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Antimicrobial Resistance Among Nontyphoidal *Salmonella* Isolated From Blood in the United States, 2003–2013

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Abstract

Background—*Salmonella* causes an estimated 100 000 antimicrobial-resistant infections annually in the United States. *Salmonella* antimicrobial resistance may result in bacteremia and poor outcomes. We describe antimicrobial resistance among nontyphoidal *Salmonella* blood isolates, using data from the National Antimicrobial Resistance Monitoring System.

Methods—Human nontyphoidal *Salmonella* isolates from 2003 to 2013 were classified as fully susceptible, resistant to ≥1 antimicrobial agent, or resistant to a first-line agent. Logistic regression was used to compare resistance patterns, serotypes, and patient characteristics for *Salmonella* isolated from blood versus stool and to determine resistance trends over time.

Results—Approximately 20% of blood isolates had antimicrobial resistance to a first-line treatment agent. Bacteremia was associated with male sex, age ≥65 years, and specific serotypes. Blood isolates were more likely to be resistant to ≥1 agent for serotypes Enteritidis, Javiana, Panama, and Typhimurium. Blood isolates were most commonly resistant to tetracycline (19%), and more likely resistant to a first-line agent (odds ratio, 1.81; 95% confidence interval, 1.56–2.11) than stool isolates. Ceftriaxone resistance increased in blood isolates from 2003 to 2013 (odd ratio, 1.12; 95% confidence interval, 1.02–1.22).

Conclusions—Resistance to first-line treatment agents in patients with *Salmonella* bacteremia is a concern for public health and for informing clinical decisions. Judicious antimicrobial use is crucial to limit resistance.

Keywords

Salmonella; nontyphoidal *Salmonella*; antimicrobial resistance; bacteremia

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Supplementary Data

Supplementary materials are available at http://jid.oxfordjournals.org. Consisting of data provided by the author to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Salmonella causes an estimated 1.2 million illnesses, 23 000 hospitalizations, and 450 deaths annually in the United States [1]. Nontyphoidal *Salmonella enterica* causes the majority of these infections and almost all *Salmonella-related* hospitalizations and deaths [2]. Most *Salmonella* infections result from the ingestion of contaminated food [2, 3] and are characterized by gastroenteritis. Invasive infection, such as bacteremia and meningitis, occurs most commonly in persons with compromised immunity [4], including those with human immunodeficiency virus infection [5], infants [6], and older adults, who may have increased risk of complications, including death [7, 8]. Invasive nontyphoidal *Salmonella* infection is most common among patients with serotypes Choleraesuis, Dublin, Enteritidis, Heidelberg, Poona, and Schwarzengrund [6].

Antimicrobial treatment can be life-saving for invasive *Salmonella* infections [2]. Antibiotics commonly prescribed for these infections include fluoroquinolones (eg, ciprofloxacin) or third-generation (extended-spectrum) cephalosporins (eg, ceftriaxone) [9]. Antimicrobial resistance may contribute to bacteremia, treatment failure, and poor clinical outcomes. Hospitalizations occur with increased frequency in persons with resistant isolates, particularly those with ceftriaxone resistance [10, 11]. *Salmonella* bacteremia is more common in drug-resistant than in susceptible infections [10–12]. For example, fluoroquinolone resistance is associated with a >3-fold increased risk of invasive illness or death within 90 days, and nalidixic acid resistance may correlate with ciprofloxacin treatment failure [13, 14]. In recent years, azithromycin use for nontyphoidal *Salmonella* treatment has increased, probably owing to increasing resistance to fluoroquinolones and extended-spectrum cephalosporins; however, there have been recent reports of azithromycin treatment failures [15]. The Clinical and Laboratory Standards Institute (CLSI) has not yet established a break point for azithromycin resistance for nontyphoidal *Salmonella* [3, 16].

Most nontyphoidal *Salmonella* infections are food borne. Resistance among nontyphoidal *Salmonella* has been linked to antimicrobial use in food animal production [17, 18]. Injudicious antimicrobial use among humans has also been linked to an increased risk of antimicrobial-resistant infection [19].

We describe and compare antimicrobial resistance patterns among nontyphoidal *Salmonella* blood and stool isolates and trends in antimicrobial resistance. We compare characteristics (sex and age) of persons with nontyphoidal *Salmonella* isolated from blood versus stool. We also assess the differences in blood isolation rates and resistance by serotype.

MATERIALS AND METHODS

The National Antimicrobial Resistance Monitoring System (NARMS) at the Centers for Disease Control and Prevention (CDC) has tracked resistance patterns among enteric pathogens from humans since 1996. NARMS is a collaboration among the CDC, the US Food and Drug Administration (FDA), the US Department of Agriculture, and state and local public health departments. Since 2003, NARMS has included health departments from all 50 states, covering >300 million persons [20]. Participating public health laboratories submit every 20th nontyphoidal *Salmonella* isolate to the CDC laboratory and include available information regarding age, sex, specimen source, and serotype.

Isolates were tested in the CDC NARMS laboratory using broth microdilution (Sensititre; Trek Diagnostics, part of Thermo Fisher Scientific). The following antimicrobial agents were tested routinely via this method from 2003 through 2013: amoxicillin–clavulanic acid, ampicillin, cefoxitin, ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfisoxazole/ sulfamethoxazole (sulfonamide), tetracycline, and trimethoprim-sulfamethoxazole (TMP-SMX). CLSI criteria were used for interpretation when available [21]. Azithromycin was not routinely tested before 2011. Before 2004, sulfamethoxazole was used instead of sulfisoxazole. NARMS break points were used for streptomycin (≥64 μg/mL) and azithromycin (≥32 μg/mL), which have no CLSI break points [20].

Isolates with specimen sources other than blood or stool and isolates of serotypes Typhi, Paratyphi A, Paratyphi B (var L+ tartrate–), and Paratyphi C were excluded from the analysis. Blood and stool isolates that were not serotyped, were partially serotyped, or were characterized as rough or nonmotile were also excluded. From this point forward, we refer to all nontyphoidal *Salmonella* isolates included in the analysis as *Salmonella.* All resistant isolates and isolates with an intermediate minimum inhibitory concentration were categorized as resistant to remain in accordance with clinical practice, except that we did not include isolates with intermediate minimum inhibitory concentrations among those with specific resistance pattern combinations (eg, resistance to ampicillin, streptomycin, sulfonamide, and tetracycline). CLSI interpretive criteria for ciprofloxacin changed in 2012 to reflect clinical significance; susceptibility was defined as ≤0.06 μg/mL, intermediate resistance as 0.12–0.5 μg/mL, and resistance as ≥1.0 μg/mL.

We analyzed data on *Salmonella* isolated from 2003 through 2013. Patients with *Salmonella* isolated from blood and stool were compared by sex and age, using odds ratios (ORs) and 95% confidence intervals (CIs). Patients were divided into 6 age groups: <1, 1–4, 5–17, 18–64, 65–84, and ≥85 years. Non-Typhimurium blood and stool isolates were compared with serotype Typhimurium, which served as the referent group. Serotypes with <10 blood isolates were combined into a category called *other.* Blood and stool isolates were compared for antimicrobial resistance. We determined the number of isolates that were fully susceptible, resistant to ≥1 agent, resistant to ≥3 CLSI classes, and resistant to ≥5 CLSI classes. We also examined the following resistance pattern combinations: resistance to ampicillin, streptomycin, sulfonamide, and tetracycline but not chloramphenicol; resistance to ampicillin, chloramphenicol, streptomycin, sulfonamide, and tetracycline; resistance to ampicillin, chloramphenicol, streptomycin, sulfonamide, tetracycline, amoxicillin–clavulanic acid, and ceftriaxone; and resistance to ampicillin, amoxicillin–clavulanic acid, and ceftriaxone. Resistance to a first-line treatment agent was defined as resistance to ≥1 of the following agents used to treat *Salmonella* infections: ampicillin, ceftriaxone, ciprofloxacin and TMP-SMX. *Salmonella* isolates from blood were compared with stool isolates for resistance to ≥1 agents by serotype using logistic regression.

Various regression models, including robust and logistic, were used to assess the sensitivity of the model choice and to identify specific trends. Estimated annual trends with associated CIs were then computed by agent and specimen source.

RESULTS

During 2003–2013, we tested 23 761 *Salmonella* isolates. Of those, 21 390 were from blood or stool, 1388 (5.9%) were from urine, and the remaining 983 (4%) were from abscesses, gallbladders, wounds, or other sites. Overall, 524 blood and stool isolates were excluded from analysis; 264 were not serotyped, 200 were partially serotyped, and 60 were rough or nonmotile. Of the 20 866 remaining isolates, 1189 (5.7%) were from blood, and 19 677 (94.3%) were from stool. Of 19 362 isolates with information on sex, 9774 (50.5%) were from female patients. Among 1117 blood isolates for which information on patient sex was available, 608 (54.4%) were from male patients, who were more likely to have bacteremia (OR, 1.23; 95% CI, 1.09–1.39).

The median age was 43 years (range, <1 to 98 years) among patients with blood isolates, compared with 22 years (<1 to 103 years) among those with stool isolates ($P < .001$). Persons aged 65–84 years (OR, 2.04; 95% CI, 1.73–2.41) or ≥85 years (OR, 2.10; 95% CI, 1.47–3.00) were more likely to have bacteremia than those in the 18–64-year age group (referent). Infants <1 year old (OR, 0.77; 95% CI, .62–.97) and children aged 1–4 (OR, 0.63; 95% CI, .52–.76) or 5–17 years (OR, 0.68; 95% CI, .56–.82) were less likely to have bacteremia.

The proportion of *Salmonella* isolates that came from blood varied by serotype, ranging from 87.0% for serotype Dublin to 2.3% for serotype Muenchen (Table 1). Compared with Typhimurium, the 3 serotypes most highly associated with bacteremia were Dublin (OR, 128.2; 95% CI, 57.19–287.40), Sandiego (OR, 4.90; 95% CI, 2.90–8.29), and Schwarzengrund (OR, 3.44; 95% CI, 2.14–5.55). Serotypes Enteritidis, Heidelberg, Oranienburg, Panama, Poona, and Rubislaw were also more likely to be isolated from blood, and serotypes Javiana, Muenchen, and Newport were less likely to be isolated from blood.

Blood isolates were further characterized by resistance pattern; 868 (73.0%) of 1189 blood isolates were susceptible to all agents tested. Among the 321 blood isolates that were resistant to ≥1 agent, resistance to a first-line treatment agent was found in 237 (73.8%). Compared with stool isolates, blood isolates were associated with resistance to ≥1 agent, ≥3 classes, ≥5 classes, and first-line treatment agents. Isolation from blood was also significantly associated with resistance to most other agents and resistance pattern combinations (Table 2).

Of the 237 blood isolates with resistance to a first-line treatment agent, the most common serotypes were Typhimurium (85 isolates), Heidelberg (38 isolates), and Dublin (33 isolates). Serotypes Dublin, Heidelberg, and Newport had the greatest number of blood isolates resistant to ceftriaxone. Serotypes Typhimurium, Heidelberg, and Dublin had the greatest number resistant to ampicillin, serotype Enteritidis had the greatest number resistant to ciprofloxacin, and serotype Typhimurium had the greatest number resistant to TMP-SMX (see Supplementary Data).

The following serotypes had the strongest association between resistance to ≥1 agent and isolation from blood: Panama (OR, 6.85; 95% CI, 1.25–37.58), Javiana (OR, 3.76; 95% CI, 1.08–13.04), Typhimurium (OR, 2.04; 95% CI, 1.52–2.73), and Enteritidis (OR, 1.61; 95%

CI, 1.13–2.29) (Table 3). In contrast, for serotype I 4,[5],12:i:–, stool isolates were significantly more likely than blood isolates to be associated with resistance to ≥1 antimicrobial agent.

During 2003–2013, ciprofloxacin resistance increased and ampicillin resistance decreased for both blood and stool isolates, though the trends were statistically significant only for stool isolates (Table 4). In contrast, ceftriaxone resistance increased significantly for blood isolates (OR, 1.12; 95% CI, 1.02–1.22) and decreased significantly for stool isolates (OR, 0.95; 95% CI, .92–.97). Resistance to TMP-SMX did not change significantly for blood or stool isolates.

DISCUSSION

We found a substantial amount of resistance to antimicrobials used for *Salmonella* bloodstream infections. Overall, approximately 5% of all *Salmonella* isolates that came from blood were resistant to ceftriaxone. Resistance to ceftriaxone has doubled since a 1996–2007 study from NARMS. In that study, only 2.5% of all *Salmonella* isolates that came from blood were resistant to ceftriaxone [12]. Ceftriaxone is considered a first-line treatment for *Salmonella* bacteremia, and increasing antimicrobial resistance is concerning for clinical treatment and patient outcomes. If this path of increasing resistance continues, we may soon be at a crossroads where first-line treatment recommendations will need to change, as occurred with gonorrhea treatment and the use of cefixime; resistance increased from 0.1% to 1.5% over 5 years and prompted a change in gonorrhea treatment guidelines [22].

Fluoroquinolones, penicillins, and cephalosporins are commonly prescribed for a variety of clinical syndromes, and increasing human exposure to these antimicrobials may lead to an increased risk of antimicrobial resistance [10, 15, 23]. Since the previous NARMS study, fluoroquinolone resistance has nearly doubled. We also found that resistance to ampicillin, *Salmonella* bacteremia. Nalidixic acid resistance correlates with resistance to ciprofloxacin and may predict treatment failure [12, 14]. We found that 4% of all *Salmonella* isolates that came from blood had nalidixic acid resistance and 4.5% had ciprofloxacin resistance; the NARMS study from 1996–2007 found that 2.7% of all *Salmonella* isolates that came from blood were resistant to nalidixic acid [12]. Resistance to ≥1 agent, and resistance to ≥3 or ≥5 classes of antimicrobials were also associated with bacteremia, supporting the finding that bacteremia is more common in drug-resistant infections than susceptible ones [10–12]. We do not know the relative contribution of each biological or clinical mechanism that may link antimicrobial resistance to bloodstream infections; these infections might be due to the failure or reduced efficacy of empirical antimicrobial treatment which would result in more severe illness, the presence of additional virulence factors that could enhance invasiveness and worsen patient outcome, or the fact that patients whose isolates are submitted to NARMS for testing are inherently more likely to be hospitalized and seek care from a provider owing to increased severity of symptoms [11].

The annual proportion of isolates that came from blood with ceftriaxone resistance increased from 2003 through 2013, whereas the proportion of stool isolates with ceftriaxone resistance decreased. This finding did not hold for the other first-line treatment agents. The reason that

blood isolates are increasingly resistant to ceftriaxone whereas stool isolates are becoming more susceptible to ceftriaxone is probably related to serotype. It is likely that the overall distribution of *Salmonella* serotypes in blood and stool is constantly evolving, and serotypes that are commonly resistant may be increasing disproportionally in blood over time. For example, host adapted, highly resistant serotypes have become associated with *Salmonella* blood infections, particularly serotypes Dublin and Choleraesuis [24–26]. *Salmonella* Choleraesuis, a serotype that is host adapted to swine, is becoming increasingly resistant, probably owing to various resistance genes and plasmids [25, 26], possibly acquired through agricultural antimicrobial use.

In our study, bacteremia was most common among patients with serotypes Dublin, Sandiego, Schwarzengrund, Poona, Panama, Heidelberg, Oranienburg, Rubislaw, and Enteritidis, compared with serotype Typhimurium. These serotype-specific findings are consistent with previous studies, with the notable exceptions of serotypes Poona and Rubislaw. A previous study showed a higher risk of invasive disease for serotype Poona compared with Typhimurium [6], but other studies have not supported this association [11, 12, 27]. Previous studies have not shown an association between bacteremia and serotype Rubislaw [6, 11, 12, 27]. The reason for the incongruous findings for serotype Poona and the new association of bacteremia with serotype Rubislaw is unknown. Most of the infections with serotypes Rubislaw and Poona in our study were among children. Both these serotypes have an historical association with reptiles [28], and reptile-associated *Salmonella* infections may place children at an increased risk of invasive infection [29]. This may explain the increased blood isolation of Rubislaw and Poona isolates in our study and may indicate that reptile exposures predispose to *Salmonella* bacteremia with certain serotypes.

We confirmed findings from previous studies regarding risk factors for *Salmonella* bacteremia, including a higher frequency of *Salmonella* bacteremia in men than in women, a higher median age among patients with bacteremia than among patients with stool isolates, and the highest rate of bacteremia among persons aged ≥64 years, consistent with invasive disease being more common in older adults [12]. Other risk factors, such as international travel, have been associated with antimicrobial resistance in patients with *Salmonella* bacteremia, [30],but travel data are not collected in NARMS. This study and a previous one that used NARMS data [12] found that the odds of *Salmonella* bacteremia was lower among infants aged <1 year than among adults aged 18–64 years. This may be due in part to differences in *Salmonella* serotype distribution. For example, in our study a lower proportion of infants than adults had *Salmonella* Enteriditis, which is known to be an invasive serotype [6,27]. Moreover, in contrast to adults with *Salmonella* gastroenteritis, it is recommended that infants <3 months of age receive treatment to avert invasive disease [31]. Further investigation is needed to characterize the vulnerability of infants to *Salmonella* bacteremia.

This study had some limitations. The NARMS protocol for the state and local laboratories requires submission of every 20th *Salmonella* isolate to the CDC. It is possible that some patients who had a stool isolate submitted to CDC NARMS also had bacteremia, but the stool isolate was the 20th isolate submitted by the health department to CDC NARMS. This would bias our associations toward the null. Differential resistance among the missing and interaction between variables, possibly regarding both serotype and age, may influence

results. We were unable to examine serotypes with regard to virulence as an explanation for their propensity cause bacteremia (or lack thereof) to. NARMS does not capture patient treatment or outcome data. For serotypes with small numbers of isolates, limited precise estimates of antimicrobial resistance could not be made because of limited power. We were also limited by the short time series of 11 years (2003–2013) to perform time trends analysis.

In conclusion, *Salmonella* blood isolates were more likely than stool isolates to be resistant to ≥1 agent and to first-line treatment agents. Resistance to first-line treatment agents in patients with *Salmonella* bacteremia is a concern for public health and clinical outcomes and is important for informing clinical decisions regarding appropriate treatment. Judicious antimicrobial use in both humans and food-producing animals is crucial to limit the emergence and spread of resistance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Proportion of Nontyphoidal *Salmonella* Isolates From Blood by Serotype, 2003–2013

Serotype[a]	Total Isolates, No.	Blood Isolates, No. (%)	OR (95% CI)
Dublin	54	47 (87.0)	128.20 (57.19–287.40)
Sandiego	93	19 (20.4)	4.90 (2.90–8.29)
Schwarzengrund	144	22 (15.3)	3.44 (2.14–5.55)
Poona	172	26 (15.1)	3.40 (2.19–5.29)
Panama	108	16 (14.8)	3.32 (1.92–5.76)
Heidelberg	811	119 (14.7)	3.28 (2.58–4.19)
Oranienburg	399	44 (11.0)	2.37 (1.68–3.34)
Rubislaw	99	10 (10.1)	2.15 (1.10–4.19)
Enteritidis	3908	250 (6.4)	1.31 (1.08–1.59)
Montevideo	549	31 (5.7)	1.14 (.77–1.69)
Other	4320	220 (5.1)	1.03 (.84–1.25)
Saintpaul	490	25 (5.1)	1.03 (.67–1.58)
Paratyphi B var L+ tartrate+	348	14 (4.0)	0.80 (.46–1.39)
Agona	286	11 (3.9)	0.76 (.41–1.42)
I 4,[5],12:i:–	790	28 (3.5)	0.70 (.47–1.05)
Infantis	446	14 (3.1)	0.62 (.36–1.08)
Newport	2398	64 (2.7)	0.52 (.39–.70)
Javiana	1159	28 (2.4)	0.47 (.32–.71)
Muenchen	474	11 (2.3)	0.45 (.25–.84)
Typhimurium	3818	190 (5.0)	Referent
Total	20 866	1189 (5.7)	

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] *Salmonella* serotypes with ≥10 blood isolates are listed individually, and those with <10 blood isolates are listed in the “Other” category.

Table 2.

Proportion of Nontyphoidal *Salmonella* Isolates From Blood by Antimicrobial Resistance Type, 2003–2013

Antimicrobial Resistance Type[a]	Total Isolates, No.	Blood Isolates, No. (%)	OR (95% CI)
Fully susceptible	16 972	868 (5.1)	Referent
Agents			
Amoxicillin-clavulanic acid	1478	120 (8.1)	1.64(1.34–2.00)
Ampicillin	2194	201 (9.2)	1.87 (1.59–2.20)
Azithromycin[b]	7	1 (14.3)	3.09 (.37–25.71)
Cefoxitin	712	59 (8.3)	1.68(1.27–2.21)
Ceftiofur	686	56 (8.2)	1.65(1.24–2.19)
Ceftriaxone	677	55 (8.1)	1.64 (1.24–2.18)
Chloramphenicol	1423	136 (9.6)	1.96 (1.62–2.37)
Ciprofloxacin	526	53 (10.1)	2.08 (1.55–2.78)
Gentamicin	355	34 (9.6)	1.97 (1.37–2.82)
Kanamycin	493	70(14.2)	3.07 (2.36–3.99)
Nalidixic acid	426	48 (11.3)	2.36 (1.73–3.21)
Streptomycin	2199	194 (8.8)	1.80 (1.53–2.11)
Sulfamethoxazole or sulfisoxazole[c]	2289	192 (8.4)	1.70(1.44–2.00)
Tetracycline	2695	227 (8.4)	1.71 (1.47–1.99)
TMP-SMX	326	34 (10.4)	2.16 (1.51–3.10)
Patterns			
First-line agent[d]	2663	237 (8.9)	1.81 (1.56–2.11)
≥1 agent	3894	321 (8.3)	1.67 (1.46–1.91)
≥3 classes	2276	205 (9.0)	1.84(1.57–2.15)
≥5 classes	1378	133 (9.7)	1.98 (1.64–2.40)
ACSSuT	1170	105 (9.0)	1.83 (1.48–2.26)
ACSSuTAuCx	395	30 (7.6)	1.53 (1.04–2.23)
ASSuTnoC	283	20 (7.1)	1.41 (.89–2.24)
AAuCx	647	53 (8.2)	1.66 (1.24–2.21)

Abbreviations: AAuCx, resistant to at least ampicillin, amoxicillin–clavulanic acid, and ceftriaxone; ACSSuT, resistant to at least ampicillin, chloramphenicol, streptomycin, a sulfonamide, and tetracycline; ACSSuTAuCx, resistant to at least ACSSuT, amoxicillin–clavulanic acid, and ceftriaxone; ASSuTnoC, resistant to at least ampicillin, streptomycin, a sulfonamide, and tetracycline, but not chloramphenicol; CI, confidence interval; OR, odds ratio; TMP-SMX, trimethoprim-sulfamethoxazole.

[a] For single antimicrobials and resistance to ≥1 agent, ≥3 classes, or ≥5 classes, resistance is defined as an intermediate or resistant minimum inhibitory concentration.

[b] Azithromycin was not routinely tested before 2011.

[c] Sulfamethoxazole, which was tested before 2004 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

[d] Resistant to ≥1 of the following agents: ampicillin, ceftriaxone, ciprofloxacin, or TMP-SMX.

Table 3.

Antimicrobial Resistance of Nontyphoidal *Salmonella* Blood and Stool Isolates, by Serotype, 2003–2013

Serotype	Blood Isolates		Stool Isolates		OR (95% CI)
	Total, No.	Resistant, No. (%)[a]	Total, No.	Resistant, No. (%)[a]	
Enteritidis	250	40 (16.0)	3658	387 (10.6)	1.61 (1.13–2.29)
Typhimurium	190	101 (53.2)	3628	1299 (35.8)	2.04 (1.52–2.73)
Heidelberg	119	52 (43.7)	692	279 (40.3)	1.15 (.78–1.70)
Newport	64	9 (14.1)	2334	311 (13.3)	1.06 (.52–2.18)
Dublin	47	35 (74.5)	7	5 (71.4)	1.17 (.20–6.82)
Oranienburg	44	3 (6.8)	355	18 (5.1)	1.37 (.39–4.85)
Montevideo	31	1 (3.2)	518	57 (11.0)	0.27 (.04–2.01)
I 4,[5],12:i:–	28	2 (7.1)	762	245 (32.2)	0.16 (.04–.69)
Javiana	28	3 (10.7)	1131	35 (3.1)	3.76 (1.08–13.04)
Poona	26	2 (7.7)	146	4 (2.7)	2.96 (.51–17.05)
Saintpaul	25	8 (32.0)	465	89 (19.1)	1.99 (.83–4.75)
Schwarzengrund	22	2 (9.1)	122	23 (18.9)	0.43 (.09–1.97)
Sandiego	19	1 (5.3)	74	3 (4.1)	1.32 (.13–13.40)
Panama	16	3 (18.8)	92	3 (3.3)	6.85 (1.25–37.58)
Infantis	14	3 (21.4)	432	49(11.3)	2.13 (.57–7.91)
Paratyphi B var L+ tartrate+	14	3 (21.4)	334	51 (15.3)	1.51 (.41–5.61)
Agona	11	5 (45.5)	275	93 (33.8)	1.63 (.49–5.48)
Muenchen	11	1 (9.1)	463	30 (6.5)	1.44 (.18–11.65)
Rubislaw	10	0(0)	89	1 (1.1)	N/A
Other	220	47 (21.4)	4100	591 (14.4)	1.61 (1.16–2.25)
Total	1189	321 (27.0)	19 677	4023 (20.4)	

Abbreviations: CI, confidence interval; N/A, not applicable; OR, odds ratio.

[a]All isolates with resistant and intermediate minimum inhibitory concentrations were categorized as resistant to remain in accordance with clinical practice.

Table 4.

Trend Effect of Year on Proportion of Nontyphoidal *Salmonella* Isolates Resistant to First-Line Treatment Agents, by Specimen Source and Agent, 2003–2013

	OR (95% CI)	
Agent	**Blood Isolates**	**Stool Isolates**
Ceftriaxone	1.12 (1.02–1.22)	0.95 (.92–.97)
Ciprofloxacin	1.09 (.99–1.20)	1.06 (1.03–1.10)
Trimethoprim-sulfamethoxazole	1.00 (.90–1.12)	0.97 (.93–1.01)
Ampicillin	0.97 (.92–1.02)	0.96 (.95–.98)

Abbreviations: CI, confidence interval; OR, odds ratio.