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___4/19/19____ Date Risk factors for hospitalization among adults aged ≥65 years with non-typhoidal Salmonella infection linked to backyard poultry contact

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Abstract

Risk factors for hospitalization among adults aged ≥65 years with non-typhoidal Salmonella infection linked to backyard poultry contact

By Florence Whitehill, DVM

Live poultry associated salmonellosis (LPAS) is a public health concern in the United States, especially among people at increased risk for hospitalization, such as older adults. Approximately 55% of adults aged \geq 65 years with non-typhoidal (NT) salmonellosis are hospitalized. To characterize the epidemiology of infections and investigate risk factors for hospitalization among older adults in the United States with LPAS, we analyzed data from people aged ≥ 65 years with NT salmonellosis who reported backyard poultry contact within 7 days of illness onset. All patients were identified during outbreak investigations reported to CDC from 2008–2017. We used logistic regression to estimate the odds of hospitalization associated with behavioral risk factors related to live poultry contact (e.g. keeping poultry inside, contacting baby poultry, purchase of live poultry for eggs or meat). Of the 1,575 LPAS patients with questionnaire data available, 127 (8.1%) were aged ≥ 65 years. Of those aged ≥ 65 years, 70 patients (55%) were hospitalized, 88% were non-Hispanic whites, 67% reported owning poultry, and 85.5% reported live poultry contact in the home. Those infected with Salmonella Hadar (26.0%) had significantly higher odds of hospitalization (OR=4.3; CI: 1.5–12.8) compared to those infected with other serotypes. Those who reported keeping poultry inside their home (33.1%) had significantly lower odds of hospitalization (OR=0.4; CI: 0.2-0.9) than those who reported not keeping poultry inside (56.7%). We did not detect additional poultry contact behaviors that were significantly associated with increased odds of hospitalization among adults aged ≥ 65 years. The high percent of non-Hispanic whites in this analysis likely represents demographics of backyard poultry owners in the United States. Based on the results of this analysis, hospitalizations resulting from LPAS may be associated with certain Salmonella serotypes, Salmonella Hadar, and behaviors such as keeping poultry inside the home. However, among adults aged ≥ 65 years in this analysis, the overall proportion of hospitalizations is similar to prior estimates for older adults. Additional infection prevention information and education targeted at poultry-owning older adults may be needed to help prevent illness and hospitalization.

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Chapter I: Introduction

Small scale and backyard poultry ownership has seen a rise in popularity in the United States over the last two decades (1). The recent uptrend of urban and peri-urban smallscale poultry keeping likely has roots in the sustainable agriculture movement and an increased cultural interest in reconnection to food origins in support of both animal welfare and healthy diet practices (2). In the last century industrial, high-density livestock production has rapidly risen on a global scale (3). In developed countries, such as the Unites States, this has led to both a physical and awareness-related separation of urban living and livestock production (2). With the renewed interest in urban agriculture, some cities have passed laws allowing poultry to be kept within city limits. However, many municipalities have not passed such legislation, citing public health and public disturbance concerns (2, 4). One of the main public health issues associated with keeping backyard flocks is the spread of zoonotic disease from live poultry to humans directly, through animal contact, or indirectly, through contact with the animal's environment. Due to the increased interest in backyard poultry in the United States, public health officials are faced with new challenges to encourage safe poultry keeping practices.

The number of backyard flocks in the United States is increasing and so are the number of zoonotic disease outbreaks linked to backyard flocks in the last 20 years (1). There are a number of diseases that can be passed from poultry to humans. For backyard flock owners, the top zoonotic disease concerns include avian influenza (bird flu), West Nile Virus, campylobacteriosis, *Escherichia coli*, and non-typhoidal salmonellosis (5). Other less common zoonotic diseases that people can contract from handling live poultry

include histoplasmosis, Exotic Newcastle disease, yersiniosis, listeriosis, psittacosis, and various parasitic diseases (5-8).

Live poultry-associated salmonellosis is a classic One Health concern. One Health is the concept that human health is closely associated with the health of animals and the environment and that through transdisciplinary collaboration and multisectoral cooperation optimal health outcomes can be achieved in all three sectors (10). To combat the growing concern of *Salmonella* infections among people in the United States with live poultry exposure, professionals from all three sectors should concert their efforts. This thesis is focused on non-typhoidal salmonellosis among patients aged ≥ 65 years in the United States who contacted live poultry in the seven days prior to becoming ill. Since 2000, 70 Salmonella outbreaks linked to live poultry contact were documented in the United States causing 4,794 illnesses, 894 hospitalizations, and seven deaths (1, 9).

To carry out an interdisciplinary such as this one requires many professionals from diverse backgrounds, including veterinarians, epidemiologists, environmental health researchers, and statisticians. The origin of the surveillance data used is a tribute to One Health collaboration. The United States Centers for Disease Control and Prevention's PulseNet laboratory network collects outbreak information from across the country so that public health professionals from many backgrounds can work together to prevent and respond to the spread of communicable diseases. Through the One Health approach, public health professionals are addressing the growing concern of live poultry-associated salmonellosis in order to protect both human and animal health within the environment that they share and to encourage safe practices that will strengthen the human-animal bond.

References

- Behravesh CB, Brinson D, Hopkins BA, et al. Backyard poultry flocks and salmonellosis: a recurring, yet preventable public health challenge. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2014;58(10):1432-8.
- 2. Pollock SL, Stephen C, Skuridina N, et al. Raising chickens in city backyards: the public health role. *Journal of community health* 2012;37(3):734-42.
- Thornton PK. Livestock production: recent trends, future prospects. *Philosophical transactions of the Royal Society of London Series B, Biological sciences* 2010;365(1554):2853-67.
- 4. Beam A, Garber L, Sakugawa J, et al. Salmonella awareness and related management practices in U.S. urban backyard chicken flocks. *Preventive veterinary medicine* 2013;110(3-4):481-8.
- U.S. Centers for Disease Control and Prevention. Healthy Pets, Healthy People: Backyard Poultry. 2018. (https://www.cdc.gov/healthypets/pets/farmanimals/backyard-poultry.html). (Accessed April 03, 2019 2018).
- Illinois Department of Public Health. Infectious Disease in Illinois: Human Health Concerns About Raising Poultry. 2012. (http://www.idph.state.il.us/health/infect/Poultry.htm). (Accessed April 03, 2019).
- Pohjola L, Nykasenoja S, Kivisto R, et al. Zoonotic Public Health Hazards in Backyard Chickens. *Zoonoses and public health* 2016;63(5):420-30.

- Brown VR, Bevins SN. A review of virulent Newcastle disease viruses in the United States and the role of wild birds in viral persistence and spread. *Veterinary research* 2017;48(1):68.
- 9. U.S. Centers for Disease Control and Prevention. Don't Play Chicken With Your Health. In: dont-play-chicken-with-your-health-P.pdf, ed. National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Foodborne, Waterborne, and Environmental Diseases (DFWED). Website, 2018.
- U.S. Centers for Disease Control and Prevention. One Health. 2019.
 (https://www.cdc.gov/onehealth/index.html). (Accessed April 03, 2019).

Chapter II: Manuscript for Submission

Title

Risk factors for hospitalization among adults aged ≥ 65 years with non-typhoidal Salmonella infection linked to backyard poultry contact

Abstract

Live poultry associated salmonellosis (LPAS) is a public health concern in the United States, especially among people at increased risk for hospitalization, such as older adults. Approximately 55% of adults aged \geq 65 years with non-typhoidal (NT) salmonellosis are hospitalized. To characterize the epidemiology of infections and investigate risk factors for hospitalization among older adults in the United States with LPAS, we analyzed data from people aged ≥ 65 years with NT salmonellosis who reported backyard poultry contact within 7 days of illness onset. All patients were identified during outbreak investigations reported to CDC from 2008–2017. We used logistic regression to estimate the odds of hospitalization associated with behavioral risk factors related to live poultry contact (e.g. keeping poultry inside, contacting baby poultry, purchase of live poultry for eggs or meat). Of the 1,575 LPAS patients with questionnaire data available, 127 (8.1%) were aged ≥ 65 years. Of those aged ≥ 65 years, 70 patients (55%) were hospitalized, 88% were non-Hispanic whites, 67% reported owning poultry, and 85.5% reported live poultry contact in the home. Those infected with Salmonella Hadar (26.0%) had significantly higher odds of hospitalization (OR=4.3; CI: 1.5–12.8) compared to those infected with other serotypes. Those who reported keeping poultry inside their home (33.1%) had

significantly lower odds of hospitalization (OR=0.4; CI: 0.2–0.9) than those who reported not keeping poultry inside (56.7%). We did not detect additional poultry contact behaviors that were significantly associated with increased odds of hospitalization among adults aged \geq 65 years. The high percent of non-Hispanic whites in this analysis likely represents demographics of backyard poultry owners in the United States. Based on the results of this analysis, hospitalizations resulting from LPAS may be associated with certain *Salmonella* serotypes, *Salmonella* Hadar, and behaviors such as keeping poultry inside the home. However, among adults aged \geq 65 years in this analysis, the overall proportion of hospitalizations is similar to prior estimates for older adults. Additional infection prevention information and education targeted at poultry-owning older adults may be needed to help prevent illness and hospitalization.

Introduction

An estimated 1.2 million illnesses, 19,000 hospitalizations, and 370 deaths are attributable to non-typhoidal *Salmonella* (NTS) each year in the United States (1). The majority of NTS infections are foodborne but approximately 11% of these infections result from animal contact (2). Live poultry are well-known carriers of NTS and may shed the pathogen in their droppings as part of their gut flora, without developing illness (3). Zoonotic NTS infections can occur via direct or indirect routes and individuals in contact with live poultry or live poultry environments are at risk for infection (4-6).

Live poultry-associated salmonellosis (LPAS) has been documented in the United States since 1955 (7). These outbreaks were previously associated with live Easter chick contact among children (3, 8). The number of reported outbreaks of LPAS has increased in the last two decades including an increasing number of outbreaks associated with backyard poultry flocks and mail-order hatcheries (3, 9). Since 2000, 70 *Salmonella* outbreaks linked to live poultry contact were documented in the United States causing 4,794 illnesses, 894 hospitalizations, and 7 deaths (10).

Although most NTS infections produce self-limiting diarrhea, certain populations, including the elderly, children, and the immunocompromised are at greater risk for developing severe outcomes that may require hospitalization (9, 11-13). Certain *Salmonella* serotypes may be more likely to cause severe clinical outcomes such as hospitalization, invasive infection, and death (14). Approximately 27% of all NTS cases in the United States are hospitalized whereas among the elderly, the proportion is estimated as high as 50% (1, 11, 12). Hospitalization and other severe outcomes among the elderly have been associated with immunosenescence and comorbidities such as gastrointestinal and immunosuppressive diseases (13, 15-18). Multiple studies have investigated risk factors for severe NTS outcomes among older adults however, none have looked at behavioral live poultry contact risk factors for severe NTS outcomes among the elderly in relation to animal contact (19-22).

To address this gap in the literature and to support public health interventions aimed at preventing NTS infections among older adults, we report the results of an epidemiologic investigation of adults aged ≥ 65 years in the United States with laboratory confirmed NTS infections and live poultry contact in the seven days before becoming ill. The objective of this investigation is to describe the epidemiology of LPAS and to investigate potential behavioral live poultry contact risk factors for hospitalization among adults aged ≥ 65 years in the United States from 2008 to 2017.

Methods

Data Source

Data were obtained from the United States Centers for Disease Control and Prevention (CDC) Outbreak Response and Prevention Branch (ORPB) within the National Center for Emerging and Zoonotic Infectious Diseases (NCEZID). Laboratory surveillance for *Salmonella* and other enteric pathogens is conducted through PulseNet. PulseNet is a national laboratory network of 83 national laboratories that performs pulsed-field gel electrophoresis (PFGE) and whole genome sequencing (WGS) of bacterial isolates. This information is used to detect temporal and geographic clusters of illnesses with isolates that are genetically related. When a *Salmonella* illness occurs in the United States, state or local health officials interview the ill person to obtain information about foods eaten, animal contact, drinking water sources, and other risk factors for illness in the 7 days prior of them becoming ill. If live poultry contact is reported on initial interview, then a supplemental questionnaire for live poultry exposure is administered.

Data were collected from individuals living in the United States with laboratoryconfirmed NTS infections and who reported live poultry contact within the 7 days prior to becoming ill. These data were collected via a standard questionnaire which asks about live poultry exposures. The dataset includes patient demographic data, patient clinical information including hospitalization resulting from salmonellosis, and variables related to live poultry contact. Patient death resulting from salmonellosis was not recorded by the questionnaire during 2008 – 2017. Behavioral live poultry contact risk factor variables described how the patient physically interacted with live poultry and animal husbandry practices. Examples of behavioral live poultry contact risk factor variables include the species of poultry contacted, keeping poultry in the home, reason for purchasing poultry, and washing practices. These data were collected between 2008 and 2017. An age-specific subset of this dataset was selected by restricting to individuals aged ≥ 65 years.

Descriptive Epidemiology

Patient state of residence was recoded into region of residence using the United States Census Bureau regions (Table 1) (23). Variables describing the type of physical contact with live poultry were recoded into one variable describing direct versus indirect contact (Table 3). Variables describing the location of live poultry contact were recoded into one variable describing any contact in the patient's home versus no contact in the patient's home (Table 3). Variables describing reasons for live poultry purchase were recoded into one variable describing purchase for food (eggs or meat) versus purchase for other reasons (Table 4). Descriptive statistics were generated for variables in the analytic dataset (Tables 1 - 4).

Risk Factor Analysis

For statistical modeling purposes, after generating descriptive statistics we further restricted the analytic dataset to those with non-missing hospitalization data and those who had primary contact with live poultry. Primary contact was defined as contact where the patient contacted live poultry or live poultry environment versus secondary contact where the patient only contacted another ill patient.

A live poultry contact risk factor analysis was performed using logistic regression modeling the dichotomous outcome of hospitalization resulting from NTS. Any predictor variables missing greater than 20% of responses were not eligible for inclusion in the risk factor analysis. Due to the substantial overrepresentation by non-Hispanic white patients in the study population race and ethnicity variables were excluded from the analysis because meaningful statistical conclusions from these variables would not be possible.

A bivariable analysis was performed to estimate the crude association between available predictor variables and hospitalization. Subsequently, multiple predictors were excluded from the multivariable analysis because of zero-cell counts in the bivariable analysis. Predictors were then classified as exposures, possible effect measure modifiers, and possible confounders based on the development of directed acyclic graphs. Behavioral live poultry contact risk factor variables were considered exposure variables. Patient age, patient sex, and patient region of residence were considered possible confounders. *Salmonella* serotype was considered a possible effect measure modifier. Predictor variables were included in the multivariable modeling analysis based on bivariable logistic regression associations, biological plausibility, and relevance to the research question.

One model was built for each exposure variable of interest (Appendix 1). The initial models included one exposure variable, the outcome, all possible effect measure modifiers, and all possible confounders. The other exposure variables were included as possible confounders if significantly associated with the exposure of interest in the bivariable analysis, otherwise all other exposure variables were included as possible effect measure modifiers.

An interaction assessment was then performed, using a likelihood ratio chunk test to detect any statistically significant interaction indicative of effect measure modification by serotype. If there was any evidence of statistically significant interaction, then a backwards elimination procedure was performed for all interaction terms. Subsequently, a confounding assessment was performed for each model. Confounding was considered present if a >10% change in the odds ratio was observed. Final models reported the odds ratio association between a behavioral live poultry contact risk factors and hospitalization (Table 5). P-values were evaluated at an alpha level of 0.05. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

Descriptive epidemiology

In the original all-ages dataset data were collected on 1575 individuals. An age-specific subset, restricted to adults aged ≥ 65 years, contained 127 (8.1%) individuals from which the descriptive statistics were generated. One individual was excluded from the multivariable analysis because of missing outcome information and 24 individuals were excluded because they did not have primary exposure to live poultry. We used the resulting dataset of 102 individuals for statistical modeling. Among patients in the study population 55.1% (70/127) were hospitalized. Table 1 shows demographic characteristics of LPAS patients in the study population. Among the 127 patients median age was 70 (range 65 - 93 years) (Table 1).

In the study population 88.2% of patients were non-Hispanic whites. The majority of patients lived in the midwestern and southern regions: 31.5% lived in the Midwest and 37.0% lived in the South.

More patient data was available from later years of data collection. From 2008 -2011, data were collected from three individuals (2.4% of the study population). In contrast, during 2015 - 2017, data were collected from 97 individuals (76.4% of the study population) (Table 2).

There were 11 *Salmonella* serotypes reported among patients. *Salmonella* Hadar was the most frequent (26.0%) followed by *Salmonella* Enteriditis (19.7%), *Salmonella* Infantis (15.8%), and *Salmonella* Braenderup (11.8%). The least frequent serotypes of infection among the study population were *Salmonella* I 4,[5],12:i:- and *Salmonella* Litchfield which were only represented by one patient each (0.8%) (Table 2).

Over 85% of patients indicated that they had contacted live poultry in their own home and 66.9% indicated they owned live poultry (Table 3). Additional behavioral live poultry risk factors reported by patients were analyzed (Tables 3 and 4).

Risk factor analysis

In the bivariable analysis *Salmonella* Braenderup and *Salmonella* Hadar infections were significantly associated with hospitalization (Table 5). Bivariable logistic regression estimated that among patients in the United States aged ≥ 65 years who contracted salmonellosis within 7 days of contacting live poultry, those who had a *Salmonella* Braenderup infection had 0.21 times lower odds of hospitalization than those who had any other serotype of *Salmonella* (OR = 0.21, 95% confidence interval: 0.05, 0.81, *P*-value = 0.02) and those who had a *Salmonella* Hadar infection had 4.33 times higher odds of hospitalization than those who had any other serotype of *Salmonella* (OR = 4.33, 95% confidence interval: 1.47, 12.77, *P*-value = 0.01) (Table 5).

Of the behavioral live poultry contact risk factors, keeping poultry inside the home was found to be significantly associated with hospitalization from salmonellosis in both the bi- and multivariable analyses. Multivariable logistic regression estimated that among patients in the United States aged ≥ 65 years who contracted salmonellosis within 7 days of contacting live poultry, those who kept poultry inside had 0.39 times lower odds of hospitalization than those who did not keep poultry inside (OR = 0.39, 95% confidence interval: 0.17, 0.92, *P*-value = 0.03) (Table 5).

In the final multivariable models for each exposure of interest, no statistically significant interaction by serotype of infection was evident in any model (Appendix 1). Based on these data, the association between behavioral live poultry contact risk factors and hospitalization did not significantly differ across different serotypes of infection.

All other predictor variables included in both bivariable and multivariable logistic regression models were not significantly associated with hospitalization among patients aged ≥ 65 years in the United States who contracted salmonellosis within 7 days of contacting live poultry (Table 5).

Discussion

This is the first known investigation of behavioral live poultry contact risk factors for severe *Salmonella* outcomes among older adults in the United States. Overall, no one behavioral live poultry contact risk factor was shown to be associated with increased odds of hospitalization. It is possible that due to a limited sample size we were not able to detect other significant associations between live poultry contact behaviors and hospitalization among older adults with LPAS. Additionally, there may be many unmeasured confounding characteristics of the study population, such as comorbidities, and other severe outcomes, such as invasive disease and death, that might have clarified the nature of the significant association that was detected. The majority of patients in the study population reported contacting live poultry at their home and owning poultry. These results may indicate that among older adults in the United States those with LPAS infections are primarily backyard poultry flock owners. Descriptive statistics revealed that the majority of the study population were non-Hispanic white patients. Few studies have been performed to investigate the demographics of poultry contact and backyard flock owners in the United States and most tend to focus on geographic location and flock management practices not owner characteristics (24-27).

A recent national survey by Elkhoraibi et al. in 2014, using different sampling methods from this investigation, found that greater than 90% of respondents across all ages who owned poultry were non-Hispanic whites (24). These figures are similar to the results of this investigation, though Elkhoraibi et al. suggested there may have been survey sampling bias present which might have caused Hispanic and black owners to be underrepresented. Sampling bias may be of importance in this investigation as well. Further investigations of the cultural characteristics of LPAS patients may need to be performed to elucidate the significance of the distinct racial and ethnic distribution of patients aged ≥65 years with LPAS in this study population and others.

About two thirds of the study population lived in the Midwest or South and a greater proportion of hospitalized individuals in the study population lived in the South though the association between region of residence and hospitalization was not statistically significant (Table 5). There are no studies currently published looking at the geographic distribution of LPAS infections in the United States. Further investigations

may be needed to illuminate where in the United States people, especially those aged ≥ 65 years, are at greater risk of contracting and experiencing severe outcomes from LPAS.

Several studies have estimated that the incidence of LPAS in the United States has increased over the last decade (3, 8, 10). The rise in number of cases per year in this study population may reflect the overall rise in LPAS incidence in the United States in this time frame. It is possible that a greater percentage of data were collected at the end of this time frame likely due to improved reporting and data management.

This investigation showed that certain Salmonella serotypes were significantly associated with hospitalization among adults aged \geq 65 years with LPAS. Certain Salmonella serotypes have been shown to have a greater rate of severe clinical outcomes among human patients (14). A study by Jones et al. analyzed Salmonella surveillance data collected from CDC FoodNet between 1996 and 2006 (14). They showed that among the cases surveyed certain Salmonella serotypes had a significantly different proportion of severe outcomes such as death, hospitalization, and invasive disease compared to *Salmonella* Typhimurium, the most common serotype in their study population. Though their referent comparison was different than the one used in this analysis, they found that *Salmonella* Braenderup infections had a lower percentage of hospitalization and invasive disease outcomes but Salmonella Hadar infection outcomes did not significantly differ from *Salmonella* Typhiumurium. It is difficult to directly compare the results of these two studies due to methodological differences but both Jones' study and this investigation show that people with certain Salmonella serotypes of infection may be at greater likelihood of severe outcomes. It may be important to further

investigate these findings to better inform diagnostics and treatment for persons, especially older adults, who are hospitalized due to severe LPAS outcomes.

The findings of this investigation are subject to several limitations. There are several measured and unmeasured confounding variables which, by not including in the multivariable risk factor analysis, may have introduced systematic bias. Socioeconomic data such as education level, occupation, and household income were not measured and therefore could not be included in the analysis. Race and ethnicity data were limited and therefore could not be used as a proxy to adjust for unmeasured socioeconomic and cultural factors. Patient clinical data including comorbidities and other severe outcomes, such as death and invasive disease, were not collected. In future revisions of the standard live poultry contact questionnaire, additional socioeconomic and additional patient health information should be considered for inclusion.

The sample size of the study population was small which was likely because of data collection and age-restriction. Due to the multi-step process of questionnaire data collection, there are likely eligible cases that are not included in LPAS outbreaks. Though these data were from a reportable disease national surveillance program, they likely are not representative of all United States cases of LPAS among adults aged ≥ 65 years because not every individual with NTS seeks medical care. This may be because the illness was self-limiting or because the individual chose to not seek medical care for reasons such as socioeconomic status or cultural practices. Furthermore, the population who can be contacted and agrees to participate in the questionnaire may be different than those who cannot be contacted or who do not agree to participate. The missing data for many variables for this study population restricted the inclusion of these variables in

analyses. In future, when possible, certain questions on the standard Live Poultry Contact Questionnaire may need to be revised or expanded to more effectively capture important patient data.

Exposure and outcome data were generated with self-reported responses to one standard questionnaire. In the presence of inaccurate responses there is potential for dependent misclassification of the exposure and the outcome which may yield biased measures of association.

Based on the results of this analysis, hospitalizations resulting from LPAS may be associated with certain *Salmonella* serotypes, *Salmonella* Hadar, and behaviors such as keeping poultry inside the home. However, among adults aged ≥ 65 years in this analysis, the overall proportion of hospitalizations is similar to prior estimates for older adults. Additional infection prevention information and education targeted at poultry-owning older adults may be needed to help prevent illness and hospitalization.

References

- Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States--major pathogens. *Emerging infectious diseases* 2011;17(1):7-15.
- 2. Hale CR, Scallan E, Cronquist AB, et al. Estimates of enteric illness attributable to contact with animals and their environments in the United States. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2012;54 Suppl 5:S472-9.
- Behravesh CB, Brinson D, Hopkins BA, et al. Backyard poultry flocks and salmonellosis: a recurring, yet preventable public health challenge. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2014;58(10):1432-8.
- Harris JR, Neil KP, Behravesh CB, et al. Recent multistate outbreaks of human salmonella infections acquired from turtles: a continuing public health challenge. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2010;50(4):554-9.
- Loharikar A, Briere E, Schwensohn C, et al. Four multistate outbreaks of human Salmonella infections associated with live poultry contact, United States, 2009. *Zoonoses and public health* 2012;59(5):347-54.
- Mettee Zarecki SL, Bennett SD, Hall J, et al. US outbreak of human Salmonella infections associated with aquatic frogs, 2008-2011. *Pediatrics* 2013;131(4):724-31.

- Anderson AS, Bauer H, Nelson CB. Salmonellosis due to Salmonella typhimurium with Easter chicks as likely source. *Journal of the American Medical Association* 1955;158(13):1153-5.
- Basler C, Nguyen TA, Anderson TC, et al. Outbreaks of Human Salmonella Infections Associated with Live Poultry, United States, 1990-2014. *Emerging infectious diseases* 2016;22(10):1705-11.
- Barton Behravesh C, Jones TF, Vugia DJ, et al. Deaths associated with bacterial pathogens transmitted commonly through food: foodborne diseases active surveillance network (FoodNet), 1996-2005. *The Journal of infectious diseases* 2011;204(2):263-7.
- U.S. Centers for Disease Control and Prevention. Don't Play Chicken With Your Health. In: dont-play-chicken-with-your-health-P.pdf, ed. National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Foodborne, Waterborne, and Environmental Diseases (DFWED). Website, 2018.
- U.S. Centers for Disease Control and Prevention. Foodborne Diseases Active Surveillance Network (FoodNet): FoodNet Surveillance Report for 2012 (Final Report). Atlanta, Georgia, USA: U.S. Department of Health and Human Services, 2014.
- Scallan E, Crim SM, Runkle A, et al. Bacterial Enteric Infections Among Older Adults in the United States: Foodborne Diseases Active Surveillance Network, 1996-2012. *Foodborne pathogens and disease* 2015;12(6):492-9.
- 13. Shimoni Z, Pitlik S, Leibovici L, et al. Nontyphoid Salmonella bacteremia: agerelated differences in clinical presentation, bacteriology, and outcome. *Clinical*

infectious diseases : an official publication of the Infectious Diseases Society of America 1999;28(4):822-7.

- Jones TF, Ingram LA, Cieslak PR, et al. Salmonellosis outcomes differ substantially by serotype. *The Journal of infectious diseases* 2008;198(1):109-14.
- Cummings PL, Kuo T, Javanbakht M, et al. Salmonellosis Hospitalizations in the United States: Associated Chronic Conditions, Costs, and Hospital Outcomes, 2011, Trends 2000-2011. *Foodborne pathogens and disease* 2016;13(1):40-8.
- Dhanoa A, Fatt QK. Non-typhoidal Salmonella bacteraemia: epidemiology, clinical characteristics and its' association with severe immunosuppression. *Annals of clinical microbiology and antimicrobials* 2009;8:15.
- Brown M, Eykyn SJ. Non-typhoidal Salmonella bacteraemia without gastroenteritis: a marker of underlying immunosuppression. Review Of cases at St. Thomas' Hospital 1970-1999. *The Journal of infection* 2000;41(3):256-9.
- Smith JL. Foodborne illness in the elderly. *Journal of food protection* 1998;61(9):1229-39.
- Chen Y, Glass K, Liu B, et al. Salmonella Infection in Middle-Aged and Older Adults: Incidence and Risk Factors from the 45 and Up Study. *Foodborne pathogens and disease* 2016;13(12):689-94.
- 20. Chui KK, Webb P, Russell RM, et al. Geographic variations and temporal trends of Salmonella-associated hospitalization in the U.S. elderly, 1991-2004: a time series analysis of the impact of HACCP regulation. *BMC public health* 2009;9:447.

- 21. Thuluvath PJ, McKendrick MW. Salmonella and complications related to age--Sheffield experience. *The Quarterly journal of medicine* 1988;67(254):497-503.
- Turgeon P, Murray R, Nesbitt A. Hospitalizations associated with salmonellosis among seniors in Canada, 2000-2010. *Epidemiology and infection* 2017;145(8):1527-34.
- U.S. Census Bureau. Census Regions and Divisions of the United States. 2015. (<u>https://www.census.gov/geo/reference/gtc/gtc_census_divreg.html</u>). (Accessed March 31, 2019).
- 24. Elkhoraibi C, Blatchford RA, Pitesky ME, et al. Backyard chickens in the UnitedStates: a survey of flock owners. *Poultry science* 2014;93(11):2920-31.
- 25. U.S. Department of Agriculture. Urban chicken ownership in four US cities. Fort Collins, CO, 2013, (USDA Animal and Plant Health Inspection Service-Veterinary Services
- Pires AFA, Peterson A, Baron JN, et al. Small-scale and backyard livestock owners needs assessment in the western United States. *PloS one* 2019;14(2):e0212372.
- 27. Smith EI, Reif JS, Hill AE, et al. Epidemiologic characterization of Colorado backyard bird flocks. *Avian diseases* 2012;56(2):263-71.
- U.S. Department of Agriculture. Poultry, Charts and Maps. 2018. (<u>https://www.nass.usda.gov/Charts_and_Maps/Poultry/index.php</u>). (Accessed March 30, 2019).

Tables

Characteristic	To	otal	Hospitalized		
	(n =	127)		70)	
	No.	%	No.	%	
Age quartiles (years)					
65 to 67	33	26.0	16	22.9	
68 to 70	32	25.2	15	21.4	
71 to 74	29	22.8	17	24.3	
75 to 93	33	26.0	22	31.4	
Sex					
Female	62	48.8	30	42.9	
Missing	3	2.4	1	1.4	
Race					
Black	1	0.8	1	1.4	
White	115	90.6	64	91.4	
Missing	11	8.7	5	7.1	
Hispanic ethnicity					
Yes	3	2.4	1	1.4	
Missing	15	11.8	8	11.4	
White non-Hispanic					
Yes	112	88.2	63	90.0	
Missing	11	8.7	5	7.14	
U.S. region of residence ^a					
Northeast	15	11.8	8	11.4	
Midwest	40	31.5	19	27.1	
South	47	37.0	29	41.4	
West	25	19.7	14	20.0	

Table 1. Demographic Characteristics of Patients Aged ≥ 65 Years with Salmonellosis Within Seven Days of Contact with Live Poultry, CDC Standard Live Poultry Questionnaire, United States, 2008–2017.

^a Region variable recoded from state of residence using United States Census Bureau regions (23).

Characteristic	Total			Hospitalized			
	(n = 127)			(n = 70)			
	No.	%	Median (SD)	No.	%	Median (SD)	
Year of illness							
2008	1	0.8		1	1.4		
2009	1	0.8		1	1.4		
2010	0	0		0	0		
2011	1	0.8		1	1.4		
2012	14	11.0		10	14.3		
2013	8	6.3		2	2.9		
2014	5	3.9		4	5.7		
2015	11	8.7		7	10.0		
2016	42	33.1		20	28.6		
2017	44	34.7		24	34.3		
Illness duration			7.0 (5.8)			8.0 (6.3)	
Missing	45	35.4		30	42.8		
Infection serotype							
Braenderup	15	11.8		3	4.3		
Enteriditis	25	19.7		14	20.0		
Hadar	33	26.0		22	31.4		
I 4,[5],12:i:-	1	0.8		0	0		
Indiana	6	4.7		3	4.3		
Infantis	20	15.8		12	17.1		
Litchfield	1	0.8		1	1.4		
Mbandaka	4	3.2		1	1.4		
Montivideo	6	4.7		5	7.1		
Newport	5	3.9		5	7.1		
Typhimurium	7	5.5		1	1.4		
Missing	4	3.2		3	4.3		

Table 2. Illness Characteristics of Patients Aged ≥ 65 Years With Salmonellosis Within Seven Days of Contact with Live Poultry, CDC Standard Live Poultry Questionnaire, United States, 2008–2017.

Abbreviations: SD, standard deviation

Characteristic		otal 127)		talized = 70)
	No.	<u>127)</u> %	No.	- 70) %
Exposure type				
Primary	103	81.1	55	78.6
Secondary	24	18.9	15	21.4
Direct contact with live poultry				
Yes	69	54.3	35	50.0
Missing	23	18.1	12	17.1
Contact at patient's home				
Yes	109	85.8	60	85.7
No or missing ^a	18	2.4	10	14.3
Contact at a store				
Yes	12	9.5	6	8.6
No or missing ^a	115	90.6	64	91.4
Contact with adult poultry				
Yes	64	50.4	34	48.6
Missing	12	9.5	6	8.6
Contact with baby poultry				
Yes	109	85.8	61	87.1
Missing	5	3.9	2	2.9
Contact with chickens				
Yes	115	90.6	63	90.0
Missing	3	2.4	2	2.9
Contact with ducks				
Yes	28	22.1	19	27.1
Missing	12	9.5	7	10.0
Contact with geese				
Yes	4	9.5	2	2.9
Missing	12	3.2	7	10.0
Contact with turkeys				
Yes	9	7.1	6	8.6
Missing	10	7.9	7	10.0
Contact with guineas				
Yes	4	3.2	2	2.9
Missing	123	96.9	68	97.1

Table 3. Live Poultry Contact Exposure Characteristics of Patients ≥ 65 Years of Age With Salmonellosis Within Seven Days of Contacting Live Poultry, CDC Standard Live Poultry Questionnaire, United States, 2008–2017.

^a Questionnaire was formatted such that for certain questions only a "Yes" check box was available for response. "No" responses were not recorded.

Characteristic	Total $(n = 127)$		Hospitalized	
-			`	= 70)
	No.	%	No.	%
Patient owned poultry	0.5	(())	4.5	(1.2
Yes	85	66.9	45	64.3
Missing	22	17.3	16	22.9
Purchase reason for eggs or meat ^a	0.0	7 0 1	. –	
Yes	89	70.1	47	67.1
Missing	25	19.7	14	20.0
Patient kept poultry inside				
Yes	42	33.1	17	24.3
Missing	13	10.2	8	11.4
Patient wore the same shoes in poultry				
environment and inside				
Yes	29	44.9	14	20.0
Missing	57	22.8	32	45.7
Handwashing frequency after handling				
live poultry				
Rarely (<30%)	1	0.8	1	1.4
Some of the time (50-30%)	4	3.2	2	2.9
Most of the time (75-50%)	9	7.1	7	10.0
Almost always (90-75%)	13	10.2	5	7.1
Always (100-95%)	51	40.2	24	34.3
Missing	49	38.6	31	44.3
Handwashing frequency after touching				
poultry environment				
Rarely (<30%)	1	0.8	1	1.4
Some of the time (50-30%)	6	4.7	4	5.7
Most of the time (75-50%)	9	7.1	7	10.0
Almost always (90-75%)	9	7.1	4	5.7
Always (100-95%)	48	37.8	21	30.0
Missing	54	42.5	33	47.1
Handwashing Type				
Soap and water	24	72.4	14	20.0
Alcohol-based hand sanitizer	3	2.4	2	2.9
Both	8	6.3	4	5.7
Missing	92	18.9	50	17.4

Table 4. Animal Husbandry Behavioral Characteristics of Patients Aged ≥65 Years With Salmonellosis Within Seven Days of Live Poultry Contact, CDC Standard Live Poultry Questionnaire, United States, 2008–2017.

^a Recoded variable using multiple reason for live poultry purchase variables.

Characteristic	Biva		Multivariable Analysis					
	(n = 102)				(n = 102)			
	OR	95%	∕₀ CI	OR	95%	ω CI		
Age quartiles (years)								
65 to 67 (referent)								
68 to 70	0.66	0.23	1.89					
71 to 74	1.34	0.43	4.18					
75 to 93	1.86	0.60	5.78					
Sex								
Female	0.56	0.25	1.22					
Region of residence ^a								
Northeast	0.54	0.22	1.30					
Midwest	0.84	0.23	3.10					
South	1.18	0.45	3.10					
West	1.58	0.71	3.51					
Serotype of infection ^b								
Braenderup	0.21*	0.05	0.81					
Enteriditis	0.71	0.27	1.85					
Hadar	4.33*	1.47	12.77					
Indiana	0.83	0.16	4.31					
Infantis	1.24	0.43	3.56					
Mbandaka	0.27	0.03	2.64					
Montivideo	3.53	0.38	32.75					
Newport [°]								
Typhimurium	0.12	0.01	1.07					
Direct contact with live poultry	0.54	0.23	1.25	1.16	0.26	5.16		
Any contact at patient's home ^d	0.72	0.22	2.37	0.25	0.04	1.62		
Contact with adult poultry	0.85	0.38	1.90	0.53	0.19	1.49		
Contact with baby poultry	0.98	0.28	3.45	1.16	0.26	5.16		
Contact with chickens	1.19	0.28	5.05	1.00	0.22	4.51		
Contact with ducks	1.58	0.61	4.06					
Contact with turkeys	5.61	0.65	48.47	4.73	0.32	70.75		
Contact with geese	0.84	0.11	6.22					
Patient owned poultry	1.38	0.71	7.42	2.67	0.49	14.45		
Patient kept poultry inside	0.39*	0.17	0.92	0.38*	0.15	0.95		
Purchase reason for eggs or meat	0.47	0.11	1.94	0.18	0.03	1.09		

Table 5. Logistic Regression Risk Factor Analysis for Hospitalization Among Patients Aged ≥ 65 Years With Salmonellosis Within Seven Days of Live Poultry Contact, CDC Standard Live Poultry Ouestionnaire, United States, 2008-2017.

Abbreviations: OR, odds ratio; CI, confidence interval

* P < 0.05, Wald chi-square test, one sided

^aRegion was coded from state of residence using United States Census Bureau regions (23).

^b Serotype referent comparison was all other serotypes.

^c Zero cell count therefore measure of association could not be calculated.

^d Recoded variable from multiple location of contact variables.

Chapter III: Conclusion

The findings from this study were subject to certain limitations including systematic biases that may exist in surveillance systems such as selection bias. In nationally notifiable disease reporting systems selection bias concerns likely stem from the specific case identification and reporting flows. Room for selection bias expands when considering *Salmonella*, which can often be a self-limiting illness that does not require medical attention when the symptoms are mild (1). Those who do not seek medical care for their illness will not be captured by surveillance systems because reporting starts with a laboratory confirmed diagnosis (2).

There are many steps that need to be completed for a person ill with *Salmonella* to be represented in the standard Live Poultry Questionnaire, from which the data for this study were collected. First, the ill person needs to seek medical attention from a health care provider who has the knowledge and ability to submit a laboratory specimen. The laboratory then needs to obtain a positive result and initiate the reporting forms which are then sent back to the health care provider (2). The health care provider, or often another staff member such as a public health professional, may complete the required forms. Based on a survey of medical professionals in Illinois ambulatory care facilities the frequency of reporting notifiable disease cases varied and was associated with knowledge and perceptions of the staff at each facility (2). Once a laboratory confirmed case of *Salmonella* is reported at the state or local level, public health professionals should then attempt follow up with the patient and administer a *Salmonella* questionnaire. If the ill person responds positively that they contacted live poultry in the 7 days prior to

becoming ill that will prompt the standard Live Poultry Contact Questionnaire to be subsequently administered.

The chain of reporting for nationally notifiable diseases in the United States is complex and requires many people to complete. There are ample opportunities for live poultry-associated salmonellosis cases to not be captured by it. Examples include those cases who do not seek medical care, those cases whose reporting forms are not completed, and those who inaccurately state that they did not contact live poultry. The population of uncaptured cases is likely different in many ways from the population of captured cases. To address this possible selection bias in the short term, a bias analysis investigation may be useful for certain links of the chain of reporting. However, much of what is needed for a selection bias analysis may be truly unknown, such as the characteristics of the population of *Salmonella* cases who do not seek medical care. In the long term much can be done to improve the efficiency of the reporting system such as increased education and training for those who complete the reporting system and its outcomes in health care establishments.

References

1. Behravesh CB, Brinson D, Hopkins BA, et al. Backyard poultry flocks and salmonellosis: a recurring, yet preventable public health challenge. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2014;58(10):1432-8.

2. Revere D, Hills RH, Dixon BE, et al. Notifiable condition reporting practices: implications for public health agency participation in a health information exchange. *BMC public health* 2017;17(1):247.

Appendices

Appendix 1

Final models used to estimate the association between live poultry contact behaviors and hospitalization due to LPAS among adults aged ≥ 65 years in the United Sates

1) Contact with baby poultry:

 $Ln(odds of Hosp) = \alpha + \beta 1(ContactBabyPoultry01) + \beta 2(PatientAgeQuartOrd) +$

 β 3(KeptPoultryInside01)

2) Contact with adult poultry:

 $Ln(odds of Hosp) = \alpha + \beta 1(ContactAdultPoultry01) + \beta 2(RegionMidwest01) + \beta 2(RegionMidw$

 β 3(RegionNortheast01) + β 4(RegionWest01) + β 5(RegionSouth01) +

 β 6(PatientSex01) + β 7(PatientAgeQuartOrd) + β 8(KeptPoultryInside01)

3) Contact with chickens:

 $Ln(odds of Hosp) = \alpha + \beta 1(ChickenContact01) + \beta 2(PatientAgeQuartOrd)$

4) Contact with turkeys:

 $Ln(odds of Hosp) = \alpha + \beta 1(TurkeyContact01) + \beta 2(RegionMidwest01) +$

 β 3(RegionNortheast01) + β 4(RegionWest01) + β 5(RegionSouth01) +

 β 6(PatientSex01) + β 7(PatientAgeQuartOrd) + β 8(KeptPoultryInside01)

5) Direct contact with poultry:

 $Ln(odds of Hosp) = \alpha + \beta 1(DirectContact01) + \beta 2(RegionMidwest01) +$

 β 3(RegionNortheast01) + β 4(RegionWest01) + β 5(RegionSouth01) +

 β 6(PatientSex01) + β 7(PatientAgeQuartOrd) + β 8(KeptPoultryInside01)

⁶⁾ Any contact in patient's home:

 $Ln(odds of Hosp) = \alpha + \beta 1(AnyHomeContact01) + \beta 2(RegionMidwest01) +$

 β 3(RegionNortheast01) + β 4(RegionWest01) + β 5(RegionSouth01) +

```
\beta6(PatientSex01) + \beta7(PatientAgeQuartOrd) + \beta8(KeptPoultryInside01)
```

7) Patient owned poultry:

```
Ln(odds of Hosp) = \alpha + \beta 1(OwnPoultry01) + \beta 2(RegionMidwest01) +
```

```
\beta3(RegionNortheast01) + \beta4(RegionWest01) + \beta5(RegionSouth01) +
```

β6(KeptPoultryInside01)

8) Patient purchased poultry for eggs or meat:

 $Ln(odds of Hosp) = \alpha + \beta 1(PurchaseReasonFood01) + \beta 2(RegionMidwest01) +$

 β 3(RegionNortheast01) + β 4(RegionWest01) + β 5(RegionSouth01) +

 β 6(PatientSex01) + β 7(PatientAgeQuartOrd) + β 8(KeptPoultryInside01)

9) Patient kept poultry inside:

 $Ln(odds of Hosp) = \alpha + \beta 1(KeptPoultryInside01) + \beta 2(PatientSex01) +$

 β 3(PatientAgeQuartOrd)