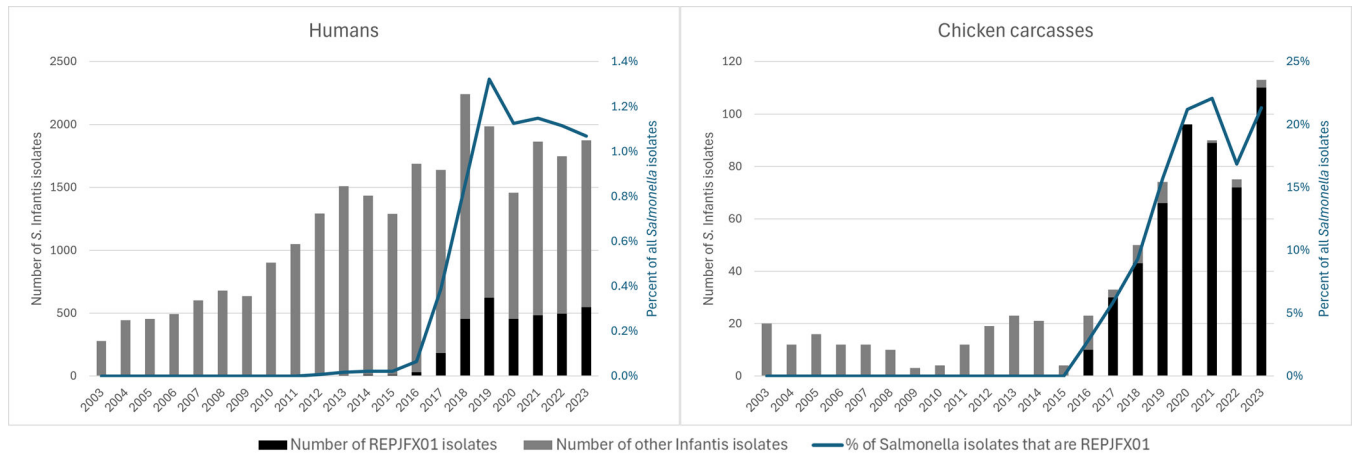


**Figure 1:** Number and percent of REPJFX01 and other *Salmonella* *Infantis* isolates in humans and chicken carcasses, PulseNet (humans) and United States Department of Agriculture (USDA) Food Safety and Inspection Service (chicken carcasses), 2003–2023

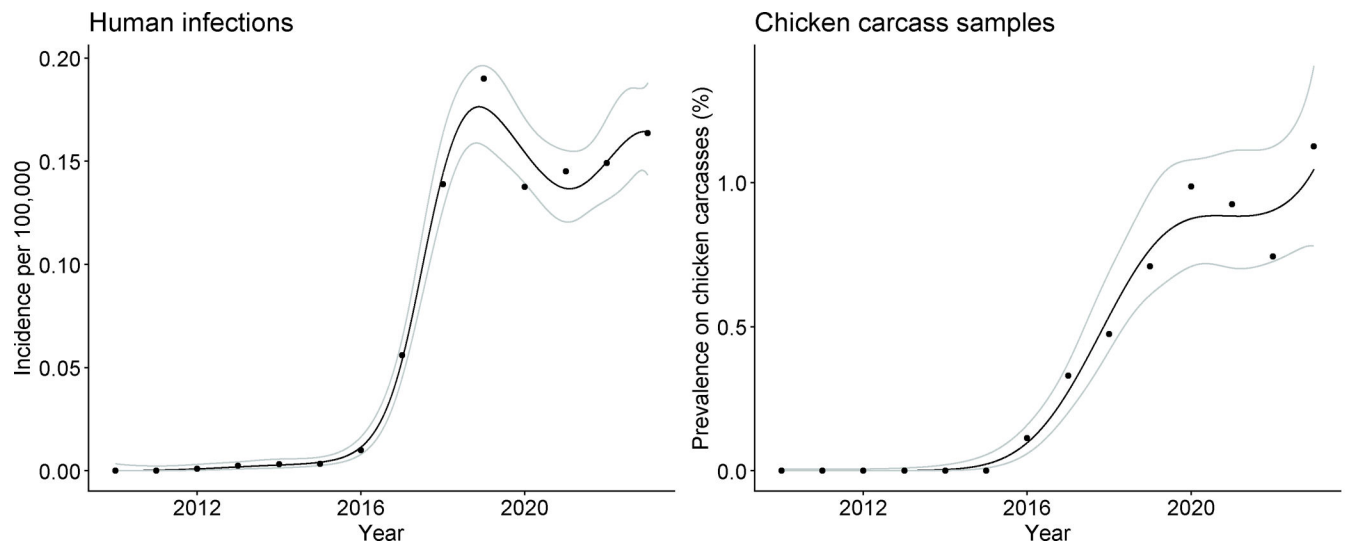


**Figure 2:**

Penalized B-spline regression of annual reported PulseNet isolates per 100,000 population of REPJFX01 infections (Human infections) and annual reported United States Department of Agriculture (USDA) Food Safety and Inspection Service chicken carcass REPJFX01 prevalence (Chicken carcass samples), 2010–2023. Black dots = observed data, black line = mean curve, gray lines = upper and lower 95% confidence band.