**Distribution Agreement**

Factors Associated with Sporadic Infections of *Salmonella enterica* Serotype Infantis, Foodborne Diseases Active Surveillance Network (FoodNet)

By

Preethi R. Sundararaman

Master of Public Health

Epidemiology

---

John E. McGowan, Jr., MD

Faculty Thesis Advisor

---

Aimee L. Geissler, PhD, MPH

Thesis Field Advisor

---

Olga L. Henao, PhD, MPH

Thesis Field Advisor

Factors Associated with Sporadic Infections of *Salmonella enterica* Serotype Infantis, Foodborne Diseases Active Surveillance Network (FoodNet)

By


Preethi R. Sundararaman

Bachelor of Science

The College of William & Mary

2011


Faculty Thesis Advisor: John E. McGowan, Jr., MD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2015

**Abstract**

Factors Associated with Sporadic Infections of *Salmonella enterica* Serotype Infantis, Foodborne Diseases Active Surveillance Network (FoodNet)

By Preethi R. Sundararaman

A recent increase in incidence of infections with *Salmonella enterica* serotype Infantis (*S.* Infantis) has been observed in the United States, but sporadic infections have not been well described. This study looked at Foodborne Diseases Active Surveillance Network (FoodNet) data from 2004-2014 to describe sporadic cases of infection with *S.* Infantis by age group, race, ethnicity, sex, season, and annual incidence. Data from a 2014 FoodNet case exposure ascertainment initiative were examined to identify foodborne, waterborne, or environmental factors associated with infection of *S.* Infantis. FoodNet surveillance includes 48 million persons, representing 15% of the U.S. population, from ten sites. This study employed a case-case comparison methodology, using persons with sporadic infections of *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, or I 4,[5],12:i:- as ill controls. Because the process by which infections are reported to surveillance is non-random, traditional case-control methodology has limitations when applied to surveillance data. Case-case comparisons have been proposed as an alternative analytic method to address these limitations. During 2004-2014, a total of 1,268 sporadic laboratory-confirmed infections of *S.* Infantis and 42,448 sporadic laboratory-confirmed infections of other *Salmonella* serotypes were reported to FoodNet. Annual incidence of sporadic infections of *S.* Infantis in 2014 was the highest observed during the 2004-2014 period. New cases of sporadic infections of *S.* Infantis were most likely to occur in children less than 5 years of age, Asian persons, and persons of Hispanic ethnicity. Exposure information was available for 96 persons with infection of *S.* Infantis and 2,040 persons with infections of other *Salmonella* serotypes reported to FoodNet in 2014. In multivariable analysis adjusting for FoodNet site, season, and exposures reported by ≥10% of cases, contact with pet birds and live poultry were significantly associated with sporadic infection of *S.* Infantis when compared to infections of other *Salmonella* serotypes. Data collection is ongoing, and replicating this analysis with more years of exposure data will help validate findings. An improved understanding of factors associated with sporadic infections of *S.* Infantis can lead to targeted public health interventions to address the observed increase in incidence of infections in the United States.

Factors Associated with Sporadic Infections of *Salmonella enterica* Serotype Infantis, Foodborne Diseases Active Surveillance Network (FoodNet)

By

Preethi R. Sundararaman

Bachelor of Science

The College of William & Mary

2011

Faculty Thesis Advisor: John E. McGowan, Jr., MD

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2015

**Acknowledgements**

My sincere gratitude to Dr. John McGowan Jr., Dr. Aimee Geissler, and Dr. Olga Henao for their continuous guidance and willingness to help throughout the thesis process. It has been an honor to work with and learn from such great experts in infectious disease epidemiology and surveillance.

I am grateful to Ellyn Marder, Stacy Crim, Mary Patrick, and the FoodNet working group, whose encouragement, assistance, and efforts to prepare the dataset made this analysis possible.

Finally, thank you to my family and friends for your endless support and belief in me. I would like to dedicate this work to the memory of my grandfather Balasubramaniam Thiagarajan, my first and most devoted supporter.

## Table of Contents

Chapter I: Literature Review ........ 1

Chapter II: Manuscript ........ 7

Introduction ........ 7

Methods ........ 9

Results ........ 11

Discussion ........ 14

References ........ 18

Tables ........ 23

Figures ........ 33

Chapter III: Summary, Public Health Implications, Possible Future Directions ........ 36

# Chapter I: Literature Review

## Foodborne illnesses

Foodborne diseases continue to be a public health concern in the United States (1, 4). An estimated 48 million foodborne illnesses, 128,000 hospitalizations, and 3,000 deaths occur each year, though most illnesses are preventable (1-4). Food can be contaminated by a variety of agents such as bacteria, viruses, and parasites. Major known pathogens include norovirus, non-typhoidal *Salmonella* spp., *Clostridium perfringens*, and *Campylobacter* spp. (1-2). Enteric pathogens commonly transmitted through food can also be transmitted through other modes, notably contaminated water and direct or indirect contact with animals (2, 5). The proportion of illnesses transmitted through food varies by pathogen (2, 4).

## *Salmonella*

*Salmonella* spp., non-typhoidal, are the second most common cause of illnesses and the leading cause of hospitalizations and deaths related to food in the United States (2). *Salmonella* is also the second most common etiology in domestic foodborne outbreaks, though 60-80% of infections occur sporadically (6-7). Approximately 94% of these infections are foodborne. Every year, non-typhoidal *Salmonella* cause an estimated 1 million domestically acquired foodborne illnesses, more than 19,000 hospitalizations, and 350 deaths.

Salmonellosis is characterized by diarrhea, fever, abdominal pain, and sometimes vomiting (6, 8). Symptoms usually develop within 6-72 hours of infection, and last 4-7 days. Most illnesses do not require treatment but severe diarrhea can occur, with which the infection may spread from the intestine to the bloodstream or elsewhere in the body. Severe illnesses may require rehydration and antibiotic therapy, and are more likely to occur in infants, the elderly, and the immunosuppressed. Asymptomatic infections can also occur (6).

*Salmonella* organisms live in the intestinal tracts of humans and other animals including poultry, pigs, cattle, rodents, and reptiles (4-6). Therefore, in addition to ingestion of food or water contaminated by feces of infected animals or humans, contact with animal reservoirs is an important route of transmission (5-6). An estimated 11% of domestically acquired non-typhoidal *Salmonella* illnesses are attributable to direct or indirect contact with animals (5). There have been salmonellosis outbreaks associated with exposures at petting zoos, farms, and animal exhibits (5).

In the United States, incidence of *Salmonella* infections was lower in 2013 compared with 2010-2012, but has not changed overall since 2006-2008 (4). A significant increase in incidence has been seen in some serotypes in 2013 compared with 2006-2008, while others have decreased or shown no change (4, 9). There are over 2,500 known serotypes of *Salmonella*, but most human infections are caused by serotypes within the *Salmonella enterica* species (6, 9-10). Differences in source of infection and severity of disease outcomes have been observed between the serotypes of non-typhoidal *Salmonella* (6, 9-10). Though sources of infection can overlap among *Salmonella* serotypes, various serotypes have been attributed to specific animal reservoirs or food commodities (9). *S.* Javiana has been associated with reptile and amphibian contact, for example, while *S.* Enteritidis has been linked to eggs and chicken (9, 11).

***Salmonella enterica* serotype Infantis**

A recent increase in incidence of infections with *Salmonella enterica* serotype Infantis (*S.* Infantis) has been observed in the United States. In 2013, incidence of *S.* Infantis infections had increased by 82% (95% CI: 40%, 137%) when compared with 2006-2008 (12). *S.* Infantis was also ranked one of the five most common *Salmonella* serotypes worldwide (13), but sporadic infections in the United States have not been well described.

*S.* Infantis has been found in poultry, pigs, and cattle, suggesting these animals could serve as reservoirs for human infection (14-16). Since 1998, more than half of U.S. foodborne disease outbreaks with *S.* Infantis as the confirmed etiology have been associated with pork (9, 17). Other food vehicles implicated in *S.* Infantis outbreaks include beef, gefilte fish, turkey, and grains/beans. Recent non-foodborne outbreaks of *S.* Infantis in the United States have been linked to contact with live chicks and ducklings from a mail-order hatchery, and contact with dry dog food (18-20). The practice of keeping chickens at urban residences has been increasing in popularity and may be contributing to the observed increase in salmonellosis associated with live poultry (21).

A matched case-control study conducted in Israel, where Infantis became the most prevalent *Salmonella* serotype in 2009, identified consumption of eggs as a significant risk factor for sporadic infection in people aged >1 year (22). Eggs have been linked to *S.* Infantis in Australia as well, where Infantis is the predominant *Salmonella* serotype in the egg industry, though overall occurrence of *Salmonella* in eggs is low (23). A study of human and chicken isolates in Japan determined that meat from broiler chickens is also a source of human *S.* Infantis infections (14). In Canada, a study of non-human isolates identified Infantis as one of the most common serovars among pigs (16). These findings are consistent with a study in the Netherlands, where Infantis was found to be one of the three most prevalent *Salmonella* serotypes in chickens and pigs (24).

**Dataset and analytic plan**

Exposure data can be used to determine current sources of *S.* Infantis infection in the United States. Identifying possible reservoirs, food vehicles, or behavioral risk factors associated with *S.* Infantis could help explain the increase in incidence, and lead to targeted interventions to reduce illness.

The Foodborne Diseases Active Surveillance Network (FoodNet) conducts active population-based surveillance of laboratory-confirmed human infections commonly transmitted through food (25). FoodNet surveillance includes 48 million persons, representing 15% of the United States population, from the following ten sites: Connecticut, Georgia, Maryland, Minnesota, New Mexico, Oregon, Tennessee, and selected counties in California, Colorado, and New York. FoodNet is a collaboration between the ten sites, the Centers for Disease Control and Prevention (CDC), the U.S. Department of Agriculture's Food Safety and Inspection Service (USDA-FSIS), and the Food and Drug Administration (FDA).

Since its inception in 1996, FoodNet data and studies have been used to estimate numbers of foodborne illnesses, monitor changes in incidence, and attribute these illnesses to specific foods and settings (25-26). FoodNet data also provide information on the number of hospitalizations and deaths, international travel, and demographics such as age, gender, race, and ethnicity. This information is disseminated and used by public health and regulatory agencies, industry, and consumer groups to evaluate and develop food safety polices and prevention efforts.

Starting in 2014, an ongoing case exposure ascertainment initiative has enhanced FoodNet surveillance data with information on dietary and behavioral exposures for sporadic infections of non-typhoidal *Salmonella.* These data are ideal for evaluating factors associated with *S.* Infantis as they include a range of foodborne exposures (e.g., consumption of eggs, chicken, and pork) as well as environmental exposures (e.g., contact with live poultry).

Laboratory-based surveillance data are an essential source of information on rates and changes in enteric disease, but are limited by low sensitivity (2, 27). Only a fraction of ill persons seek medical care, submit a specimen for laboratory testing, and are reported to public health agencies. It is estimated that less than 3% of *Salmonella* infections in the United States are laboratory-confirmed (27). Because the process by which infections are reported to surveillance is non-random, traditional case-control methodology using randomly selected controls may be subject to selection bias (28). Another limitation of case-control studies is recall bias, as cases may have a better memory of exposures simply due to the presence of disease (28).

An alternative analytic method has been proposed to address these biases, where reported cases of infection are compared to cases of another similar laboratory-confirmed infection (27-28). A previous FoodNet study determined the utility of this case-case comparison methodology in identifying risk factors for sporadic cases of *Salmonella* serotype Enteritidis (27). Laboratory-confirmed infections of other *Salmonella* serotypes served as the comparison group, resulting in equal sensitivities of ascertainment, and allowing for reduced recall bias.

Case-case comparisons are most effective when the cases and ill controls do not share a causal exposure, which would result in a measure of association biased toward the null (27). Though some *Salmonella* serotypes overlap in exposures, the impact can be minimized by using a variety of serotypes in the comparison group, thus reducing the proportion of ill controls attributable to a particular exposure (27-28). The results of case-case comparison analyses could be used to determine changes in attribution of *Salmonella* serotypes to specific exposures, identify risk factors for sporadic infections, help determine differences between risk factors for sporadic and outbreak-associated infections, and generate hypotheses for further investigation.

This study aimed to identify risk factors associated with sporadic infection of *S.* Infantis, using newly acquired FoodNet case exposure ascertainment data in case-case comparisons. Characteristics and annual incidence of sporadic cases of infection with *S.* Infantis are described using eleven years of FoodNet surveillance data.

# Chapter II: Manuscript

Factors Associated with Sporadic Infections of *Salmonella enterica* Serotype Infantis, Foodborne Diseases Active Surveillance Network (FoodNet)

## Introduction

*Salmonella* spp., non-typhoidal, are the second most common cause of illnesses and the leading cause of hospitalizations and deaths related to food in the United States (2). *Salmonella* is also the second most common etiology in domestic foodborne outbreaks, though 60-80% of infections occur sporadically (6-7). Every year, non-typhoidal *Salmonella* cause an estimated 1 million domestically acquired foodborne illnesses, more than 19,000 hospitalizations, and 350 deaths.

In the United States, incidence of *Salmonella* infections was lower in 2013 compared with 2010-2012, but has not changed overall since 2006-2008 (4). A significant increase in incidence has been seen in some serotypes in 2013 compared with 2006-2008, while others have decreased or shown no change (4, 9). A recent increase in incidence of infections with *Salmonella enterica* serotype Infantis (*S.* Infantis) has been observed in the United States. In 2013, incidence of *S.* Infantis infections had increased by 82% (95% CI: 40%, 137%) when compared to 2006-2008 (12). *S.* Infantis was also ranked one of the five most common *Salmonella* serotypes worldwide (13), but sporadic infections in the United States have not been well described.

*S.* Infantis has been found in poultry, pigs, and cattle, suggesting these animals could serve as reservoirs for human infection (14-16). Since 1998, more than half of national foodborne disease outbreaks with *S.* Infantis as the confirmed etiology have been associated with pork (9, 17). Other food vehicles implicated in *S.* Infantis outbreaks include beef, gefilte fish, turkey, and grains/beans. Recent non-foodborne outbreaks of *S.* Infantis in the United States have been linked to contact with live chicks and ducklings from a mail-order hatchery, and contact with dry dog food (18-20). The practice of keeping chickens at urban residences has been increasing in popularity and may be contributing to the observed increase in salmonellosis associated with live poultry (21).

The Foodborne Diseases Active Surveillance Network (FoodNet) conducts active population-based surveillance of laboratory-confirmed human infections commonly transmitted through food (25). FoodNet data provide information on the number of hospitalizations and deaths, international travel, and demographics such as age, gender, race, and ethnicity. Starting in 2014, an ongoing case exposure ascertainment initiative has enhanced FoodNet surveillance data with information on 48 dietary and behavioral exposures for sporadic infections of non-typhoidal *Salmonella.* These data are ideal for evaluating factors associated with *S.* Infantis as they include a range of foodborne exposures (e.g., consumption of eggs, chicken, and pork) as well as environmental exposures (e.g., contact with live poultry).

Since less than 3% of salmonellosis cases in the United States are laboratory-confirmed, traditional case-control methodology may be subject to selection bias when applied to surveillance data (27-28). An alternative analytic method has been proposed to address these biases, where reported cases of infection are compared to cases of another similar laboratory-confirmed infection (27-28). Case-case comparisons where cases and ill controls share a causal exposure may result in a measure of association biased toward the null (27). Though some *Salmonella* serotypes overlap in exposures, the impact can be minimized by using a variety of serotypes in the comparison group, thus reducing the proportion of ill controls attributable to a particular exposure (27-28). Case-case comparisons may help determine changes in attribution of *Salmonella* serotypes to specific exposures, identify risk factors for sporadic infections, help determine differences between risk factors for sporadic and outbreak-associated infections, and generate hypotheses for further investigation.

This study aimed to identify risk factors associated with sporadic infection of *S.* Infantis, using newly acquired FoodNet case exposure ascertainment data in case-case comparisons. Characteristics and annual incidence of sporadic cases of infection with *S.* Infantis are described using eleven years of FoodNet surveillance data.

**Methods**

The hypothesis evaluated in this study is that persons with non-outbreak-associated infections of *Salmonella* Infantis are more likely to have had contact with food-producing animals (poultry, pigs, and cattle) when compared to persons with non-outbreak-associated infections of other non-typhoidal *Salmonella* serotypes.

Cases were defined as persons with sporadic laboratory-confirmed infections of *S.* Infantis reported to the Foodborne Diseases Active Surveillance Network (FoodNet). Persons with sporadic laboratory-confirmed infections of *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, or Heidelberg reported to FoodNet served as the comparison group. FoodNet surveillance includes 48 million persons, representing 15% of the United States population, from the following ten sites:

Connecticut, Georgia, Maryland, Minnesota, New Mexico, Oregon, Tennessee, and selected counties in California, Colorado, and New York (25). An "outbreak" variable allowed for differentiation of infections that were sporadic, or not outbreak-associated.

Chi-squared tests were used to compare cases of *S.* Infantis with persons infected with the other *Salmonella* serotypes by age group, gender, race, ethnicity, seasonality, and frequency of hospitalizations, deaths, and international travel from 2004 to 2014. A p-value of <0.05 was considered statistically significant. Annual incidence was calculated by dividing the number of sporadic infections by U.S. Census estimates of the surveillance area population for that year (4).

Data collected in 2014 from a new case exposure ascertainment (CEA) initiative were evaluated to determine behavioral and dietary factors associated with sporadic infections of *S.* Infantis. Persons with sporadic infections of the other *Salmonella* serotypes served as ill controls in case-case comparisons. As part of the CEA initiative, FoodNet sites transmit data on 48 foodborne, waterborne, and environmental exposures mapped to their respective state health department *Salmonella* case report forms. Cases of infection were excluded if they were less than 1 year of age, associated with a known outbreak, reported international travel, or had an undetermined serotype. California was excluded from this portion of the analysis as exposure data were not available for cases of infection with serotype Infantis.

Chi-squared tests were conducted for the 2014 CEA data subset, to verify that differences in characteristics between cases and ill controls were comparable to those observed in the 2004-2014 dataset. First, associations of sporadic infections of *S.* Infantis with individual exposures were assessed using odds ratios adjusting for FoodNet site and season, which are known confounders for *Salmonella* spp. (27, 29). Season was categorized using month of illness onset as follows: winter (December, January, February); spring (March, April, May); summer (June, July, August); and fall (September, October, November). Next, a multivariable logistic regression model was created to calculate odds ratios adjusted for exposures reported by at least 10% of cases. Standard backwards elimination was used to evaluate age group, race, ethnicity, sex, FoodNet site, and season as potential confounders. FoodNet site and season were identified as confounders and kept in the final model. Data manipulation and analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). All data for 2014 were preliminary as of February 17, 2015. A determination request was submitted to the Emory IRB, and the study was deemed exempt from review.

## Results

During the 2004-2014 period, a total of 1,268 sporadic laboratory-confirmed infections of *S.* Infantis were reported to FoodNet [**Table 1**]. A total of 42,448 sporadic laboratory confirmed infections were reported for the comparison group of *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg. In 2014, incidence of sporadic infections of *S.* Infantis was the highest observed during the 11-year period at 0.42 per 100,000 population; two times the rate observed in 2004 (0.21 per 100,000) [**Figure 1a**]. In contrast, incidence of sporadic infections of the other non-typhoidal *Salmonella* serotypes was similar throughout the period (7.95 per 100,000 in

2014 vs. 7.56 per 100,000 in 2004) except for a peak in infections observed in 2010 (10.21 per 100,000) [**Figure 1b**].

Average annual incidence varied among FoodNet sites. Incidence of *S.* Infantis infections was highest in California (0.60 per 100,000 population) and lowest in Maryland (0.15 per 100,000 population) [**Table 2**]. Average annual incidence of the other non-typhoidal *Salmonella* serotypes varied from 13.05 per 100,000 in Georgia to 4.29 per 100,000 in Oregon.

For both cases and ill controls, average annual incidence rates of infection were substantially higher in children <5 years of age compared to other age groups (0.80 per 100,000 for *S.* Infantis; 34.20 per 100,000 for other *Salmonella* serotypes) [**Table 3; Figures 2a-b**]. The second highest average annual incidence of infections was observed in adults aged 65 years and older for *S.* Infantis (0.27 per 100,000), while children aged 5-9 years had the second highest rates for the other serotypes (11.26 per 100,000). Cases with infections of *S.* Infantis were significantly less likely to be white (65.3% vs. 73.1%, $p<0.001$) or black (12.5% vs. 19.4%, $p<0.001$), and more likely to be Asian (14.8% vs. 3.4%, $p<0.001$) or of other race (7.4% vs. 4.1%, $p<0.001$) when compared to persons infected with other non-typhoidal *Salmonella* serotypes [**Table 3**]. Average annual incidence of sporadic infections of *S.* Infantis was highest among Asian persons (0.61 per 100,000), while incidence of infections of other serotypes was highest among black persons (8.77 per 100,000). Cases of *S.* Infantis were also significantly more likely to be Hispanic (15.2% vs. 10.7%, $p<0.001$). Compared to ill controls, a higher proportion of cases of *S.* Infantis were female (55.8% vs. 51.0%, $p=0.001$).

Of those infected with *S.* Infantis during the 11-year period, 2 persons died (0.2%) [**Table 4**]. Approximately one third of persons infected with *S.* Infantis were hospitalized (27.5%) and one tenth reported international travel (9.7%). No significant differences were observed in the frequencies of hospitalizations, deaths, or international travel between cases and ill controls.

Seasonal variation was observed in incidence rates of sporadic infections of *S.* Infantis and other non-typhoidal *Salmonella* serotypes [**Table 5; Figure 3**]. Incidence of infections peaked in July-September for both *S.* Infantis and other serotypes, and smaller peaks appeared in April-May and January for infections of *S.* Infantis.

Exposure information was available for a total of 96 persons with *S*. Infantis infection and a total of 2,040 persons with other *Salmonella* serotypes infections reported to FoodNet in 2014 [**Table 6**]. The distribution of serotypes in the comparison group was similar to that observed in the 2004-2014 data, with Enteritidis responsible for approximately a third (35.1%) and Typhimurium responsible for nearly a fifth (22.5%) of ill controls. New York contributed the most cases (23, 24.0%) while Maryland contributed the most ill controls (392, 19.2%) [**Table 7**].

When assessing exposures individually and adjusting for site and season, infection with *S.* Infantis was strongly associated with contact with pet birds (aOR 7.27, 95% CI: 3.40, 15.56) and live poultry (aOR 3.48, 95% CI: 1.73, 7.01) [**Table 8**]. Cases of *S.* Infantis were also more likely to report consumption of fish when compared to persons infected with other *Salmonella* serotypes (aOR 2.12, 95% CI: 1.17, 3.83). In multivariable analysis including exposures reported by at least 10% of cases, and again adjusting for site and season, associations between infection of *S.* Infantis and contact with pet birds (aOR 12.91, 95% CI: 2.71, 61.48) and live poultry (aOR 6.34, 95% CI: 1.31, 30.71) remained, though estimates were less precise [**Table 9**].

## Discussion

This study looked at eleven years of FoodNet surveillance data to describe characteristics and annual incidence of sporadic cases of infection with *S.* Infantis, and examined 2014 FoodNet exposure data to identify factors associated with infection of *S.* Infantis in case-case comparisons.

Contact with pet birds was most significantly associated with infection of *S.* Infantis when compared to infections of other *Salmonella* serotypes. Pet birds have been previously identified as a reservoir for *Salmonella* spp., but association with serotype Infantis may need to be further explored (30). Contact with live poultry was also significantly associated with infection of *S.* Infantis when compared to ill controls. This finding is consistent with the study hypothesis, and with recent zoonotic outbreaks linking infections of *S.* Infantis to contact with live poultry including chicks and ducklings (18-19). Cases of *S.* Infantis were more likely than ill controls to report consumption of fish, but this association did not remain significant when adjusting for exposures reported by at least 10% of cases in addition to adjusting for site and season.

Annual incidence of sporadic infections of *S.* Infantis in 2014 was the highest observed during the 2004-2014 period. New cases of sporadic infections of *S.* Infantis were most likely to occur in children less than 5 years of age, followed by adults aged 65 years and older. Incidence of sporadic infections of both *S.* Infantis and other *Salmonella* serotypes displayed a distinct summer peak, a seasonal trend that is characteristic of *Salmonella* spp. (8, 29). Smaller peaks in incidence of infections of *S.* Infantis appeared in April-May and January. Outbreaks linked to backyard poultry and birds obtained as pets for Easter holiday celebrations have shown peaks in the spring, so the peak in sporadic infections of *S.* Infantis observed in April-May could be related to this seasonal variation in exposures (21).

This study is subject to several limitations. First, methods of data collection varied among FoodNet sites. Sites used different questionnaires to collect exposure information, which could explain the varied levels of missing data for some exposures. Most sites interviewed all persons with reported infections of *Salmonella* who met eligibility criteria, but some sites interviewed or transmitted exposure data on selected cases of infection only. Cases of known outbreaks were excluded to limit the analyses to sporadic cases of infection, but some cases of infection reported as sporadic may actually be unrecognized as outbreak cases, or may be part of undetected outbreaks (7). Because of the low number of cases of *S.* Infantis, associations with some exposures could not be assessed. Additionally, it is possible that an overlap in causal exposures between cases of *S.* Infantis and controls infected with other *Salmonella* serotypes resulted in certain associations being unidentified or underestimated. For example, persons with infections of *S.* Enteritidis were included in the comparison group, and previous case-control studies have associated infections of this serotype with consumption of eggs and chicken (9, 27, 30). Studies conducted outside of the United States have linked *S.* Infantis to consumption of eggs and chicken as well (14, 22-23). Finally, the findings in this study may not be generalizable to the national population due to variations in health-careseeking behaviors and other characteristics of the population in the FoodNet surveillance area (4).

The study benefited from certain advantages. The range of exposures collected in FoodNet CEA data provided a rare opportunity to evaluate associations between sporadic infections of *S.* Infantis and factors linked to different modes of transmission, including foodborne, waterborne, and animal contact. The use of ill controls as the comparison group likely allowed for reduction of selection and recall biases that are limitations of traditional case-control methodology applied to surveillance data. Ill controls are more likely than randomly selected healthy controls to have sensitivities of ascertainment and memory of exposures that are comparable with cases (27-28). Previous FoodNet studies have determined the utility of this case-case comparison methodology in identifying risk factors for sporadic infections of *Salmonella* serotypes. Studies that assessed factors associated with *S.* Enteritidis and *S.* Typhimurium found similar conclusions when comparing cases to ill controls as when comparing cases to healthy controls (27, 31). These studies suggest case-case comparisons could be a cost-effective means to monitor changes in the attribution of *Salmonella* serotypes to specific exposures, identify risk factors for sporadic infections, and generate hypotheses for further investigation (27).

This was the first analysis of FoodNet case exposure ascertainment data to assess factors associated with sporadic infections of *S.* Infantis. Though infections of *Salmonella* are primarily attributed to foodborne exposures, individual serotypes have been attributed to contact with specific animal reservoirs (6-7, 9). Because non-significant exposure associations in this study may be a result of sparse data or shared causal exposures between cases and ill controls, we cannot conclude that sporadic infections of *S.* Infantis are not associated with foodborne exposures. However, the results of this study may indicate that sporadic cases of infection with *S.* Infantis are more likely to be associated with environmental factors such as contact with birds and live poultry when compared to other *Salmonella* serotypes. Data collection is ongoing, and replicating this analysis with more years of exposure data will help validate findings. An improved understanding of factors associated with sporadic infections of *S.* Infantis can lead to targeted public health interventions to address the observed increase in incidence of infections in the United States.

**References**


1. Khabbaz RF, Moseley RR, Steiner RJ, et al. Challenges of infectious diseases in the USA. *Lancet*. 2014; 384(9937):53-63.

2. Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States—major pathogens. *Emerg Infect Dis*. 2011; 17(1):7-15.

3. Scallan E, Griffin PM, Angulo FJ, et al. Foodborne illness acquired in the United States – unspecified agents. *Emerg Infect Dis*. 2011; 17(1):16-22.

4. Crim SM, Iwamoto M, Huang JY, et al. Incidence and trends of infection with pathogens transmitted commonly through food – Foodborne Diseases Active Surveillance Network, 10 U.S. sites, 2006-2013. *MMWR Morb Mortal Wkly Rep*. 2014; 63(15):328-32.

5. Hale CR, Scallan E, Cronquist AB, et al. Estimates of enteric illness attributable to contact with animals and their environments in the United States. *Clin Infect Dis.* 2012; 54 Suppl 5:S472-9.

6. Heymann DL, editor. *Control of communicable diseases manual*. 19th ed. Washington, DC: American Public Health Association; 2008.

7. Gould LH, Walsh KA, Vieira AR, et al. Surveillance for foodborne disease outbreaks – United States, 1998-2008. *MMWR Surveill Summ*. 2013; 62(2):1-34.

8. Centers for Disease Control and Prevention, US Department of Health and Human Services. General Information on Salmonella. http://www.cdc.gov/salmonella/general/index.html. Accessed January 27, 2015.

9. Jackson BR, Griffin PM, Cole D, et al. Outbreak-associated *Salmonella enterica* serotypes and food commodities, United States, 1998-2008. *Emerg Infect Dis*. 2013; 19(8):1239-44.

10. Jones TF, Ingram LA, Cieslak PR, et al. Salmonellosis outcomes differ substantially by serotype. *J Infect Dis*. 2008; 198(1):109-14.

11. Clarkson LS, Tobin-D'Angelo M, Shuler C, et al. Sporadic *Salmonella enterica* serotype Javiana infections in Georgia and Tennessee: a hypothesis-generating study. *Epidemiol Infect*. 2010; 138(3):340-6.

12. Centers for Disease Control and Prevention, US Department of Health and Human Services. Table 9 FoodNet-Percent Change and 95% CI in Incidence of Laboratory-Confirmed *Salmonella* Infections 2013. http://www.cdc.gov/foodnet/data/trends/tables/2013/table9.html. Updated April 17, 2014. Accessed March 11, 2015.

13. Galanis E, Lo Fo Wong DM, Patrick ME, et al. Web-based surveillance and global *Salmonella* distribution, 2000-2002. *Emerg Infect Dis*. 2006; 12(3):381-8.

14. Noda T, Murakami K, Ishiguro Y, et al. Chicken meat is an infection source of *Salmonella* serovar Infantis for humans in Japan. *Foodborne Pathog Dis*. 2010; 7(6):727-35.

15. Najjar Z, Furlong C, Stephens N, et al. An outbreak of *Salmonella* Infantis gastroenteritis in a residential aged care facility associated with thickened fluids. *Epidemiol Infect*. 2012; 140(12):2264-72.

16. Guerin MT, Martin SW, Darlington GA, et al. A temporal study of *Salmonella* serovars in animals in Alberta between 1990 and 2001. *Can J Vet Res*. 2005; 69(2):88-99.

17. Centers for Disease Control and Prevention, US Department of Health and Human Services. Foodborne Outbreak Online Database. http://wwwn.cdc.gov/foodborneoutbreaks. Accessed March 21, 2014.

18. Basler C, Forshey TM, Machesky K, et al. Multistate outbreak of human *Salmonella* infections linked to live poultry from a mail-order hatchery in Ohio—March-September 2013. *MMWR Morb Mortal Wkly Rep*. 2014; 64(10):222.

19. Centers for Disease Control and Prevention (CDC). Notes from the field: Multistate outbreak of *Salmonella* Infantis, Newport, and Lille infections linked to live poultry from a single mail-order hatchery in Ohio—March-September, 2012. *MMWR Morb Mortal Wkly Rep*. 2013; 62(11):213.

20. Imanishi M, Rotstein DS, Reimschuessel R, et al. Outbreak of *Salmonella enterica* serotype Infantis infection in humans linked to dry dog food in the United States and Canada, 2012. *J Am Vet Med Assoc*. 2014; 244(5):545-53.

21. Barton Behravesh C, Brinson D, Hopkins BA, et al. Backyard poultry flocks and salmonellosis: a recurring, yet preventable public health challenge. *Clin Infect Dis.* 2014; 58(10):1432-8.

22. Bassal R, Reisfeld A, Nissan I, et al. Risk factors for sporadic infection with *Salmonella* Infantis: a matched case-control study. *Epidemiol Infect*. 2014; 142(4):820-5.

23. Chousalkar KK, Roberts JR. Recovery of *Salmonella* from eggshell wash, eggshell crush, and egg internal contents of unwashed commercial shell eggs in Australia. *Poult Sci*. 2012; 91(7):1739-41.

24. Van Duijkeren E, Wannet WJ, Houwers DJ, et al. Serotype and phage type distribution of *Salmonella* strains isolated from humans, cattle, pigs, and chickens in the Netherlands from 1984 to 2001. *J Clin Microbiol*. 2002; 40(11):3980-5.

25. Centers for Disease Control and Prevention, US Department of Health and Human Services. About FoodNet. http://www.cdc.gov/foodnet/about.html. Updated November 5, 2013. Accessed September 14, 2014.

26. Scallan E, Mahon BE. Foodborne Diseases Active Surveillance Network (FoodNet) in 2012: a foundation for food safety in the United States. *Clin Infect Dis*. 2013; 57(5):779.

27. Voetsch AC, Poole C, Hedberg CW, et al. Analysis of the FoodNet case-control study of sporadic *Salmonella* serotype Enteritidis infections using persons infected with other *Salmonella* serotypes as the comparison group. *Epidemiol Infect*. 2009; 137(3):408-16.

28. McCarthy N, Giesecke J. Case-case comparisons to study causation of common infectious diseases. *Int J Epidemiol*. 1999; 28(4):764-8.

29. Centers for Disease Control and Prevention (CDC). Foodborne Diseases Active Surveillance Network (FoodNet): FoodNet surveillance report for 2012 (final report). Atlanta, Georgia: U.S. Department of Health and Human Services, CDC; 2014.

30. Marcus R, Varma JK, Medus C, et al. Re-assessment of risk factors for sporadic *Salmonella* serotype Enteritidis: a case-control study in five FoodNet Sites, 2002-2003. *Epidemiol Infect*. 2007; 135(1):84-92.

31. Glynn MK, Reddy V, Hutwagner L, et al. Prior antimicrobial agent use increases the risk of sporadic infections with multidrug-resistant *Salmonella* enterica serotype Typhimurium: a FoodNet case-control study, 1996-1997. *Clin Infect Dis*. 2004; 38 Suppl 3:S227-36.

## Tables

**Table 1.** Number of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis and other non-typhoidal *Salmonella* serotypes[a] reported to the Foodborne Diseases Active Surveillance Network (FoodNet), 2004-2014.

| Serotype | No. | % |
|---|---|---|
| Cases | | |
| Infantis | 1,268 | 100.0 |
| Ill Controls | | |
| Enteritidis | 12,882 | 30.4 |
| Typhimurium | 10,540 | 24.8 |
| Newport | 7,891 | 18.6 |
| Javiana | 5,823 | 13.7 |
| I 4,[5],12:i:- | 3,138 | 7.4 |
| Heidelberg | 2,174 | 5.1 |
| Total | 42,448 | 100.0 |

[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

**Table 2.** Number, percentage, and average annual incidence of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis and other non-typhoidal *Salmonella* serotypes[a], by site – FoodNet, 2004-2014.

| | ***S.* Infantis (n=1,268)** | | | **Other non-typhoidal *Salmonella*[a] (n=42,448)** | | | |
|---|---|---|---|---|---|---|---|
| Site | No. | % | Avg. incidence (per 100,000)[b] | No. | % | Avg. incidence (per 100,000)[b] | $\chi 2$ p-value |
| California | 224 | 17.7 | 0.60 | 2,786 | 6.6 | 7.60 | <0.001[c] |
| Colorado | 64 | 5.1 | 0.21 | 1,808 | 4.3 | 6.00 | 0.172 |
| Connecticut | 99 | 7.8 | 0.25 | 2,762 | 6.5 | 7.07 | 0.065 |
| Georgia | 248 | 19.6 | 0.23 | 13,726 | 32.3 | 13.05 | <0.001[c] |
| Maryland | 97 | 7.7 | 0.15 | 5,615 | 13.2 | 8.88 | <0.001[c] |
| Minnesota | 182 | 14.4 | 0.31 | 3,914 | 9.2 | 6.75 | <0.001[c] |
| New Mexico | 41 | 3.2 | 0.19 | 1,588 | 3.7 | 7.14 | 0.347 |
| New York | 89 | 7.0 | 0.19 | 2,864 | 6.8 | 6.02 | 0.704 |
| Oregon | 91 | 7.2 | 0.22 | 1,786 | 4.2 | 4.29 | <0.001[c] |
| Tennessee | 133 | 10.5 | 0.19 | 5,599 | 13.2 | 8.10 | 0.005[c] |

[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

[b]Annual incidence per 100,000 population was calculated by dividing the number of sporadic infections by U.S. Census estimates of the surveillance area population for each site and averaged over the 11 years.

[c]Significant result in chi-squared test (p-value <0.05).

**Table 3.** Number, percentage, and average annual incidence of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis and other non-typhoidal *Salmonella* serotypes[a], by age group, race, ethnicity, and sex – FoodNet, 2004-2014.

| | ***S.* Infantis (n= 1,268)** | | | **Other non-typhoidal *Salmonella*[a] (n= 42,448)** | | | |
|---|---|---|---|---|---|---|---|
| | No. | % | Avg. incidence (per 100,000)[b] | No. | % | Avg. incidence (per 100,000)[b] | χ2 p-value |
| Age Group (years) | | | | | | | |
| <5 | 263 | 20.7 | 0.80 | 11,286 | 26.6 | 34.20 | <0.001[c] |
| 5-9 | 62 | 4.9 | 0.19 | 3,749 | 8.8 | 11.26 | <0.001[c] |
| 10-19 | 107 | 8.4 | 0.15 | 4,393 | 10.4 | 6.26 | 0.027[c] |
| 20-64 | 655 | 51.7 | 0.21 | 18,230 | 43.0 | 5.85 | <0.001[c] |
| ≥65 | 181 | 14.3 | 0.27 | 4,754 | 11.2 | 7.27 | 0.001[c] |
| Race | | | | | | | |
| White | 704 | 65.3 | 0.18 | 26,720 | 73.1 | 6.86 | <0.001[c] |
| Asian | 160 | 14.8 | 0.61 | 1,254 | 3.4 | 4.91 | <0.001[c] |
| Black | 135 | 12.5 | 0.17 | 7,085 | 19.4 | 8.77 | <0.001[c] |
| Other[d] | 80 | 7.4 | 0.45 | 1,488 | 4.1 | 8.58 | <0.001[c] |
| Ethnicity | | | | | | | |
| Hispanic | 154 | 15.2 | 0.28 | 3,510 | 10.7 | 6.32 | <0.001[c] |
| Non-Hispanic | 861 | 84.8 | 0.19 | 29,367 | 89.3 | 6.41 | |
| Sex | | | | | | | |
| Female | 704 | 55.8 | 0.27 | 21,614 | 51.0 | 8.27 | 0.001[c] |
| Male | 558 | 44.2 | 0.22 | 20,746 | 49.0 | 8.24 | |

[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

[b]Annual incidence per 100,000 population was calculated by dividing the number of sporadic infections by U.S. Census estimates of the surveillance area population for each subgroup and averaged over the 11 years.

[c]Significant result in chi-squared test (p-value <0.05).

[d]Includes persons identified as American Indian or Alaskan Native, Pacific Islander or Native Hawaiian, multi-racial, or other race.

**Table 4.** Frequency of hospitalizations, deaths, and international travel among cases with sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis and other non-typhoidal *Salmonella* serotypes[a] – FoodNet, 2004-2014.

| | ***S.* Infantis (n= 1,268)** | | **Other non-typhoidal *Salmonella*[a] (n= 42,448)** | | |
|---|---|---|---|---|---|
| | No. | % | No. | % | $\chi 2$ p-value[b] |
| Hospitalizations | 328 | 27.5 | 11,991 | 29.7 | 0.097 |
| Deaths | 2 | 0.2 | 189 | 0.5 | 0.123 |
| International Travel | 97 | 9.7 | 2,617 | 8.5 | 0.172 |

[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

[b]A p-value <0.05 was considered a significant result in chi-squared tests.

**Table 5.** Number, percentage, and average incidence of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis and other non-typhoidal *Salmonella* serotypes[a], by month of illness onset – FoodNet, 2004-2014.

| | ***S.* Infantis (n= 1,268)** | | | **Other non-typhoidal *Salmonella*[a] (n= 42,448)** | | |
|---|---|---|---|---|---|---|
| Month of Illness Onset | No. | % | Avg. incidence (per 100,000)[b] | No. | % | Avg. incidence (per 100,000)[b] |
| Jan | 102 | 8.0 | 0.24 | 2,121 | 5.0 | 4.97 |
| Feb | 53 | 4.2 | 0.12 | 1,644 | 3.9 | 3.85 |
| Mar | 53 | 4.2 | 0.12 | 1,979 | 4.7 | 4.64 |
| Apr | 106 | 8.4 | 0.25 | 2,415 | 5.7 | 5.65 |
| May | 105 | 8.3 | 0.24 | 3,011 | 7.1 | 7.04 |
| Jun | 124 | 9.8 | 0.29 | 4,137 | 9.8 | 9.67 |
| Jul | 142 | 11.2 | 0.33 | 5,892 | 13.9 | 13.77 |
| Aug | 170 | 13.4 | 0.40 | 6,290 | 14.8 | 14.70 |
| Sep | 146 | 11.5 | 0.34 | 5,421 | 12.8 | 12.67 |
| Oct | 101 | 8.0 | 0.24 | 4,324 | 10.2 | 10.11 |
| Nov | 79 | 6.2 | 0.18 | 2,872 | 6.8 | 6.73 |
| Dec | 87 | 6.9 | 0.20 | 2,342 | 5.5 | 5.49 |

[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

[b]Average monthly incidence per 100,000 population was calculated by dividing the number of sporadic infections for each month by one twelfth of U.S. Census estimates of the surveillance area population and averaged over the 11 years.

**Table 6.** Number of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis and other non-typhoidal *Salmonella* serotypes[a] included in exposure analyses – FoodNet CEA[b], 2014.

| Serotype | No. | % |
|---|---|---|
| Cases | | |
| Infantis | 96 | 100.0 |
| Ill Controls | | |
| Enteritidis | 715 | 35.1 |
| Typhimurium | 459 | 22.5 |
| Newport | 328 | 16.1 |
| Javiana | 247 | 12.1 |
| I 4,[5],12:i:- | 189 | 9.3 |
| Heidelberg | 102 | 5.0 |
| Total | 2,040 | 100.0 |

[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

[b]Case exposure ascertainment (CEA) data were collected for case patients greater than 1 year of age, not associated with a known outbreak, and who did not report international travel.

**Table 7.** Number and percentage of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis and other non-typhoidal *Salmonella* serotypes[a] included in exposure analyses, by site – FoodNet CEA[b], 2014.

| | ***S.* Infantis (n=96)** | | **Other non-typhoidal *Salmonella*[a] (n=2,040)** | | |
|---|---|---|---|---|---|
| Site[c] | No. | % | No. | % | $\chi$2 p-value |
| Colorado | 7 | 7.3 | 148 | 7.3 | 0.989 |
| Connecticut | 19 | 19.8 | 174 | 8.5 | <0.001[d] |
| Georgia | 10 | 10.4 | 278 | 13.6 | 0.368 |
| Maryland | 6 | 6.3 | 392 | 19.2 | 0.001[d] |
| Minnesota | 14 | 14.6 | 245 | 12.0 | 0.450 |
| New Mexico | 3 | 3.1 | 110 | 5.4 | 0.332 |
| New York | 23 | 24.0 | 234 | 11.5 | <0.001[d] |
| Oregon | 4 | 4.2 | 157 | 7.7 | 0.201 |
| Tennessee | 10 | 10.4 | 302 | 14.8 | 0.234 |

[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

[b]Case exposure ascertainment (CEA) data were collected for case patients greater than 1 year of age, not associated with a known outbreak, and who did not report international travel.

[c]California was excluded because exposure information was not collected for cases of *S.* Infantis.

[d]Significant result in chi-squared test (p-value <0.05).

**Table 8.** Frequency, percentage, and site and season adjusted odds ratios of exposures associated with sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis compared to infections of other non-typhoidal *Salmonella* serotypes[a] – FoodNet CEA[b], 2014.

| | ***S.* Infantis (n= 96)** | | | **Other non-typhoidal *Salmonella*[a] (n= 2,040)** | | | **Odds ratios adjusted for site and season** | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. | % | *No. Unknown*[c] | No. | % | *No. Unknown*[c] | aOR[d] | 95% CI | χ2 p-value |
| **Foodborne exposures** | | | | | | | | | |
| Chicken | 53 | 69.7 | *20* | 1,243 | 73.4 | *346* | 0.81 | (0.48, 1.35) | 0.415 |
| Turkey | 12 | 23.1 | *44* | 354 | 25.0 | *626* | 0.57 | (0.23, 1.38) | 0.211 |
| Beef | 34 | 54.0 | *33* | 797 | 53.4 | *547* | 1.24 | (0.68, 2.27) | 0.483 |
| Pork | 27 | 43.6 | *34* | 549 | 36.6 | *541* | 1.27 | (0.74, 2.15) | 0.385 |
| Fish | 21 | 32.3 | *31* | 338 | 22.0 | *505* | 2.12 | (1.17, 3.83) | 0.013[e] |
| Seafood | 13 | 20.3 | *32* | 238 | 15.2 | *475* | 1.63 | (0.83, 3.17) | 0.155 |
| Dairy | 50 | 75.8 | *30* | 1,214 | 77.5 | *474* | 0.76 | (0.41, 1.39) | 0.373 |
| Eggs | 47 | 55.3 | *11* | 998 | 56.9 | *285* | 1.01 | (0.63, 1.63) | 0.955 |
| Lettuce/spinach | 29 | 44.6 | *31* | 817 | 51.6 | *456* | 0.71 | (0.42, 1.18) | 0.187 |
| Tomatoes | 37 | 43.0 | *10* | 761 | 43.2 | *277* | 0.98 | (0.63, 1.54) | 0.938 |
| Berries | 16 | 25.0 | *32* | 520 | 33.6 | *490* | 0.64 | (0.35, 1.15) | 0.135 |
| Melon | 13 | 19.7 | *30* | 441 | 27.5 | *438* | 0.65 | (0.34, 1.24) | 0.193 |
| **Animal exposures** | | | | | | | | | |
| Dog | 28 | 44.4 | *33* | 858 | 52.7 | *413* | 0.69 | (0.41, 1.16) | 0.160 |
| Cat | 15 | 23.4 | *32* | 365 | 22.5 | *416* | 0.93 | (0.51, 1.71) | 0.814 |
| Reptile/amphibian | 6 | 6.7 | *7* | 118 | 6.2 | *135* | 1.09 | (0.46, 2.59) | 0.853 |
| Bird | 11 | 16.9 | *31* | 42 | 2.6 | *414* | 7.27 | (3.40, 15.56) | <0.001[e] |
| Sick pet | 1 | 1.5 | *31* | 39 | 2.5 | *470* | 0.59 | (0.08, 4.50) | 0.614 |
| Farm/ranch | 8 | 8.9 | *6* | 142 | 7.4 | *124* | 1.40 | (0.65, 3.02) | 0.392 |

| | *S.* Infantis (n= 96) | | | Other non-typhoidal *Salmonella*[a] (n= 2,040) | | | Odds ratios adjusted for site and season | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. | % | *No. Unknown*[c] | No. | % | *No. Unknown*[c] | aOR[d] | 95% CI | χ2 p-value |
| Live poultry | 21 | 26.6 | *17* | 91 | 5.4 | *339* | 3.48 | (1.73, 7.01) | 0.001[e] |
| Pig [f] | 0 | 0.0 | *31* | 18 | 1.1 | *410* | <0.001 | (<0.001, >999.99) | 0.986 |
| Ruminants | 1 | 1.5 | *31* | 71 | 4.4 | *407* | 0.37 | (0.05, 2.71) | 0.325 |
| **Waterborne exposures** | | | | | | | | | |
| Septic system | 10 | 23.8 | *54* | 320 | 29.4 | *953* | 0.58 | (0.27, 1.25) | 0.167 |
| Well water | 14 | 19.7 | *25* | 300 | 17.5 | *327* | 0.73 | (0.37, 1.46) | 0.378 |
| Swim treated water | 3 | 4.6 | *31* | 172 | 10.4 | *378* | 0.50 | (0.15, 1.66) | 0.257 |
| Swim untreated water | 1 | 1.5 | *30* | 113 | 6.7 | *360* | 0.21 | (0.03, 1.58) | 0.130 |
| Drink untreated water | 2 | 2.2 | *6* | 39 | 2.1 | *157* | 1.32 | (0.30, 5.77) | 0.709 |
| **Person-person exposures** | | | | | | | | | |
| Sick contact | 7 | 10.6 | *30* | 189 | 11.2 | *425* | 0.88 | (0.39, 2.00) | 0.754 |

[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

[b]Case exposure ascertainment (CEA) data were collected for case patients greater than 1 year of age, not associated with a known outbreak, and who did not report international travel.

[c]Number unknown includes persons for which exposure status was missing or reported as unknown.

[d]Odds ratios for each exposure were adjusted for site and season.

[e]Significant result in chi-squared test (p-value <0.05).

[f]Model did not converge for contact with pig because no cases reported exposure.

**Table 9.** Multivariable analysis of exposures[a] associated with sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis compared to infections of other non-typhoidal *Salmonella* serotypes[b] – FoodNet CEA[c], 2014.

| | **Odds ratios adjusted for site, season, and exposures reported by ≥10% of cases** | | |
|---|---|---|---|
| | aOR[d] | 95% CI | $\chi 2$ p-value |
| **Foodborne exposures** | | | |
| Chicken | 0.54 | (0.17, 1.72) | 0.301 |
| Turkey | 0.67 | (0.17, 2.60) | 0.561 |
| Beef | 1.71 | (0.54, 5.49) | 0.364 |
| Pork | 2.39 | (0.83, 6.90) | 0.108 |
| Fish | 1.67 | (0.58, 4.82) | 0.347 |
| Seafood | 2.04 | (0.60, 6.91) | 0.252 |
| Dairy | 0.53 | (0.16, 1.69) | 0.282 |
| Eggs | 0.95 | (0.32, 2.84) | 0.928 |
| Lettuce/spinach | 1.24 | (0.39, 3.97) | 0.721 |
| Tomatoes | 0.52 | (0.16, 1.67) | 0.273 |
| Berries | 0.54 | (0.16, 1.81) | 0.314 |
| Melon | 0.38 | (0.09, 1.60) | 0.189 |
| **Animal exposures** | | | |
| Dog | 0.43 | (0.15, 1.22) | 0.111 |
| Cat | 0.62 | (0.17, 2.20) | 0.457 |
| Bird | 12.91 | (2.71, 61.48) | 0.001[e] |
| Live poultry | 6.34 | (1.31, 30.71) | 0.022[e] |
| **Waterborne exposures** | | | |
| Septic system | 0.40 | (0.09, 1.87) | 0.247 |
| Well water | 0.74 | (0.12, 4.43) | 0.740 |
| **Person-person exposures** | | | |
| Sick contact | 0.65 | (0.08, 5.55) | 0.693 |

[a]The multivariable logistic regression model was limited to exposures for which at least 10% of cases reported exposure.

[b]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

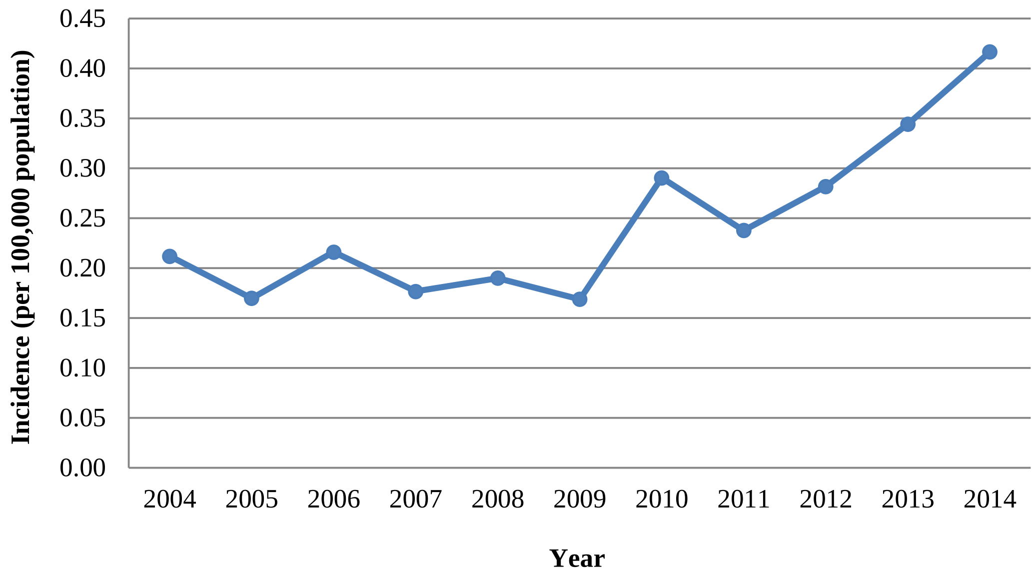
[c]Case exposure ascertainment (CEA) data were collected for case patients greater than 1 year of age, not associated with a known outbreak, and who did not report international travel.

[d]Odds ratios were adjusted for site, season, and exposures reported by at least 10% of cases.

[e]Significant result in chi-squared test (p-value <0.05).

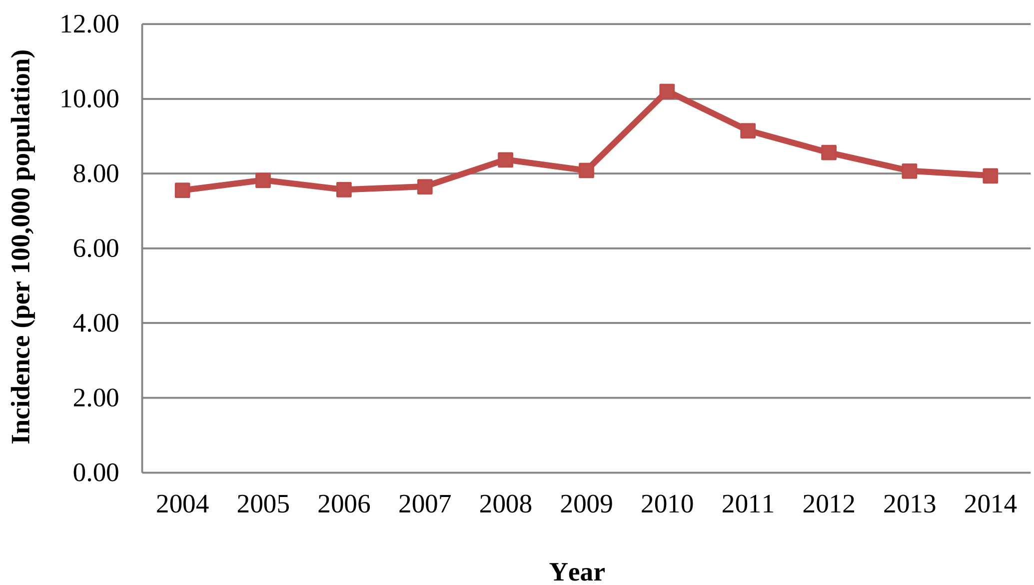
# Figures

**Figure 1a.** Annual incidence[a] of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis (N=1,268) – FoodNet, 2004-2014.




[a]Annual incidence per 100,000 population was calculated by dividing the number of sporadic infections by U.S. Census estimates of the surveillance area population.

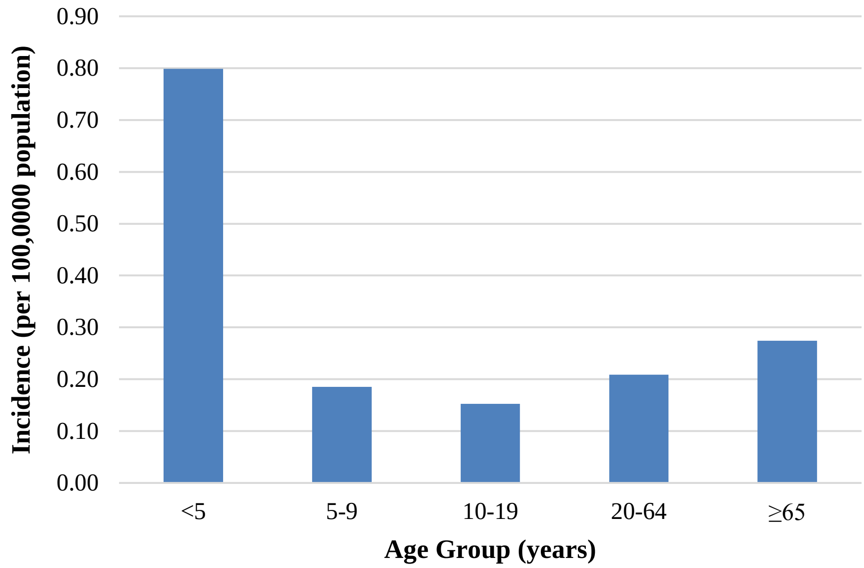
**Figure 1b.** Annual incidence[a] of sporadic laboratory-confirmed infections of other non-typhoidal *Salmonella* serotypes[b] (N=42,448) – FoodNet, 2004-2014.




[a]Annual incidence per 100,000 population was calculated by dividing the number of sporadic infections by U.S. Census estimates of the surveillance area population.

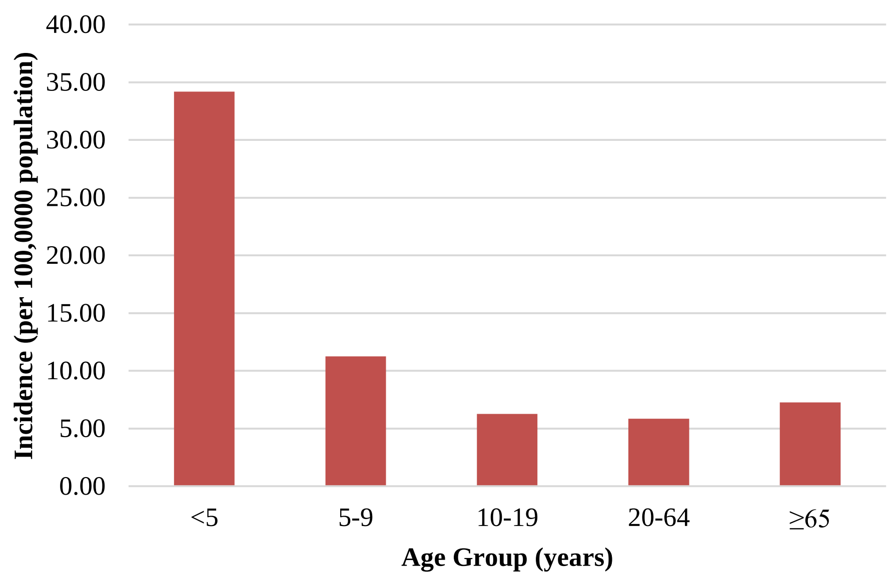
[b]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

**Figure 2a.** Average annual incidence[a] of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis (N=1,268), by age group – FoodNet, 2004-2014.




[a]Annual incidence per 100,000 population was calculated by dividing the number of sporadic infections by U.S. Census estimates of the surveillance area population for each age group and averaged over the 11 years.

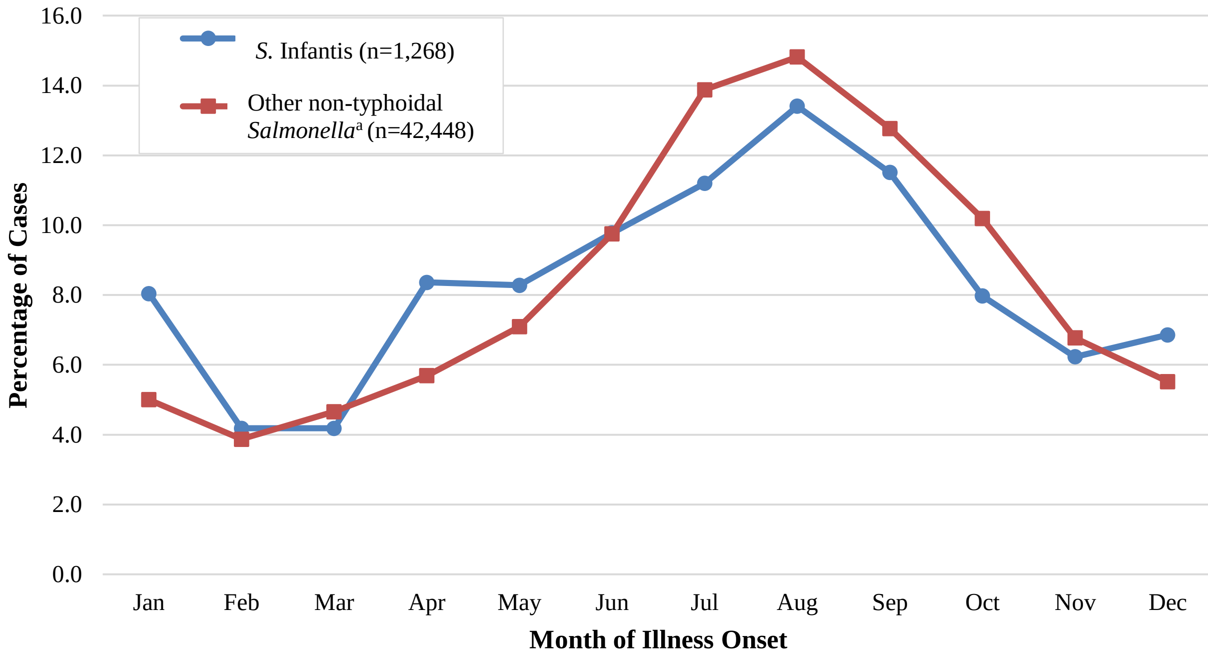
**Figure 2b.** Average annual incidence[a] of sporadic laboratory-confirmed infections of other non-typhoidal *Salmonella* serotypes[b] (N=42,448), by age group – FoodNet, 2004-2014.




[a]Annual incidence per 100,000 population was calculated by dividing the number of sporadic infections by U.S. Census estimates of the surveillance area population for each age group and averaged over the 11 years.

[b]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

**Figure 3.** Seasonality of sporadic laboratory-confirmed infections of *Salmonella enterica* serotype Infantis and other non-typhoidal *Salmonella* serotypes[a], by month of illness onset – FoodNet, 2004-2014.




[a]The ill controls comparison group was limited to *Salmonella* serotypes Enteritidis, Typhimurium, Newport, Javiana, I 4,[5],12:i:-, and Heidelberg.

# **Chapter III: Summary, Public Health Implications, Possible Future Directions**

A recent increase in incidence of infections with *Salmonella enterica* serotype Infantis (*S.* Infantis) has been observed in the United States, but sporadic infections of *S.* Infantis have not been well described. This study looked at eleven years of FoodNet surveillance data to describe characteristics and annual incidence of sporadic cases of infection with *S.* Infantis, and examined 2014 FoodNet exposure data to identify factors associated with infection of *S.* Infantis in case-case comparisons.

Annual incidence of sporadic infections of *S.* Infantis in 2014 was the highest observed during the 2004-2014 period. New cases of sporadic infections of *S.* Infantis were most likely to occur in children less than 5 years of age, followed by adults aged 65 years and older. Average annual incidence of sporadic infections of *S.* Infantis was highest among Asian persons and persons of Hispanic ethnicity. Prevention efforts may be most effective if directed at these demographic subgroups.

This study found contact with live poultry to be significantly associated with sporadic infections of *S.* Infantis when compared to ill controls. This finding corresponds with observations associating recent zoonotic outbreaks of *S.* Infantis infections with contact with live poultry including chicks and ducklings (18-19). Contact with pet birds was also significantly associated with sporadic infection of *S.* Infantis when compared to infections of other *Salmonella* serotypes. While pet birds have previously been identified as a reservoir for *Salmonella*, the association with serotype Infantis in particular may need further exploration (30).

There were limitations in our analysis, including varying methods of data collection among sites. In addition, due to the low number of cases of *S.* Infantis, associations with some exposures could not be assessed. It is also possible that an overlap in causal exposures between cases of *S.* Infantis and controls infected with other *Salmonella* serotypes resulted in certain associations being unidentified or underestimated.

Despite these limitations, the case-case comparison methodology used in this study has valuable applications for surveillance data. The use of ill controls as the comparison group likely allowed for reduction of selection and recall biases that are limitations of traditional case-control methodology applied to surveillance data. Case-case comparisons could be a cost-effective means to monitor changes in the attribution of *Salmonella* serotypes to specific exposures, identify risk factors for sporadic infections, and generate hypotheses for further investigation.

This was the first analysis of FoodNet case exposure ascertainment data to assess factors associated with sporadic infections of *S.* Infantis. The results of this study may indicate that sporadic cases of infection with *S.* Infantis are more likely to be associated with environmental factors such as contact with birds and live poultry when compared to other *Salmonella* serotypes. Data collection is ongoing, and replicating this analysis with more years of exposure data will help validate findings. An improved understanding of factors associated with sporadic infections of *S.* Infantis can lead to targeted public health interventions to address the observed increase in incidence of infections in the United States.