Outbreaks of Salmonella enterica Linked to Animal Contact: Demographic and Outbreak Characteristics and Comparison to Food Outbreaks — United States, 2009–2014

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Outbreaks of *Salmonella enterica* Linked to Animal Contact: Demographic and Outbreak Characteristics and Comparison to Food Outbreaks — United States, 2009–2014

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Abstract

Introduction: Each year in the United States, *Salmonella enterica* infections cause an estimated 1.2 million illnesses that result in 19,000 hospitalizations and 390 deaths. Illnesses occur sporadically throughout the year, but might also occur as part of an outbreak. Outbreaks are most commonly linked to a food source, but contact with live animals can also result in human outbreaks of illness.

Methods: Outbreaks of *Salmonella* reported to the Centers for Disease Control and Prevention through National Outbreak Reporting System (NORS) from 2009–2014 with a primary mode of transmission listed as animal contact or food were analyzed to characterize the demographics of zoonotic outbreaks and examine how they differ from foodborne outbreaks. Missing data for age or sex categories were recoded as age or sex unknown. Chi-square tests were used to compare proportions of categorical variables. Logistic regression was used to calculate odds ratios for age, sex, health outcomes and multistate exposure. Wilcoxon rank-sum tests were used to compare medians for outbreak size and duration. Analyses were conducted using SAS 9.3.

Results: During 2009–2014, a total of 484 outbreaks were reported through NORS; of these, 99 (20.5%) resulted from *Salmonella* transmission through animal contact and 385 (79.5%) resulted from foodborne transmission. These outbreaks resulted in 3,604 (19.8%) and 13,568 (80.2%) illnesses, respectively. A higher proportion of outbreak-associated illnesses among children aged <1 year were linked to animal contact outbreaks compared to food outbreaks (15.2% vs. 1.4%, p<0.01). Similarly, more animal contact outbreak-associated illnesses were noted among children aged 1–4 years compared to food outbreak-associated illnesses (24.5% vs 5.6%, p<0.01). Outbreak-associated illnesses that were hospitalized (OR 1.81, 95% CI: 1.62, 2.02), visited the emergency room (OR 1.58, 95% CI: 1.14, 2.18), or visited a healthcare provider (OR 2.67, 95% CI: 2.07, 3.43) were more likely to be associated with animal contact compared to food. No significant difference was noted in the outbreak size between animal contact (Median: 10, IQR: 4-42) and food outbreaks (Median: 14, IQR: 7-30) (p =0.2). Animal contact outbreaks reported to NORS were more likely to be multistate compared to foodborne outbreaks (OR 5.43, 95% CI: 3.37, 8.76) and had a longer median duration in days (p<0.001).

Conclusions: Outbreaks of *Salmonella* resulting from animal contact frequently have characteristics that are distinct from food outbreaks. Findings are consistent with reports in the literature where young children are disproportionately affected by animal contact outbreaks. Animal contact outbreaks might have a higher proportion of hospitalizations, emergency room visits, and healthcare provider visits. Animal contact outbreaks might also be longer in duration and are more likely to be multistate. Future investigations of multistate *Salmonella* outbreaks that are consistent with these differences should collect epidemiologic information regarding animal exposures to determine if contact with animals resulted in the transmission of the outbreak.
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CHAPTER I
INTRODUCTION

Background

Every year in the United States, non-typhoidal Salmonella enterica infections cause an estimated 1.2 million gastrointestinal illnesses, resulting in approximately 19,000 hospitalizations and 370 deaths [1]. Most human infections result in gastrointestinal symptoms that onset between 12 and 72 hours post exposure, and can last between 4 and 7 days [2]. The most common symptom is diarrhea, with fever, abdominal cramps, and vomiting frequently accompanying. The disease is usually self-limiting, and most people do not need medical treatment to recover. However, high risk groups, such as children under 5, elderly persons, and immune-compromised persons may be at risk of serious infection that can travel outside of the gastrointestinal tract, leading to complications and possibly death [2]. Non-typhoidal Salmonella accounts for the highest number of hospitalizations and deaths among all enteric pathogens in the United States [1]. Salmonella infections tend to have a seasonal trend, with more cases reported in the warmer months, and a peak of high numbers of cases tends to happen in the late summer [3]. Most cases of salmonellosis are foodborne in origin, acquired by consuming contaminated animal-derived products including meat, eggs, and dairy products, or fresh produce contaminated with the bacteria; in addition, contact with live animals or environmental contamination can spread the disease [4]. Although food sources of infection comprise the largest public health burden, outbreaks of Salmonella associated with live animal contact continue to increase, with an estimated 11% of all non-typhoidal Salmonella infections being attributed to animal contact annually [5]. The bacteria is transmitted through the fecal-oral route; contaminated fecal particles can be introduced into the oral cavity through consuming contaminated foods, bacteria on improperly washed hands, or from person-to-person contact.
Purpose of Study

Although there are numerous documented outbreak investigations of zoonotic *Salmonella* outbreaks in the literature, there have been no overarching studies conducted to describe the demographics of outbreaks associated with live animal contact. Demographic information is compiled each year for all *Salmonella* infections, both outbreak and sporadic, and literature reviews have been conducted to describe the demographics of foodborne *Salmonella* outbreaks[3]. Until the creation of the National Outbreak Reporting System (NORS) in 2009, there was no centralized agency to report outbreaks where the primary mode of transmission was animal contact[6]. The purpose of this study is to describe outbreaks of *Salmonella* associated with live animal contact and analyze any potential demographic differences between zoonotic outbreaks and foodborne outbreaks. The outcome of this analysis could help guide future *Salmonella* outbreak investigations where there are no clear or probable hypotheses for primary mode of transmission. If the demographics of an outbreak are consistent with zoonotic demographics, investigators can request that the local health department gather epidemiologic information about live animal contact the case may have had in the seven days leading up to illness onset.
CHAPTER II
REVIEW OF THE LITERATURE

DEMOGRAPHIC INFORMATION ON SALMONELLA INFECTIONS

Every year, the Centers for Disease Control and Prevention compile an annual surveillance report for all *Salmonella* infections, which includes all sporadic and outbreak associated cases. In the latest edition of the National *Salmonella* Surveillance Annual Report (2012), the age distribution of cases showed the highest incidence rate per 100,000 to be children under 5 years of age [3]. The incidence rate was higher for males compared to females for cases below 20 years of age, and higher for females for cases aged 20 to 80 years. As of 2012, the top four most common serotypes that cause human illness are *S. Enteritidis*, *S. Typhimurium*, *S. Newport*, and *S. Javiana* [3]. These serotypes have commonly been among the top 5 most common, but with ever changing food production and distribution, importation, and animal-human interaction practices, novel serotypes of *Salmonella* continue to increase in prevalence or appear in previously unknown sources [7].

SALMONELLA INFECTION OUTBREAKS IN THE UNITED STATES

Illnesses of salmonellosis occur sporadically throughout the year and are rarely linked to a specific source, but cases also may occur as part of an outbreak [3, 8]. State and local health departments are responsible for monitoring, investigating, and reporting all lab-confirmed cases of *Salmonella* [8]. An outbreak is defined as two or more similar illnesses arising from a common exposure [9]. Outbreaks can be isolated, single-state clusters, as the case would be for a “church potluck” type outbreak, or they can be more widespread, multi-state outbreaks, as would happen if a widely distributed food product were contaminated and shipped for consumer purchase [6, 7]. In 2009, the National Outbreak Reporting System (NORS) was created for reporting of all outbreaks of acute
gastroenteritis [6]. This new surveillance system expanded upon the previous reporting systems, which were specific only to foodborne (FDOSS) and waterborne (WDOSS) outbreaks and illnesses [10]. Now, all enteric illness outbreaks can be reported with any mode of transmission, including person-to-person transmission, environmental contamination, or animal contact transmission [10]. Although NORS has greatly expanded and enhanced surveillance, one limitation is that reporting to NORS is voluntary, and underreporting of outbreaks is very likely.

The incidence of multi-state foodborne disease outbreaks has been on the rise since 1973, and every year, about 47% of those outbreaks are non-typhoidal Salmonella infections [7]. This increase may be attributed to changes in the way food is produced and distributed, but better outbreak detection through PulseNet, an online database of bacterial disease surveillance may also contribute to this increase [7, 11]. Early detection and epidemiologic investigation of outbreak scenarios are essential for containing the outbreak, removing the affected product or exposure, and preventing further illness.

MONITORING SALMONELLA INFECTIONS IN THE UNITED STATES

In the United States, Salmonella is a nationally notifiable infectious disease, which means that all lab confirmed cases must be reported [2]. When a patient comes into a healthcare facility with gastrointestinal symptoms consistent with Salmonella, a stool sample is taken and cultured. If the bacterial culture grows Salmonella, the bacteria will be isolated and tested further. This pure sample of the case patient’s Salmonella bacteria is called their isolate. Within the species of Salmonella enterica, there are different subspecies called serotypes [12]. Serotypes are identified based on their surface antigens and flagellar antigens [13]. Based on a type of molecular subtyping called pulsed-field gel electrophoresis, or PFGE, the serotypes can further be narrowed down and linked together by this
“genetic fingerprint” [11]. In the past few years, whole genome sequencing has been conducted with some outbreak investigations which can provide an exact genetic match between case patient isolates, helping to more accurately determine if the illnesses came from the same source. All of these methods of genetically linking isolates and cases of *Salmonella* are important for outbreak response and investigations because they provide the framework for the epidemiologic investigation.

All isolates of *Salmonella* must be sent to a state public health laboratory, which uploads the PFGE pattern into a national database called PulseNet [11, 14]. PulseNet monitors all bacterial enteric illnesses in the United States. Advanced algorithms determine what the expected baseline number of *Salmonella* infections should be for any given week in the country through a system called CODA. If the number of cases of a certain PFGE pattern rises above the normal baseline, the system will flag to alert the change. When a cluster of illnesses that have the same genetic fingerprint are identified, an epidemiologic investigation can begin by contacting the state or local health department who reported the case to determine what information is known about exposures [15]. The outbreak or cluster will be assigned a unique identifying code based on the month and year of detection, serotype of *Salmonella*, and the location of the cluster [15]. This helps to facilitate the investigation by ensuring the accuracy of the information in each outbreak line list. It is important to note that just because a cluster has matching PFGE patterns, it does not necessarily mean that they are arising from a common source; an epidemiologic investigation must occur to link the cases through exposure information [11].

The PulseNet network has allowed for improved detection of multi-state outbreaks by identifying clusters of cases with matching PFGE patterns [14, 16]. When cases occur in different states, they may seem sporadic or unrelated, but PulseNet can link the PFGE patterns to show a genetically related cluster of disease [17]. This is especially true for zoonotic *Salmonella* outbreaks, as animals infected with a common serotype may have been shipped all over the country for sale as pets.
BURDEN OF ZOONOTIC SALMONELLA INFECTIONS

Studies have been conducted to estimate the burden of *Salmonella enterica* infections in the United States that are attributable to animal contact, along with the resulting hospitalization and death estimates. Approximately 11% of all non-typhoidal *Salmonella* illnesses can be attributed to contact with live animals, accounting for 127,155 (90% CrI: 66,502-219,886) domestically acquired illnesses, resulting in 2,392 (90% CrI: 935-4956) hospitalizations and 47 (90% CrI: 0-131) deaths [5]. Among all enteric zoonoses, non-typhoidal *Salmonella* accounts for 48% of all hospitalizations and 62% of all deaths [5]. Reptile associated salmonellosis seems to disproportionately affect infants and young children [18, 19]. In addition, outbreaks of *Salmonella* associated with turtles and live poultry have also had low median ages and a high proportion of infants and children aged less than five years who were affected [20-23]. In very young children and infants, it is likely that infection occurs as a result of indirect contact.

ZOONOTIC TRANSMISSION OF SALMONELLA BACTERIA

*Salmonella* bacteria can be transmitted through direct contact with the animal itself, or indirect contact with the environment where the animal lives and roams [24]. Even when animals appear healthy, they still may harbor the *Salmonella* bacteria in their intestinal tract and shed it intermittently, thereby contaminating their bodies and their environment [25, 26]. Because *Salmonella* is transmitted through the fecal-oral route, animals can shed the bacteria in their feces, which can then contaminate their feet, fur, feathers, skin, or mouths; transmission to humans can occur through touching, petting, feeding, or being licked by an animal, for example [27]. The bacteria can also be excreted in the feces...
of apparently healthy animals and then contaminate food for human consumption during the slaughter or production process[26].

In recent years, outbreaks of *Salmonella* have been associated with many different types of animal carriers, and cases have been exposed in public settings, private homes, farms, or other educational settings [25]. *Salmonella* outbreaks have been linked to small turtles, guinea pigs, bearded dragons and other reptiles, and live poultry, including baby ducklings and chicks from mail-order hatcheries [18, 21, 28, 29]. Pet food products that are derived from animal sources can also harbor *Salmonella* bacteria and cause illness in humans. Recent outbreaks of human illness have been associated with products such as dry dog food, pet jerky treats, and frozen feeder rodents meant for snake consumption [30-32].

**A ONE HEALTH APPROACH TO THE CONTROL OF ZOOLECTIC SALMONELLA INFECTIONS**

Zoonotic transmission of *Salmonella* can occur through human contact with an animal directly, or indirectly through contact with its environment [33]. Because of the complex interactions between human health, animal health, and the environment, a One Health approach is fundamental for preventing outbreaks of enteric illness associated with live animal contact [34]. This approach means that professionals in human medicine, veterinary sciences, and environmental sciences must work together with a common health goal to solve the complex issues that arise with zoonotic disease transmission [35]. An outbreak of *Salmonella* serotype Braenderup was detected in July of 2012, and through epidemiologic investigation, was found to be associated with live poultry exposure [28]. Traceback information revealed that the infection was associated with mail-order hatcheries that shipped live baby poultry to consumers and feed stores, but the complex nature of the industry presented challenges. Through a One Health approach, the investigators worked with veterinarians,
human healthcare providers, and industry experts to find the source of the outbreak, and because of the collaboration, were able to establish Hatchery D as the source, which ultimately yielded the outbreak strain through environmental sampling [28]. This is one example of how important a One Health approach can be when investigating zoonotic outbreaks of Salmonella and other enteric illnesses, in addition to any disease that is zoonotic in origin and poses a threat to public health.

**TURTLE ASSOCIATED SALMONELLOSIS**

Turtles have been implicated as the source in many multi-state Salmonella outbreaks in recent years. Tiny turtles are an especially risky vehicle for human salmonellosis in children because they are attractive pets that frequently given to children due to their small size and ease of care, but their water based environment becomes heavily contaminated with Salmonella bacteria and young children have a tendency to put small objects, including turtles, in their mouths [36, 37]. Small turtles are not appropriate pets for households with infants or young children, elderly family members, or immune-compromised persons due to the high risk of salmonellosis[38]. In 1975, the FDA banned the sale of pet turtles with a carapace (shell) length of less than four inches in an effort to prevent human illness associated with these animals [39]. Studies conducted before the implementation of the ban estimated that approximately 280,000 cases of human salmonellosis may be linked to turtle exposure, either through direct or indirect contact; after the ban was put into place, there was a 77% reduction in the frequency of Salmonella serotypes that had previously been associated with turtles, whereas no consistent change was observed in non-turtle associated serotypes [39]. It is also estimated that 100,000 cases of turtle-associated salmonellosis were prevented in children aged 1-9 years as a result of the ban [39]. Despite the success of the ban, outbreaks of Salmonella associated with turtle exposure continue to occur, possibly due enforcement issues [37]. A clause in the ban allows for the
sale of undersized turtles if they are used for “bona fide” educational purposes, scientific uses, or exhibition [20]. Despite the restrictions of the ban, tiny turtles are still sold illegally as pets through online vendors, flea markets, roadside stands and vans, or street vendors [20]. While the ban remains in place in the United States, worldwide international shipment of baby turtles bred in the US still occurs, potentially increasing turtle-associated salmonellosis in other countries [36].

Prior to 2006, no large-scale multi-state outbreaks of turtle-associated salmonellosis were reported, most likely due to the sporadic nature of zoonotic Salmonella infections, which made them difficult to detect before the implementation of PulseNet [16]. Many single state cases and outbreaks can be found in the literature, including cases related to turtles acquired at state fairs [40]. In 1994, a six-week-old infant was hospitalized for 56 days with severe complications from an infection of S. Stanley [41]. The family had a pet turtle, which yielded the same serotype of Salmonella upon testing. Although the infant had no contact with the turtle, the turtle’s bowl was cleaned in the kitchen sink, likely leading to cross contamination. An outbreak in Wyoming in 2004 sickened 3 children and 1 adult with S. Pomona, which led to an investigation of small turtles being sold at souvenir shops [42]. More cases were identified through the investigation, and regulatory action was taken to prevent the sale of small turtles.

Since 2006, multistate outbreaks of Salmonella associated with turtle exposure occur regularly. In 2006, an outbreak of Salmonella I4,[5],12:i:- was identified in Ohio and Tennessee, where both patients reported exposure to tiny turtles that had been purchased from flea-market type vendors [43]. For both cases, the turtles and their environment were sampled, yielding the outbreak strain. In 2007, a three week old infant presented to an emergency department in Florida with poor feeding and lethargy, and despite being immediately transferred to a pediatric hospital, the infant died [43]. Cultures yielded Salmonella Pomona, and upon interview by the Florida Department of health, the
parents revealed that they had received a 1.25 inch turtle as a gift. Laboratory testing yielded S. Pomona in the turtle, which was indistinguishable from the patient’s isolate by PFGE [43]. Nineteen other cases of the outbreak strain were identified in multiple states, and of the 15 patients interviewed, 12 (80%) reported contact with turtles in the 7 days before they became ill. The median age for these patients was 3 years, with a range of 2 months to 59 years [43]. In 2008, an outbreak of *Salmonella Typhimurium* possibly related to turtle exposure was reported to CDC by the Philadelphia Department of Health when the cluster was identified by PulseNet [16]. Laboratory testing of the turtle yielded the outbreak strain, which led to a multi state outbreak investigation of *S. Typhimurium* with the outbreak PFGE pattern. Using PulseNet, 135 cases from 25 states and CD were identified, with a median age of 7 years (range: <1-94 years). Of the 70 primary cases with exposure information, 26 (37%) reported exposure to turtles, which led to the initiation of a case-control study. The study included 37 cases and 47 controls. The matched odds ratio for turtle exposure was 16.5, and 16 (94%) of the 17 case-patients with exposure information reported that the turtle was less than 4 inches long [16]. Turtle associated outbreaks continue to occur. In 2007 and 2008, *Salmonella Paratyphi* B var Java was identified and linked to turtle exposure [44]. An outbreak of *Salmonella Paratyphi* B var. L (+) tartrate + associated with turtle exposure was reported in 2011 [37], an outbreak of *Salmonella Poona* associated with pet turtle exposure was reported in 2014 [20]. From 2012 to 2013, eight turtle-associated multi-state *Salmonella* outbreaks were reported, with 473 cases, and 70% of ill persons were children 10 years of age or younger; this event is referred to as “Turtlepocalypse” among outbreak investigators due to the widespread and complicated nature of the investigation [45]. Turtle-associated salmonellosis continues to be a public health challenge, with more efforts needed in ban enforcement and consumer education for potential turtle owners.
LIVE POULTRY ASSOCIATED SALMONELLOSIS

Live poultry has long been recognized as a source of human salmonellosis, because the bacteria naturally live in the intestinal tract of the birds, which shed it into their environment [33, 46]. From 1990 to 2012, there were 45 outbreaks of Salmonella linked to live poultry exposure, with 8 separate outbreaks in 2012 [47]. While past outbreaks of Salmonella associated with live poultry were linked to the Easter tradition of giving children artificially dyed baby chicks as gifts [48, 49], the trend of backyard poultry ownership has been increasing as a result of the movement toward local, sustainable foods, and with it, an increase in live-poultry associated salmonellosis [47]. Chicks and ducklings are often implicated in outbreaks together, and historically there have been springtime Easter-related increases in illness [48, 50]. The number of outbreaks associated with live poultry has been increasing over the last decade, as well as the number of cases included in each outbreak [47]. A large number of these outbreaks are associated with mail-order hatcheries, which ship baby poultry directly to people’s homes or to agricultural feed stores for retail sale [51]. Traceback for these outbreaks can be difficult, as there is no regulatory agency for mail-order hatcheries to ensure best practices. Hatcheries may drop-ship or trans-ship birds for other hatcheries when they cannot complete an order, making it complicated to determine the source of infected birds linked to human illness.

Young children are largely affected in Salmonella outbreaks associated with live poultry, especially when chicks or ducklings are implicated. An outbreak of S. Typhimurium in 2009 in New York and Pennsylvania was investigated, and a case control study showed statistically significant matched odds ratios for contact with baby poultry, contact with chicks, contact with ducklings, and visiting an agricultural feed store [51]. Traceback for this outbreak led to a single agricultural feed store supplied by a single hatchery, and recommendations for prevention included interventions at the hatchery and
feed stores, as well as recommending that pediatricians speak with patients and their families about the risk of salmonellosis associated with live poultry contact. 36% of the patients in this outbreak were less than five years of age. In 2012, an outbreak of S. Infantis, S. Newport, and S. Lille were linked to live poultry from a single mail order hatchery in Ohio, and 33% of the patients were less than 10 years of age [52]. In 2011, an outbreak of S. Johannesburg and S. Altona were linked to a single mail-order hatchery; 32% of the S. Altona patients and 75% of the S. Johannesburg patients were less than 5 years of age [53]. Most of the live poultry were purchased for pets or for backyard flocks.

Risky behaviors associated with live poultry contact can increase the chances of acquiring a *Salmonella* infection. Treating the birds as indoor pets and keeping them inside the home can increase the risk of exposure or surface contamination, especially if they are allowed to roam freely [22, 47, 50]. Many case patients report very close contact with the birds, including holding, snuggling, or kissing them [22, 47]. Ducklings have been allowed to swim in bathwater with children, which can spread *Salmonella* bacteria through the water and onto tub surfaces [50]. Interventions in the agricultural feed stores have helped to educate consumers, especially novice poultry owners, on proper handling of live baby poultry to decrease the risk of salmonellosis.

**REPTILE ASSOCIATED SALMONELLOSIS**

Aside from turtles, many other species of reptiles have been associated with outbreaks of *Salmonella*. Iguanas have been implicated in smaller single state outbreaks dating back to the 1990s, and these infections have often been very rare serotypes. In 1990, two infants in Indiana were diagnosed with S. marina, a rare serotype [54]. In both cases, the only indoor pet was an iguana, which both tested positive for S. marina. Neither infant had direct contact with the iguanas, and the parents reported handwashing after handling the reptiles. Morbidity and Mortality Weekly Reports report
many other cases of *Salmonella* infection associated with iguana exposure and confirmed through testing of the reptile’s environment. In 1995 in Connecticut, a 40 year old man was hospitalized with osteomyelitis from an infection of *S. wassenaar*, which was later linked to his two pet iguanas when stool samples yielded the same strain [41]. Many cases of iguana-associated salmonellosis have been seen in very young children and infants, which have led to severe infections and complications. In 1994 in New Jersey, a 5-month-old girl was hospitalized with severe septicemia and meningitis, and her cerebrospinal fluid and blood cultures yielded *S. rubislaw*. Although the family did not own an iguana, the infant frequently stayed at the home of a babysitter who did, and subsequent testing of the iguana yielded *S. rubislaw* [41]. In the same year, a 3-week-old infant was hospitalized with *S. poona*, and the family’s pet iguana tested positive for the strain [41]. In Arizona in 1996, a 3-week old boy developed a severe infection of an extremely rare serotype, *S. IV 44:z4,z23*, which led to a 10 day hospitalization [19]. After the pet iguana tested positive for *S. IV 44:z4,z23*, the family gave it to a relative. One month later, the boy was treated in the emergency department for fever and diarrhea after visiting the relative who then kept the iguana, and stool cultures yielded the same serotype as his first infection. A lack of awareness of the risk of salmonellosis associated with iguanas can lead to risky behaviors. After purchasing an iguana at a pet store in Massachusetts in 1997 where the store owner was reportedly unaware that iguanas can carry *Salmonella*, an 8 year old immunocompromised boy contracted *S. St. Paul* after handling the iguana and placing it on his head and face [19]. In Wisconsin in 1998, a 5 month old infant died suddenly at home; later testing showed *S. marina* yielded from the autopsy testing and the iguana in the family’s home [19]. The family was unaware of the risk of salmonellosis through direct or indirect contact.

*Salmonella* infections have also been associated with aquatic amphibians. In 2009, a multistate outbreak of *S. Typhimurium* primarily affecting children was detected through PulseNet [55]. 85
patients from 31 states were identified with the outbreak strain, and the median age was 5 years (3 weeks–54 years) with 79% of the patients aged less than 10 years. A multistate case control study was conducted to examine the association between illness and two exposures of note: consumption of cheese flavored crackers, and exposure to aquatic animals. A total of 19 patients and 31 controls were enrolled, and exposure to frogs was statistically significant [mOR= 24.4, 95%CI 4.0-infinity]. No association between food and illness was found. A total of 14 patients could identify the type of frog they had, and all 14 identified the African Dwarf frog [55]. Subsequent testing of the frog’s environment and habitat in case-patient homes yielded the outbreak strain, and traceback investigations led to a California breeder, and positive samples of the outbreak strain were found in the breeding facility.

Other types of lizards and snakes may also transmit Salmonella. Salmonellosis has been associated with handling corn snakes [19], bearded dragons [40], and Savannah monitor lizards [56]. Indirect transmission has been noted in these cases as well. For the 8-week-old infant associated with the aforementioned monitor lizard, the father reported having to climb into the cage to care for the lizard due to the size of enclosure. He reported cleaning the cage with bare feet and then walking around the home, as well as cleaning cage accessories in the kitchen sink [56]. In California in 2001, a 3-month-old infant was seen in the emergency department and stool samples yielded S. Nima [40]. Although there were no reptiles in the home, the father taught high school biology, where he had a classroom boa constrictor that he would drape across his shoulders and would not change clothes before holding his child. Subsequent testing of the stool of the snake yielded S. Nima.
OTHER ZOONOTIC ASSOCIATED SALMONELLOSIS

Outbreaks of salmonellosis can also be associated with other zoonotic modes of transmission, including small mammals, pet foods, and other animal-derived pet products. Human salmonellosis was first linked to dry dog and dry cat foods in 2007 when a multistate outbreak of S. Schwarzengrund was identified through PulseNet [57]. Between 2006 and 2008, a total of 79 patients in 21 states were identified, and 48% of the patients were two years of age or younger. To determine the source of the outbreak, two multistate case-control studies were conducted. The first study included all ages of patients and examined exposures to canines and pet foods. The second study included only children aged two years or younger who had exposure to dogs. Dog contact (mOR:3.6) and purchase of X brand dry dog food (mOR:6.9) were statistically significantly associated with cases. For the infant case-patients, illness was associated with feeding pets in the kitchen (OR:4.4). FDA testing in August of 2007 yielded the outbreak strain in unopened bags of dry dog food from plant X, which initiated a recall and eventually led to the permanent closure of that plant [57]. In 2012, an unopened bag of dry dog food yielded S. Infantis during routine surveillance, and human cases with the same genetic fingerprint were identified through PulseNet [30]. A total of 53 cases in the United States and Canada were identified, and 38% of the cases were children aged 2 years or younger. Epidemiologic and traceback investigations identified a plant in South Carolina, and the outbreak strain was also isolated from fecal samples of dogs that ate the implicated food [30]. In 2013, an outbreak of S. Typhimurium was identified by the New Hampshire Department of Health and Human Services that was linked to locally made pet chicken jerky treats, the production of which was not regulated by any agency due to the small scale production and single-ingredient product [32]. Public health recommendations from all of these investigations include a One Health approach to preventing salmonellosis associated with pet food products, and hypothesized that pet foods or treats may be an under-recognized vehicle for
outbreaks of *Salmonella* or a source of sporadic infections. These recommendations include proper handwashing after handling pet foods, avoiding cross-contamination, and preventing young children from contact with pet food products [30, 32, 57]. In addition, pediatricians, veterinarians, and public health workers should be aware of the risk of salmonellosis associated with pet food products.

Salmonellosis can also be associated with rodents and other small mammals. A multistate outbreak of *S. Typhimurium* was linked to hedgehogs between 2011 and 2013, which totaled 20 cases with a median age of 13 years [58]. In 2010, a 7-year-old female was hospitalized with a severe infection of *Salmonella Enteritidis*, and the epidemiologic investigation revealed that the patient had two pet guinea pigs, which died prior to her hospital admission [29]. Because serotype enteritidis is so common, the case definition included PFGE match by XbaI and BlnI patterns, and reported guinea pig exposure. Ten cases were identified, and the median age was 9.5 years. Traceback identified one breeder who was potentially supplying the stores, but a definitive environmental source of guinea pig infection was not identified. Another interesting outbreak of *Salmonella I 4,[5],12:i:-* was associated with frozen feeder rodents meant for consumption by snakes or other reptiles. From 2008-2010, there were over 500 cases internationally, and illness was significantly associated with exposure to frozen feeder rodents [31]. Traceback and environmental testing yielded the outbreak strain and initiated an international recall of all frozen feeder rodent products from Company A.
CHAPTER III
MANUSCRIPT

Outbreaks of *Salmonella enterica* Linked to Animal Contact: Demographic and Outbreak Characteristics and Comparison to Food Outbreaks — United States, 2009–2014

Introduction

Every year in the United States, non-typhoidal *Salmonella enterica* infections cause an estimated 1.2 million gastrointestinal illnesses, resulting in approximately 19,000 hospitalizations and 390 deaths [1]. Most human infections result in gastrointestinal symptoms that onset between 12 and 72 hours post exposure, and can last between 4 and 7 days [2]. The most common symptom is diarrhea, which is often accompanied by fever, abdominal cramps, and vomiting. The disease is usually self-limiting, and most people do not need medical treatment to recover. However, high risk groups, such as children aged less than five years, elderly persons, and immune-compromised persons might be at risk of serious infection that can travel outside of the gastrointestinal tract, leading to complications and possibly death [2]. Non-typhoidal *Salmonella* accounts for the highest number of hospitalizations and deaths among all enteric pathogens in the United States [1]. *Salmonella* infections tend to have a seasonal trend, with a higher frequency reported in the warmer months, peaking in the late summer [59]. Illnesses resulting from *Salmonella* infection occur sporadically throughout the year and most illnesses are rarely linked to a specific source, but illnesses might also occur as part of an outbreak [3, 8]. In 2013, 6% of all reported *Salmonella* infections were linked to an outbreak [59].

In the United States, salmonellosis is a nationally notifiable infectious disease, which means that all laboratory-confirmed infections are required to be reported [2]. Within the species of *Salmonella enterica*, there are different subspecies called serotypes [12]. Serotypes are identified based on their surface antigens and flagellar antigens [13]. Based on a type of molecular subtyping
called pulsed-field gel electrophoresis, or PFGE, the serotypes can further be narrowed down and linked together by this “genetic fingerprint” [11]. All isolates of *Salmonella* must be sent to a state public health laboratory, which uploads the PFGE pattern into a national database called PulseNet [11, 14].

Although most infections are foodborne, *Salmonella* infections can also be acquired through contact with animals and their environment or habitat [5, 33]. These zoonotic infections comprise an estimated 11% of all salmonellosis annually [5]. Among all enteric zoonoses, non-typhoidal *Salmonella* accounts for an estimated 48% of all hospitalizations and 62% of all deaths [5]. Reptile associated salmonellosis seems to disproportionately affect infants and young children [18, 19, 33]. In addition, outbreaks of *Salmonella* infections linked to turtles and live poultry have also had low median ages and a high proportion of infants and children aged less than five years who became ill [20-23, 33, 45, 47, 53]. Animal contact outbreaks have been documented to have long durations, often spanning several years [44, 45, 47, 55, 58]. Outbreaks linked to live poultry often have an onset date in the early spring, coinciding with the Easter holidays and the practice of giving baby chicks or ducklings as gifts [22, 33, 47, 53].

Since 2009, state and local health departments voluntarily report outbreaks of enteric illness through the Centers for Disease Control and Prevention (CDC) National Outbreak Reporting System (NORS) [6]. Before the implementation of NORS, there was no national surveillance system for outbreaks of enteric illness associated with animal contact [10]. For surveillance and reporting purposes, an outbreak is defined as two or more similar illnesses arising from a common exposure [6]. Outbreaks can be single state or local outbreaks where all the ill persons are located in one region, or they can be multistate outbreaks with illnesses in many regions. The incidence of multistate foodborne disease outbreaks has been on the rise since 1973, and every year, about 47% of those outbreaks
result from non-typhoidal *Salmonella* [7]. This increase might be attributed to changes in the way food is produced and distributed, but better outbreak detection through PulseNet, an online database of bacterial disease surveillance might also contribute to this increase [7, 11]. Many of these large, multistate outbreaks have also been linked to contact with animals, including live poultry, turtles, other reptiles, and some small mammals [20-23, 52, 55, 58].

Although the literature describes some potential differences between outbreaks linked to food and outbreaks linked to animal contact, no nationwide studies have been conducted to assess these differences. In the beginning of an outbreak investigation, there is not always a clear hypothesis of the source of the outbreak. This might especially be true in multistate outbreaks, where the same genetic fingerprint of a serotype of *Salmonella* links infections in different states. Once a vehicle has been implicated, prevention efforts and interventions can be implemented to prevent further illness. If the common source is animal contact, but there is a lack of epidemiologic information gathered on potential animal exposures, the investigation could be delayed, potentially leading to additional illnesses. Therefore, the objective of this analysis was to compare outbreaks of *Salmonella* infections linked to animal contact to outbreaks of *Salmonella* infections linked to food and determine differences in the demographic and outbreak characteristics by mode of transmission. Determination of an animal vehicle earlier in an outbreak investigation based on demographic characteristics might reduce the burden of additional outbreak-associated illness.

**Methods**

This study was conducted using surveillance data from the CDC. A dataset was obtained from CDC’s NORS with the following outbreak inclusion criteria: outbreak report date from January 1, 2009 to December 31, 2014, laboratory-confirmed etiology of *Salmonella enterica*, and a primary mode of
transmission either animal contact or food. The dataset was further subdivided to include only outbreaks where the primary mode of transmission was confirmed to be either animal contact or food; any outbreaks with a food vehicle undetermined (where the investigating agency could not confirm the food source of the outbreak) were excluded from the analysis.

*Measures and Definitions*

The outcome of interest for this study was category of outbreak, defined dichotomously as either animal contact outbreak or food outbreak based NORS (reported to CDC by state health department investigations). The exposures of interest for this study included demographics of cases and outbreak characteristics. A case was defined as any person who was reported to have an illness linked to an outbreak. Ages of cases in each outbreak were reported by number in each age category or percentage in each category. Sexes of cases in each category were also reported by count or percentage. Hospitalizations, deaths, emergency room visits, and healthcare provider visits were reported as number of cases with the healthcare outcome, with a second variable for number of cases for whom this information is known.

Outbreak size was reported using three definitions: estimated primary ill, laboratory-confirmed primary ill, and probably primary ill. Estimated primary ill included all laboratory-confirmed and probable primary cases; age and sex categories included all the cases in estimated primary ill. Laboratory-confirmed primary cases included only those in which an isolate had been confirmed in either a state or CDC laboratory. Probable primary cases included only cases who had a gastrointestinal illness after exposure to the implicated item, but did not have a laboratory test that confirmed diagnosis. Total secondary cases was defined as cases who became ill after contact with a primary case, but did not have exposure to the implicated vehicle.
Duration of the outbreak was calculated in days by subtracting the date of onset for the last illness in an outbreak from the date of onset for the first illness in the outbreak. Month of onset was also determined using date of the first illness in each outbreak. Multistate exposure indicated whether an outbreak occurred in a single state or in multiple states, which is based on the states in which the illness is diagnosed. Serotype indicates the laboratory-confirmed subspecies of *Salmonella* bacteria implicated in the outbreak.

If categorical counts were not reported, case counts for age categories and sex categories were recreated based on reported percentages and estimated primary ill. Missing data was recoded as age or sex unknown and was treated as missing for the purpose of this analysis.

*Statistical Methods*

Statistical analyses were performed to determine differences in the characteristics of animal contact outbreaks and food outbreaks. All statistical analyses were performed using SAS 9.3. For age categories, sex categories, and healthcare and survival outcomes, the number of cases per category in each outbreak were summed across all animal contact and food outbreaks, and collectively were referred to as outbreak-associated illnesses. Proportions for categorical variables were analyzed using chi-square tests. Logistic regression was used to calculate odds ratios and 95% confidence intervals for age categories, sex categories, healthcare outcomes, and multistate exposure. Number of reported deaths, hospitalizations, emergency room visits, and healthcare provider visits were analyzed for animal contact outbreaks compared to food outbreaks based on illnesses for whom information was available. Due to differences in reporting of these outcomes, the number of illnesses with this information missing is different for each outcome. Fisher’s Exact Test was used to compare deaths due to the small expected cell frequencies.
Case counts per outbreak and duration of outbreak in days were compared by outbreak type using Wilcoxon rank-sum tests. Month of outbreak onset was determined from outbreak onset date to examine any differences in seasonality by mode of transmission. The top 15 most common serotypes of *Salmonella* for animal contact and food outbreaks were compiled by number of total outbreaks and percentage of total outbreaks. P-values less than 0.05 were considered statistically significant for all analyses.

**Results**

From 2009–2014, there were 99 outbreaks of *Salmonella* infections reported to NORS with a primary mode of transmission listed as animal contact. These outbreaks resulted in 3,604 estimated primary illnesses, 586 hospitalizations, and 6 deaths. In the same time period, 385 outbreaks of *Salmonella* infections were reported with food as the primary mode of transmission and confirmed food vehicle. Food outbreaks resulted in 13,568 estimated primary illnesses, 1,616 hospitalizations, and 15 deaths.

Demographic differences between animal contact and food outbreaks were observed (Table 1.). A higher proportion of outbreak-associated illnesses were children aged <1 year in animal contact outbreaks compared to food outbreaks (15.2% vs. 1.4%, p<0.01). Similarly, more animal contact outbreak-associated illnesses were noted among children aged 1–4 years compared to food outbreak-associated illnesses (24.5% vs 5.6%, p<0.01) (Figure 1). Outbreak associated illnesses aged < 1 year had 25.0 (95% CI: 20.2, 30.8) times the odds of being linked to animal contact compared to food when compared to the reference group aged 20-49 years. Children aged 1 to 4 years (OR: 10.0 95% CI: 8.7, 11.6) and children aged 5 to 9 years (OR: 5.48 95% CI: 4.65, 6.46) also were more likely to be linked to animal contact outbreaks compared to the reference age group. For animal contact outbreaks, 1,056
outbreak-associated illnesses had an unknown age category and were treated as age missing. For food outbreaks, 3,235 outbreak-associated illnesses had an unknown age category and were treated as age missing. Females were more likely than males to be linked to an animal contact outbreak compared to a food outbreak (OR: 1.22, 95% CI: 1.13, 1.32).

We did not observe a significant difference in the proportion of deaths comparing animal contact and food outbreaks (0.2% vs 0.2%, Fisher’s Exact Test=0.143). Outbreak-associated illnesses that included hospitalization were more likely to be linked to animal contact outbreaks than food outbreaks (OR: 1.81, 95% CI: 1.62, 2.02). Outbreak-associated illnesses that visited the emergency room (OR: 1.58, 95% CI: 1.14, 2.18) or visited a healthcare provider (OR: 2.67, 95% CI: 2.07, 3.43) were also more likely to be linked to animal contact.

The median size of animal contact outbreaks was 10 cases (IQR 4–42) compared to a median of 14 cases (IQR: 7–30) among food outbreaks (p=0.24). The median number of probable primary illnesses for food outbreaks (median: 4, IQR: 0–14) was greater than animal contact outbreaks (median: 0, IQR: 0–1) (p<0.01). The duration of animal contact outbreaks (median 98.0 days, IQR: 26.0–216.0) was significantly longer than food outbreaks (median: 8.0 days, IQR: 2.0–26.0) (p <0.01). Multistate exposure was more common among animal contact outbreaks compared to food outbreaks (OR 5.43, 95% CI: 3.37–8.76) (Table 2).

Food outbreaks by calendar month of onset showed the peak of outbreak onsets occurred during the mid-summer months. Animal contact outbreaks by month of onset were more sporadic, with peaks in the early spring months, early summer, and mid-winter. (Figure 2.) The top 15 serotypes of Salmonella for animal contact and food outbreaks are listed in Table 3.
Discussion

Differences between outbreaks of Salmonella enterica linked to animal contact and outbreaks linked to food were observed in this study. The findings of this analysis are consistent with previous observations in the literature and past outbreak reports that report that young children are disproportionately affected by animal contact outbreaks of Salmonella [18-22, 33]. Although 20.5% of all outbreak-associated illnesses in this analysis resulted from animal contact, when stratified by age category, a majority of outbreak-associated illnesses among children aged <1 year and aged 1–4 years resulted from animal contact (72.7% and 51.7%, respectively). This is the first analysis using NORS data that compares animal contact outbreaks to food outbreaks to support this hypothesis.

Outbreak-associated illnesses that were hospitalized had 1.81 times the odds of being linked to animal contact compared to food. Illnesses with emergency room visits and healthcare provider visits also had greater odds of being linked to animal contact outbreaks. This might indicate that illnesses linked to animal contact have the potential to be more severe, resulting in more hospitalizations, more emergency room visits, and more healthcare provider visits.

The difference in median number of laboratory-confirmed primary illnesses might be associated with the difference in hospitalizations, emergency room visits, and healthcare provider visits for animal contact and food outbreak illnesses. During these healthcare visits, stool samples would be collected and Salmonella isolated to confirm etiology. Once confirmed, the isolate of Salmonella is sent to state public health laboratories, and the illness is reported to the state or local health department. In addition, differences in case definition might also contribute to these differences. For foodborne outbreaks, it is possible that the case definition might not include a lab-confirmed PFGE match, but a gastrointestinal illness after exposure to a common food. More animal contact outbreaks might include a PFGE match in the case definition, which might not account for as many probable illnesses.
The difference in outbreak duration between animal contact and food outbreaks is consistent with previous observations in the literature where animal contact outbreaks lasted many months or years. This finding is plausible because animals shed *Salmonella* bacteria intermittently, which can contaminate their environments or spread to humans long after the animal has been acquired [33]. Unless an affected food is shelf stable, food outbreaks might be shorter in duration because the entirety of the affected food is consumed over a short period of time, or because food outbreaks might be associated with seasonal, perishable items such as produce.

Number and percentage of outbreaks were reported for the top 15 serotypes of *Salmonella* in Table 3. For food outbreaks, the top 15 serotypes are include nearly all of the top 15 laboratory-confirmed serotypes reported in 2012 [3]. The top 15 serotypes for animal contact outbreaks included 9 of the same serotypes as food outbreaks, but also included some that were less common overall. These include S. Poona, S. Pomona, and S. Sandiego, which are often linked to turtle-associated outbreaks, and S. Hadar, which has been linked to live-poultry outbreaks [20, 45].

Month of outbreak onset also varied between animal contact and food outbreaks. The onset of food outbreaks by month was consistent with yearly trends for overall *Salmonella* infections, with a peak in the late summer months [59]. Animal contact outbreaks peaked in the early spring, which is consistent with the literature regarding live baby poultry and human salmonellosis [5, 22, 47, 53].

There were limitations to this analysis. First, outbreaks of acute gastrointestinal illness are voluntarily reported to NORS by state and local health departments, so underreporting likely influenced the number of total outbreaks, as well as the number of outbreak-associated illnesses that could be included in this analysis. Reporting also varies by state, depending on the funding, resources, and manpower each state has to conduct outbreak investigations. Second, incomplete reports and missing data for demographic variables presented challenges for this analysis. Data was recreated in
the most thorough manner possible to account for missing information, but it is likely that some error still occurred. Hospitalizations, deaths, emergency room visits, and healthcare provider visits had to be analyzed based on number of cases for whom this information was available, which might have led to an overestimation of the proportions of cases with each outcome. Additionally, although the differences in sex were statistically significant, the effect size was small and might be of little practical significance due to the large sample size of outbreak-associated illnesses. Third, conducting analyses on data at the outbreak level also presented some challenges and limitations to the analysis. Because specific age, gender, and outcomes were not available for each case in the outbreak and were only represented through aggregate outbreak level data, no multivariable analysis could be conducted to control for the effect of certain variables. It is possible that hospitalizations, emergency room visits, and healthcare provider visits were more likely among animal contact outbreak-associated illnesses due to the influence of age. Animal contact outbreaks had a higher proportion of young children, who might be more likely to be taken to the hospital or healthcare provider when ill.

The form to report animal contact outbreaks to NORS captures only a small amount of information related to animal contact. Animal type and setting are reported, but this information can be inconsistent between outbreak reports. We would recommend that NORS include additional variables regarding animal contact that might provide better data for future investigations. For example, a category for animal type (reptile, mammal, poultry, etc.) and then a separate category for species would be helpful to eliminate reporting confusion. In addition, it would be useful to include whether the animal exposure occurred in multiple settings (i.e., many different homes where people keep live poultry as pets) or in a single setting where multiple people were exposed (i.e., a petting zoo). Gathering more information on animal contact outbreaks would provide more information for future
analyses and would better inform public health agencies on implementing control and prevention measures.

Although outbreaks of *Salmonella* comprise only a small proportion of all infections annually, it is important to identify them, investigate sources, and implement control measures to reduce the burden of disease. It is possible that past outbreaks with unconfirmed primary mode of transmission or unconfirmed but suspected food vehicle might have been associated with live animal contact that was not discovered. Based on this analysis, it is also possible that animal contact outbreaks may result in more severe illnesses, which supports the importance of investigating and reporting these outbreaks and the local, state, and national level. Future investigations of multistate *Salmonella* outbreaks where the demographic characteristics are consistent with the results of this report should include collection of epidemiologic information on animal exposures, as animal contact might be the source of the outbreak.
Table 1. Number and percentage of illnesses associated with animal contact and foodborne illness outbreaks, by age group, sex, healthcare, and survival – National Outbreak Reporting System, United States, 2009–2014

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Animal Contact n=3,604 (19.8%)</th>
<th>Foodborne n=13,568 (80.2%)</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Age Group (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1</td>
<td>387 (15.2)</td>
<td>145 (1.4)</td>
<td>24.98 (20.25, 30.83)</td>
</tr>
<tr>
<td>1–4</td>
<td>623 (24.5)</td>
<td>583 (5.6)</td>
<td>10.00 (8.67, 11.55)</td>
</tr>
<tr>
<td>5–9</td>
<td>312 (12.2)</td>
<td>533 (5.2)</td>
<td>5.48 (4.65, 6.46)</td>
</tr>
<tr>
<td>10–19</td>
<td>248 (9.7)</td>
<td>1,267 (12.3)</td>
<td>1.83 (1.56, 2.16)</td>
</tr>
<tr>
<td>20–49</td>
<td>546 (21.4)</td>
<td>5,112 (49.5)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>50–74</td>
<td>362 (14.2)</td>
<td>2,184 (21.1)</td>
<td>1.55 (1.35, 1.79)</td>
</tr>
<tr>
<td>75+</td>
<td>70 (2.8)</td>
<td>509 (4.9)</td>
<td>1.29 (0.99, 1.68)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1,487 (46.5)</td>
<td>5,601 (51.6)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Female</td>
<td>1,708 (53.5)</td>
<td>5,255 (48.4)</td>
<td>1.22 (1.13, 1.32)</td>
</tr>
<tr>
<td>Healthcare and Survival*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>586 (28.2)</td>
<td>1,616 (17.8)</td>
<td>1.81 (1.62, 2.02)</td>
</tr>
<tr>
<td>No</td>
<td>1,495 (71.8)</td>
<td>7,447 (82.2)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1,523</td>
<td>4,505</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6 (0.2)</td>
<td>15 (0.2)</td>
<td>Fisher’s Exact Test</td>
</tr>
<tr>
<td>No</td>
<td>2,549 (99.8)</td>
<td>9,288 (99.8)</td>
<td>p = 0.14</td>
</tr>
<tr>
<td>Missing</td>
<td>1,049</td>
<td>4,265</td>
<td></td>
</tr>
<tr>
<td>ER Visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Missing</td>
</tr>
<tr>
<td>----------------</td>
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<td>-----</td>
<td>---------</td>
</tr>
<tr>
<td><strong>Healthcare Visit</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>176</td>
<td>(64.0)</td>
<td>2,443</td>
</tr>
<tr>
<td>No</td>
<td>99</td>
<td>(36.0)</td>
<td>3,666</td>
</tr>
<tr>
<td>Missing</td>
<td>3,329</td>
<td></td>
<td>7,459</td>
</tr>
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Variables are reported based on information available.
<table>
<thead>
<tr>
<th></th>
<th>Animal Contact</th>
<th>Foodborne</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N= 99 (20.5%)</td>
<td>N=385 (79.5%)</td>
<td></td>
</tr>
<tr>
<td><strong>Outbreak Size</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated Primary Ill</td>
<td>10 (4–42)</td>
<td>14 (7–30)</td>
<td>0.236</td>
</tr>
<tr>
<td>(No. of Illnesses)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lab Confirmed Primary</td>
<td>9 (3–41)</td>
<td>7 (4–15)</td>
<td>0.053</td>
</tr>
<tr>
<td>(No. of Illnesses)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable Primary (No.</td>
<td>0 (0–1)</td>
<td>4 (0–14)</td>
<td>0.001</td>
</tr>
<tr>
<td>of Illnesses)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Secondary (No.</td>
<td>0 (0–0)</td>
<td>0 (0–1)</td>
<td>0.079</td>
</tr>
<tr>
<td>of Illnesses)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of Outbreak</strong></td>
<td>Median (IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days</td>
<td>98.0 (26.0–216.0)</td>
<td>8.0 (2.0–26.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Multistate Exposure</strong></td>
<td>No. of outbreaks (%)</td>
<td>Odds Ratio (95% CI: 3.37, 8.76)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>63 (16.4)</td>
<td>322 (83.6)</td>
<td>5.43</td>
</tr>
<tr>
<td>No</td>
<td>51(51.5)</td>
<td>48 (48.5)</td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Top 15 most commonly reported *Salmonella enterica* serotypes: Number and Percentage of all Outbreaks, by Primary Mode of Transmission—National Outbreak Reporting System, United States, 2009–2014

<table>
<thead>
<tr>
<th>Animal Contact Outbreaks</th>
<th></th>
<th>Food Outbreaks</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotype</td>
<td>No.</td>
<td>%</td>
<td>Serotype</td>
<td>No.</td>
</tr>
<tr>
<td>1. Typhimurium</td>
<td>26</td>
<td>23.0</td>
<td>1. Enteritidis</td>
<td>101</td>
</tr>
<tr>
<td>2. I 4,[5],12:i:-</td>
<td>10</td>
<td>8.8</td>
<td>2. Typhimurium</td>
<td>57</td>
</tr>
<tr>
<td>4. Infantis</td>
<td>7</td>
<td>6.2</td>
<td>4. Heidelberg</td>
<td>30</td>
</tr>
<tr>
<td>5. Hadar</td>
<td>6</td>
<td>5.3</td>
<td>5. I 4,[5],12:i:-</td>
<td>19</td>
</tr>
<tr>
<td>7. Enteritidis</td>
<td>5</td>
<td>4.4</td>
<td>7. Infantis</td>
<td>14</td>
</tr>
<tr>
<td>8. Pomona</td>
<td>5</td>
<td>4.4</td>
<td>8. Braenderup</td>
<td>13</td>
</tr>
<tr>
<td>10. Johannesburg</td>
<td>4</td>
<td>3.5</td>
<td>10. Saintpaul</td>
<td>9</td>
</tr>
<tr>
<td>11. Newport</td>
<td>4</td>
<td>3.5</td>
<td>11. Uganda</td>
<td>8</td>
</tr>
<tr>
<td>12. Paratyphi B</td>
<td>4</td>
<td>3.5</td>
<td>12. Mbandaka</td>
<td>7</td>
</tr>
<tr>
<td>13. Poona</td>
<td>4</td>
<td>3.5</td>
<td>13. Muenchen</td>
<td>7</td>
</tr>
<tr>
<td>14. Muenchen</td>
<td>3</td>
<td>2.6</td>
<td>14. Thompson</td>
<td>7</td>
</tr>
<tr>
<td>15. Thompson</td>
<td>3</td>
<td>2.6</td>
<td>15. Typhimurium var Cope</td>
<td>7</td>
</tr>
</tbody>
</table>
Figure 1. Percent of Total Illnesses in Each Age Group by Primary Mode of Transmission—
Figure 2. Month of Outbreak Onset by Primary Mode of Transmission—National Outbreak Reporting System, United States, 2009–2014
REFERENCES

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