

## Antimicrobial resistance in *Salmonella* that caused foodborne disease outbreaks: United States, 2003–2012

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Received 9 August 2016; Final revision 19 October 2016; Accepted 7 November 2016;  
first published online 6 December 2016

### SUMMARY

Although most non-typhoidal *Salmonella* illnesses are self-limiting, antimicrobial treatment is critical for invasive infections. To describe resistance in *Salmonella* that caused foodborne outbreaks in the United States, we linked outbreaks submitted to the Foodborne Disease Outbreak Surveillance System to isolate susceptibility data in the National Antimicrobial Resistance Monitoring System. Resistant outbreaks were defined as those linked to one or more isolates with resistance to at least one antimicrobial drug. Multidrug resistant (MDR) outbreaks had at least one isolate resistant to three or more antimicrobial classes. Twenty-one per cent (37/176) of linked outbreaks were resistant. In outbreaks attributed to a single food group, 73% (16/22) of resistant outbreaks and 46% (31/68) of non-resistant outbreaks were attributed to foods from land animals ( $P < 0.05$ ). MDR *Salmonella* with clinically important resistance caused 29% (14/48) of outbreaks from land animals and 8% (3/40) of outbreaks from plant products ( $P < 0.01$ ). In our study, resistant *Salmonella* infections were more common in outbreaks attributed to foods from land animals than outbreaks from foods from plants or aquatic animals. Antimicrobial susceptibility data on isolates from foodborne *Salmonella* outbreaks can help determine which foods are associated with resistant infections.

**Key words:** Antibiotic resistance, foodborne infections, outbreaks, *Salmonella*.

### INTRODUCTION

Non-typhoidal *Salmonella* is the most common cause of bacterial foodborne illness in the United States, with an estimated 1 million infections occurring

annually [1]. *Salmonella* is also the leading cause of bacterial foodborne disease outbreaks in the United States [2].

Although most *Salmonella* infections are self-limiting, antimicrobial treatment is critical for severe salmonellosis. Antimicrobial resistance has been associated with more severe illness and more adverse outcomes, including higher rates of hospitalizations, longer duration of hospital stays, and higher mortality [3–5]. In a recent study, bloodstream infections and hospitalizations were significantly more common in patients with resistant than pansusceptible *Salmonella* [6]. Other studies have pointed to adverse clinical

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Preliminary results from this study were presented at the 2015 ASM Conference on Antimicrobial Resistance in Zoonotic Bacteria and Foodborne Pathogens (A. C. Brown).

outcomes from resistant infections in outbreaks [7, 8], including one that showed 22% of patients from resistant outbreaks were hospitalized compared to 8% of patients from non-resistant outbreaks ( $P < 0.01$ ) [8].

Antimicrobial susceptibility testing of patients' isolates from foodborne *Salmonella* outbreaks can help determine which foods are associated with resistant infections. Testing outbreak isolates can also shed light on the food sources of non-resistant outbreaks. We analysed data from two national enteric disease surveillance systems to compare the foods associated with resistant *Salmonella* outbreaks with foods associated with non-resistant outbreaks from 2003 to 2012.

## METHODS

### Outbreak reporting and categorization

The Centers for Disease Control and Prevention (CDC) define a foodborne outbreak as the occurrence of two or more cases of a similar illness from ingestion of a common food. Local, state, and territorial health departments report foodborne disease outbreaks voluntarily to CDC through the Foodborne Disease Outbreak Surveillance System (FDOSS). Outbreak reports submitted to FDOSS include information on the aetiology, patient demographics, implicated food(s), and the month and year when the outbreak began. We included data on outbreaks of non-typhoidal *Salmonella* infections reported from 2003 to 2012.

Using the Interagency Food Safety Analytics Collaboration (IFSAC) food categorization scheme [9], we classified the foods implicated in outbreaks into food categories (e.g. beef, poultry, dairy, eggs) and food groups (e.g. land animals, aquatic animals, plants). We were able to classify implicated foods when either a single ingredient was implicated or all ingredients belonged to a single food group or category. We were unable to classify outbreaks for which no food was reported or if the implicated food had ingredients from more than one food category or group. We used only classifiable outbreaks for our analyses of foods that caused resistant and non-resistant outbreaks.

### Isolates

During January 2003–June 2011, CDC asked state public health laboratories to submit representative patient and food isolates from single-state outbreaks

caused by *Salmonella* serotypes Enteritidis, Newport, and Typhimurium to CDC's National Antimicrobial Resistance Monitoring System (NARMS) laboratory. CDC also asked the ten state health departments in CDC's Foodborne Disease Active Surveillance Network (FoodNet) [10] to submit isolates from all single-state *Salmonella* outbreaks in the FoodNet catchment area, regardless of serotype. Beginning in July 2011, CDC NARMS asked all 54 participating public health laboratories to routinely submit isolates from single-state outbreaks of all *Salmonella* serotypes. For multistate outbreaks, CDC contacted states involved to request isolates.

We tested outbreak isolates for antimicrobial susceptibility using broth microdilution to determine the minimum inhibitory concentration for the following 15 antimicrobial agents: amikacin, gentamicin, kanamycin, streptomycin, ampicillin, amoxicillin-clavulanic acid, ceftiofur, ceftriaxone, cefoxitin, sulfamethoxazole/sulfoxazole, trimethoprim-sulfamethoxazole, chloramphenicol, ciprofloxacin, nalidixic acid, and tetracycline. These agents were categorized into eight classes defined by Clinical and Laboratory Standards Institute (CLSI) guidelines [11].

### Linking and analysis

We linked isolate susceptibility data to outbreak reports using a combination of epidemiological and microbiological variables, including laboratory identification number, specimen collection date, illness onset date, state, and serotype. We validated linkages using additional isolate and outbreak data from PulseNet, the national molecular subtyping network for foodborne disease surveillance.

We categorized linked outbreaks into two groups. If all isolates tested from an outbreak had no resistance to any of the 15 antimicrobials tested by NARMS, we considered that outbreak to be caused by strains with no resistance detected ('non-resistant' outbreak). If one or more isolates tested from a given outbreak was resistant to one or more of the antimicrobials tested by NARMS, we considered that outbreak to be caused by a strain in which resistance was detected ('resistant' outbreaks). Resistant outbreaks were multidrug resistant (MDR) if at least one isolate was resistant to three or more classes of antimicrobials. If a resistant outbreak had one or more isolates that was resistant to ampicillin, ceftriaxone, ciprofloxacin, or trimethoprim-sulfamethoxazole, we described that outbreak as having resistance to a clinically important

Table 1. Characteristics of linked outbreaks of *Salmonella* infections, by resistance, United States, 2003–2012 (*N* = 176)

Characteristics	Non-resistant	Resistant*	<i>P</i> value
Number of outbreaks (%)	139 (79%)	37 (21%)	
Number of outbreak-associated illnesses	11 312	2531	
Median number of illnesses (range)	26 (2–1939)	42 (2–365)	0·51
Age group, years	<i>N</i> (%)	<i>N</i> (%)	
<5	602 (5)	255 (10)	<0·01
≥ 50	2039 (18)	491 (19)	0·11
Male	400 (35)	1509 (60)	<0·01
Hospitalizations†	1539/6784 (23)	315/1587 (20)	0·01
Deaths†	25/6962 (0·4)	1/1333 (0·1)	0·11
Blood isolation	7/139 (5)	7/37 (19)	0·01
Single state	99 (71)	25 (68)	0·69
US census region‡			
West§	33 (33)	6 (25)	0·47
South	38 (42)	8 (38)	0·65
Midwest	15 (15)	6 (17)	0·37
Northeast	13 (13)	5 (21)	0·36

\* Outbreaks were defined as ‘resistant’ if at least 1 isolate resistant to ≥ 1 antimicrobial tested on the NARMS panel; outbreaks were ‘non-resistant’ if all isolates tested were susceptible to all antimicrobials on the panel.

† Denominators differ because of the number of persons for whom data were collected.

‡ Geography of single state outbreaks is described using US Census Regions [33].

§ West region includes Pacific census region.

drug (defined as drugs commonly used to treat severe salmonellosis or patients with salmonellosis who are at high risk for developing invasive infections).

We compared the characteristics of resistant outbreaks to those of non-resistant outbreaks, including patients’ demographics, frequency of blood infections, implicated food categories, and occurrence of MDR and clinically important resistance. To determine whether resistant outbreaks were more likely to have patients with bloodstream infections, we compared the frequency of blood isolation between isolates linked to resistant outbreaks and non-resistant outbreaks.

We used Fisher’s exact and Wilcoxon rank sums tests for statistical comparisons. All denominators depended on the number of persons for whom data were collected. We considered *P* values <0·05 to be significant. All *P* values were two-tailed. We conducted all analyses using SAS v. 9.3 (SAS Institute, USA).

## RESULTS

### Linking and outbreak demographics

We linked 701 isolates from foodborne *Salmonella* outbreaks to 176 outbreak reports for the years

2003–2012. Of linked outbreaks, 21% (37/176) were resistant; 78% (29/37) of resistant outbreaks were MDR, and 70% (26/37) of these had resistance to a clinically important drug (Table 1). A significantly higher percentage of children aged <5 years were patients in resistant outbreaks compared to non-resistant outbreaks (*P* < 0·01). We found a significantly higher proportion of males in patients in resistant outbreaks (*P* < 0·01). Exposures to the implicated food occurred in a single state for 71% (125/176) of outbreaks. Nearly the same proportion of resistant (71%) and non-resistant (68%) outbreaks occurred in single states. There were no major differences between resistant and non-resistant outbreaks with regard to the US census regions in which they occurred.

Non-resistant outbreaks were associated with 11 312 cases of illness; 2531 cases were associated with resistant outbreaks (Table 1). Resistant outbreaks had a median size of 42 cases (range 2–365) compared to a median size of 26 cases (range 2–1939) in non-resistant outbreaks (*P* = 0·33). Although the proportion of patients hospitalized in all resistant outbreaks (20%, 315/1587) was lower than for non-resistant outbreaks (23%, 1539/6784) (*P* = 0·01) (Table 1), outbreaks with clinically important resistance had a higher hospitalization rate (28%, 150/528) than non-resistant outbreaks

( $P < 0.01$ ). Nineteen per cent (7/37) of resistant outbreaks had at least one blood isolate compared to 5% (7/139) of non-resistant outbreaks ( $P = 0.01$ ). Death was a rare outcome; in non-resistant outbreaks, 0.4% (25) of patients died and 0.1% (1) of patients in resistant outbreaks died ( $P = 0.11$ ).

### Foods causing outbreaks

Ninety (51%) of the 176 outbreaks were attributed to a single food group ('classifiable') (Table 2). Twenty-four per cent (22/90) of classifiable outbreaks and 17% (15/86) of non-classifiable outbreaks were resistant ( $P = 0.25$ ).

In classifiable outbreaks, 46% (31/68) of non-resistant outbreaks were attributed to foods from land animals, compared to 73% (16/22) of resistant outbreaks ( $P < 0.05$ ). Outbreaks attributed to foods from plants caused 50% (34/68) of non-resistant outbreaks and 27% (6/22) of resistant outbreaks. Foods from aquatic animals caused 4% (3/68) of non-resistant outbreaks and no resistant outbreaks.

Thirty-three per cent (16/48) of outbreaks attributed to foods from land animals were resistant, compared to 15% (6/40) of outbreaks attributed to foods from plants ( $P = 0.05$ ). Eighty-two per cent (14/17) of MDR outbreaks were attributed to foods from land animals; these 14 outbreaks also accounted for the 82% (14/17) of all outbreaks with resistance to at least one clinically important drug (Table 2). Eighty-nine per cent (8/9) of outbreaks with resistance to quinolones or third-generation cephalosporins were attributed to land animals.

The most common foods associated with resistant outbreaks were beef (27%, 6/22), chicken (18%, 4/22), and turkey (18%, 4/22) (Table 2). Turkey and beef also caused most outbreaks (59%, 10/17) with MDR and clinically important resistance. The most common foods associated with non-resistant outbreaks were eggs (15%, 10/68), tomatoes (10%, 7/68), and melons (9%, 6/68).

### Serotypes causing outbreaks

The top three serotypes causing foodborne *Salmonella* outbreaks were Enteritidis, Typhimurium, and Newport (Table 3). In resistant outbreaks, the most common serotypes were Typhimurium, Newport, and Heidelberg. In non-resistant outbreaks, the most common serotypes were Enteritidis, Typhimurium, and Newport.

Resistant outbreaks caused by serotypes Typhimurium and Newport were associated most often with foods from land animals (80% each) whereas non-resistant outbreaks caused by these two serotypes were associated most often with foods from plants (73% and 70%, respectively). Other serotypes were more closely associated with either resistance (present or absent) or a specific food group. For example, although *S. Enteritidis* was associated more often with outbreaks from land animals ( $n = 14$ ) than outbreaks from plants ( $n = 2$ ), this serotype was not linked to any resistant outbreaks.

## DISCUSSION

Our study is the first to link data from two national enteric disease surveillance systems to characterize the food sources of outbreaks caused by antimicrobial-resistant *Salmonella*. During this ten year period we found that foods from land animals were the primary source of resistant foodborne *Salmonella* outbreaks. Of particular concern was our finding that resistant strains in all beef outbreaks and most poultry outbreaks were both MDR and resistant to at least one antimicrobial considered to be clinically important for the management of severe salmonellosis. Consistent with previous reports suggesting that resistant infections are associated with more adverse clinical outcomes [6, 8, 12], our findings also suggest that severe infections, as measured by frequency of blood isolation or rate of hospitalization, occurred more frequently in resistant outbreaks. Together, the findings from this study have important implications for our understanding of the origins and management of antimicrobial resistance in humans with foodborne *Salmonella* infections.

Outbreak investigations and case-control studies of sporadic infections have found strong associations between some serotypes and food vehicles. For example, serotype Enteritidis outbreaks are commonly attributed to undercooked eggs, whereas infections from serotype Javiana are often associated with fruit [13]. Infections with serotypes Typhimurium and Newport have been linked previously to a variety of food vehicles but resistant infections from these serotypes were attributed to consumption of chicken and beef [14–17]. In our study, serotypes Typhimurium and Newport were among the most common causes of outbreaks. Most of the resistant outbreaks caused by these two serotypes were attributed to meat or poultry (Table 3). (Supplementary Table S1 describes the specific outbreak and resistance characteristics of every resistant *Salmonella* outbreak of foodborne

Table 2. Foods causing outbreaks of Salmonella infections, by resistance, United States, 2003–2012 (N = 176)\*

Food	Number of outbreaks (%)									
	Non-resistant (n = 139)		Resistant† (n = 37)		MDR3* (n = 29)		Clinically important resistance‡ (n = 26)		Quinolone or cephalosporin§ resistance (n = 15)	
<b>Classifiable</b>	<b>68</b>	<b>(48·9)</b>	<b>22</b>	<b>(59·5)</b>	<b>17</b>	<b>(58·6)</b>	<b>17</b>	<b>(65·4)</b>	<b>9</b>	<b>(60·0)</b>
<b>Land animals</b>	<b>31</b>	<b>(47·15·6)</b>	<b>16</b>	<b>(72·7)</b>	<b>14</b>	<b>(82·4)</b>	<b>14</b>	<b>(82·4)</b>	<b>8</b>	<b>(88·9)</b>
Beef	7	(10·3)	6	(27·3)	6	(37·5)	6	(37·5)	5	(55·6)
Dairy	3	(4·4)	1	(4·5)	0	(0·0)	0	(0·0)	0	(0·0)
Poultry	4	(5·9)	8	(36·4)	6	(37·5)	6	(37·5)	2	(22·2)
(Chicken)	2	(2·9)	4	(18·2)	2	(12·5)	2	(12·5)	2	(22·2)
(Turkey)	2	(2·9)	4	(18·2)	4	(25·0)	4	(25·0)	0	(0·0)
Eggs	10	(14·7)	0	(0·0)	1	(6·3)	1	(6·3)	1	(11·1)
Pork	3	(4·4)	1	(4·5)	1	(6·3)	1	(6·3)	0	(0·0)
Other	4	(5·9)	0	(0·0)	0	(0·0)	0	(0·0)	0	(0·0)
<b>Plants</b>	<b>34</b>	<b>(50·0)</b>	<b>6</b>	<b>(27·3)</b>	<b>3</b>	<b>(17·6)</b>	<b>3</b>	<b>(17·6)</b>	<b>1</b>	<b>(11·1)</b>
Seeded vegetables	9	(13·2)	2	(9·1)	2	(11·7)	2	(11·7)	1	(11·1)
(Tomatoes)	7	(10·3)	0	(0·0)	0	(0·0)	0	(0·0)	0	(0·0)
Fruits	10	(14·7)	1	(4·5)	0	(0·0)	0	(0·0)	0	(0·0)
(Melons)	6	(8·8)	0	(0·0)	0	(0·0)	0	(0·0)	0	(0·0)
Sprouts	5	(7·4)	0	(0·0)	0	(0·0)	0	(0·0)	0	(0·0)
Leafy vegetables	3	(4·4)	0	(0·0)	0	(0·0)	0	(0·0)	0	(0·0)
Nuts	4	(5·9)	0	(0·0)	0	(0·0)	0	(0·0)	0	(0·0)
Herbs	0	(0·0)	2	(9·1)	0	(0·0)	0	(0·0)	0	(0·0)
Grains-beans	0	(0·0)	1	(4·5)	1	(5·9)	1	(5·9)	0	(0·0)
Other	3	(4·4)	0	(0·0)	0	(0·0)	0	(0·0)	0	(0·0)
<b>Aquatic animals</b>	<b>3</b>	<b>(4·4)</b>	<b>0</b>	<b>(0·0)</b>	<b>0</b>	<b>(0·0)</b>	<b>0</b>	<b>(0·0)</b>	<b>0</b>	<b>(0·0)</b>
Fish	3	(4·4)	0	(0·0)	0	(0·0)	0	(0·0)	0	(0·0)
<b>Non-classifiable</b>	<b>71</b>	<b>(51·1)</b>	<b>15</b>	<b>(40·5)</b>	<b>12</b>	<b>(41·4)</b>	<b>9</b>	<b>(34·6)</b>	<b>6</b>	<b>(40·0)</b>
Unclassifiable	31	(22·3)	5	(13·5)	4	(13·8)	3	(11·5)	1	(6·7)
No food reported	40	(28·8)	10	(27·0)	8	(27·6)	6	(23·1)	5	(33·3)

Text font reflects the IFSAC categorization scheme [9] of foods implicated in outbreaks. Food groups are in bold, food categories are in plain text, and specific foods within food categories are italicized. All values are inclusive of subcategories listed below.

\* Resistant outbreaks were multidrug resistant (MDR3) if at least one isolate was resistant to  $\geq 3$  classes of antimicrobials.

† Outbreaks were defined as ‘resistant’ if at least one isolate resistant to  $\geq 1$  antimicrobial tested on the NARMS panel; outbreaks were ‘non-resistant’ if all isolates tested were susceptible to all antimicrobials on the panel.

‡ Clinically important resistance included isolates resistant to ampicillin, ceftriaxone, ciprofloxacin, or trimethoprim-sulfamethoxazole.

§ Third-generation cephalosporins.

|| Outbreaks for which implicated ingredients could not be assigned to one food category or food group were unclassifiable.

Table 3. *Salmonella* serotypes causing foodborne outbreaks, by food group implicated and resistance\*, United States, 2003–2012 (N = 87†)

Serotype	Number of outbreaks (%)															
	Total	Land animals				Plants				Aquatic animals				Total		
		Resistant	Non-resistant	Resistant	Non-resistant	Resistant	Non-resistant	Resistant	Non-resistant	Resistant	Non-resistant	Resistant	Non-resistant			
Enteritidis	16	0 (0)	14 (100)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	16 (100)		
Typhimurium	15	4 (57)	4 (43)	1 (14)	6 (86)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (31)	10 (69)		
Newport	15	4 (57)	3 (43)	1 (12)	7 (88)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (33)	10 (67)		
Montevideo	5	0 (0)	4 (100)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)		
Heidelberg	5	4 (80)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (80)	1 (20)		
Saintpaul	4	0 (0)	1 (100)	0 (0)	3 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (100)		
Berta	3	1 (50)	1 (50)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33)	2 (67)		
Braenderup	3	0 (0)	0 (0)	1 (50)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33)	2 (67)		
I 4,[5],12:i:-	2	1 (100)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33)	2 (67)		
Muenchen	2	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)		
Paratyphi B var. L(+)	2	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	2 (100)		
Hadar	1	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)		
Istanbul	1	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)		
Agona	1	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)		
Rissen	1	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)		
Senftenberg	1	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)		
Amager	1	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Anatum	1	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Infantis	1	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Bredeney	1	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Carrau	1	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Cubana	1	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Javiana	1	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Oranienburg	1	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Tennessee	1	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		
Litchfield	1	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)		

\* Row percentages were calculated by dividing the number of outbreaks in each resistance category by the total number of outbreaks attributed to each food group for that serotype.

† Three multi-aetiology outbreaks were not included in this table. All three multi-aetiology outbreaks were non-resistant; two were attributed to foods from plants and one was attributed to foods from aquatic animals.

disease during 2003–2012.) These findings lend further support to the association between *Salmonella* serotypes with known food animal reservoirs and transmission of resistant strains of those serotypes to humans through contaminated food products.

Our findings are consistent with other studies that show the use of antimicrobials in food animals can select for antimicrobial-resistant bacteria and that these resistant bacteria can cause resistant infections in people [12, 18]. Whether a food was more frequently associated with resistant outbreaks can be explained, in part, by the ways in which antimicrobials are used in food production [19, 20]. Foods from land animals, such as beef or poultry, can carry bacteria that have been exposed to antimicrobial drugs administered to cattle, broiler chickens, or turkeys. These bacteria may develop resistance to those drugs. Animals can also carry resistant bacteria or resistance genes that they have picked up from their environment. Whatever their source, resistant bacteria in animals can contaminate food products made from those animals, and humans who consume those contaminated products can become infected with the resistant bacteria.

Unlike most other serotypes that caused outbreaks from land animal foods, all outbreaks of *S. Enteritidis* were non-resistant. Most *S. Enteritidis* outbreaks in our dataset were associated with consumption of eggs. Vaccination programmes, flock husbandry practices, and enhanced biosecurity measures are frequently used in place of antimicrobials to prevent and control disease in egg-laying hens (written communication, J. M. Gilbert, human food safety team lead at the Office of New Animal Drug Evaluation, FDA, June 2015) because most antimicrobial drugs for chickens carry warnings that indicate they should not be used in hens laying eggs intended for human consumption (called ‘table eggs’) [21, 22]. FDA requires that drugs approved for use in layer hens not be present in eggs in amounts that could harm consumers [23]. Injection of table eggs with antimicrobial drugs is not permitted, although the external shell might be treated using an antimicrobial wash.

Finally, we found that children aged <5 years represented a larger proportion of cases in resistant outbreaks than in non-resistant outbreaks. This was true even when we stratified by food group or category (data not shown), thus pointing to an increased susceptibility to resistant bacteria. One reason may be that they are more likely to have received a recent course of antibiotic therapy [24, 25]. A recent study

found that outpatient antibiotic prescribing rates in 2011 were higher in children (889/1000) than adults (789/1000) and that counties with higher populations of infants and children aged <2 years were more likely to have high antibiotic prescribing rates [26]. No matter the reason, treating salmonellosis in children becomes more difficult when infections are resistant to the antimicrobials (e.g. extended-spectrum cephalosporins) that are most effective in treating invasive disease. We also found that the proportion of patients who were men was higher in resistant outbreaks than non-resistant outbreaks. Although studies have shown increased consumption and tendencies toward riskier preparations of meat and poultry in men [27–29], men did not represent a larger proportion of cases in outbreaks caused by foods from land animals (data not shown).

Our study had several limitations. First, outbreak-associated infections are only a small fraction of all *Salmonella* illnesses [1, 30]. Thus, our findings do not address the food sources of sporadic cases of antimicrobial resistant salmonellosis in the United States. Second, approximately half of all outbreaks reported to FDOSS were not attributed to a single food group and so were not included in the food source analysis. Third, the characteristics of linked outbreaks might not be the same as unlinked outbreaks. For example, 29% of our linked outbreaks were multistate, compared to 10% of all non-typhoidal *Salmonella* outbreaks reported to CDC during our study period. Moreover, the median size of linked outbreaks was larger than that of unlinked outbreaks. Fourth, isolates were submitted for only 14% of foodborne *Salmonella* outbreaks reported to CDC, so our findings might not be generalizable to all foodborne outbreaks in the United States. State and local health department often do not have the time or resources to submit isolates from each outbreak investigation. CDC is working to support programmes that would increase submission rates. For this study, we linked 47% of submitted outbreak isolates to outbreak reports, and our ability to link is improving each year. Our enhanced outbreak submission scheme, initiated in 2012, improved linking by twofold for the final year of our study period compared with earlier years. Fifth, for most of our study period, isolate collection from most single-state outbreaks was focused on characterizing outbreaks of *Salmonella* serotypes Enteritidis, Newport, and Typhimurium because these serotypes were consistently among the most common causes of outbreak-associated

*Salmonella* infections [30] and the top serotypes exhibiting clinically important resistance patterns [31]. Nevertheless, these serotypes were represented equally in both linked and unlinked outbreaks, and the number of linked outbreaks from states asked to submit isolates from only these serotypes was not disproportionately higher than the number of linked outbreaks from states asked to submit isolates from outbreaks of any serotype. Sixth, we defined an outbreak as resistant or non-resistant based on the isolates submitted, but an outbreak can be caused by resistant strains with more than one resistance pattern and some isolates in an outbreak can be resistant whereas others are non-resistant. Nevertheless, because the protocol for selecting isolates for testing was independent of the outbreak food source, we do not believe our results were biased toward detecting resistance in foodborne outbreaks from any one food category. Finally, we were unable to link outbreaks caused by foods from land animals back to the producer or farm of that animal. Thus, we cannot make a causal association between specific on-farm practices and the development of resistance.

Throughout our study period, sites typically submitted outbreak isolates for susceptibility testing after the outbreak investigation was well underway or it was over. This decreases the potential bias toward investigating resistant outbreaks because resistance was rarely known until after the investigation concluded. However, antimicrobial susceptibility testing of outbreak isolates will soon be timelier. CDC's initiatives in support of the 2014 National Action Plan for Combating Antibiotic Resistant Bacteria [32], propose susceptibility testing on all *Salmonella* isolates, including those associated with outbreaks. This expanded testing capacity would inform ongoing investigations and help prioritize resources so that transmission vehicles, including foods, are identified sooner and more often, thereby preventing more *Salmonella* infections.

In our study, *Salmonella* outbreaks associated with consumption of foods from land animals were more often resistant than outbreaks associated with foods from plants. Furthermore, outbreaks caused by land animal products were more often MDR, including resistance to at least one drug that is clinically important for the treatment of severe *Salmonella* infections. Our findings highlight that antimicrobial resistance is an important public health issue that requires coordinated action in human and animal medicine. Our study also demonstrates the value of obtaining antimicrobial

resistance data on *Salmonella* outbreak isolates. By helping us to better understand the epidemiology of food source contamination, these data can assist with hypothesis generation during outbreak investigations and inform source attribution studies. Antimicrobial resistance data from outbreaks also can help inform research priorities as well as policy decisions and prevention efforts.

## SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit <https://doi.org/10.1017/S0950268816002867>.

## DECLARATION OF INTEREST

None.

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