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Antimicrobial-Resistant Nontyphoidal *Salmonella* Infection Following International Travel—United States, 2018–2019

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Abstract

Background.—Antimicrobial resistance in nontyphoidal *Salmonella* (NTS) can limit treatment options. We assessed the contribution of international travel to antimicrobial-resistant NTS infections.

Methods.—We describe NTS infections that were reported to the Foodborne Diseases Active Surveillance Network during 2018–2019 and screened for genetic resistance determinants, including those conferring decreased susceptibility to first-line agents (ciprofloxacin, ceftriaxone, or azithromycin). We used multivariable logistic regression to assess the association between resistance and international travel during the 7 days before illness began. We estimated the contribution of international travel to resistance using population-attributable fractions, and we examined reported antimicrobial use.

Results.—Among 9301 NTS infections, 1159 (12%) occurred after recent international travel. Predicted resistance to first-line antimicrobials was more likely following travel; the adjusted odds ratio varied by travel region and was highest after travel to Asia (adjusted odds ratio, 7.2 [95% confidence interval, 5.5–9.5]). Overall, 19% (95% confidence interval, 17%–22%) of predicted resistance to first-line antimicrobials was attributable to international travel. More

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Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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travelers than nontravelers receiving ciprofloxacin or other fluoroquinolones had isolates with predicted resistance to fluoroquinolones (29% vs 9%, respectively; $P < .01$).

Conclusions.—International travel is a substantial risk factor for antimicrobial-resistant NTS infections. Understanding risks of resistant infection could help target prevention efforts.

Keywords

salmonella; drug resistance; foodborne disease; travel

Globally, nontyphoidal *Salmonella* (NTS) are responsible for the highest burden of all foodborne diseases [1]. Most people with NTS infection experience diarrhea, fever, and stomach cramps, and symptoms usually start 6 hours to 6 days after infection [2, 3]. An estimated 1.35 million NTS infections occur each year in the United States, and approximately 16% of these infections are resistant to antimicrobials recommended for treatment [4, 5]. Although most episodes of NTS infection do not require antimicrobial therapy, antibiotics are critical to treat invasive infections. Antimicrobial resistance may also be associated with virulence genes, resulting in more severe illness [6]. The growing proportion of antimicrobial-resistant NTS limits treatment options and creates opportunities for acquired resistance determinants (resistance genes or mutations) to spread to other pathogens [5, 7].

International travel is an important risk factor for antimicrobial-resistant NTS infections [7, 8] and has been associated with 6-fold increased odds of infection with quinolone-nonsusceptible NTS [7]. Understanding the contribution of international travel to NTS resistance and resistance genes, and the role of travel region, can help inform prevention efforts and treatment guidelines.

We describe NTS infections associated with international travel among persons investigated in US sentinel surveillance sites during 2018–2019, including characterization of resistance determinants by travel region, and reported use of antimicrobials. We examine risk factors for resistant infections and estimate the contribution of international travel to antimicrobial-resistant NTS infections in the United States.

METHODS

The Foodborne Diseases Active Surveillance Network (FoodNet) conducts active, population-based surveillance for laboratory-confirmed *Salmonella* infections in 10 sites covering approximately 15% of the US population (an estimated 49 million persons in 2018) [9, 10]. FoodNet epidemiologists collect demographic, clinical information, and travel history during the 7 days before illness began, using a standard case report form. Since 2018, FoodNet has collected expanded information, including international travel history for the person infected and their household members during the 6 months before illness began.

PulseNet, a national surveillance laboratory network has monitored *Salmonella* and other strains of enteric bacteria since 1996 and has used whole-genome sequencing (WGS) since 2015 [11, 12]. We linked FoodNet patient data from 2018 and 2019 with WGS results in PulseNet. Reads with a base call quality score ≥28, and coverage ≥40× were assembled

using Shovill software, version 1.1.0 (https://github.com/tseemann/shovill), with a *–min-cov* of 10% of the average genome coverage. Resistance determinants were identified using Staramr software, version 0.4.0 (https://github.com/phac-nml/staramr), with cutoffs of 90% identity and 50% coverage, and the PointFinder scheme for *Salmonella.*

Predicted resistance to antimicrobials was assigned using ResFinder and PointFinder drug keys used as part of National Antimicrobial Resistance Monitoring System surveillance [13–16]. Resistance was predicted for amikacin, ampicillin, amoxicillin–clavulanic acid, azithromycin, cefoxitin, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, streptomycin, sulfisoxazole, tetracycline, and trimethoprim-sulfamethoxazole; we defined predicted resistance to any antimicrobials ("any resistance") as the presence of a resistance gene or mutation expected to confer decreased susceptibility or resistance to ≥1 of these antimicrobials [17]. We defined predicted resistance to first-line antimicrobials ("first-line resistance") as the presence of a resistance gene or mutation conferring decreased susceptibility or resistance to ciprofloxacin, ceftriaxone, or azithromycin.

We performed analyses using Stata SE 16 software (StataCorp) and figures were made using R version 4.2. We defined NTS serotypes as all *Salmonella* serotypes except serotypes Typhi and Paratyphi A, C, and tartrate-negative B. We limited analyses to symptomatic infections with NTS serotypes that included information from WGS and on international travel during the 7 days before illness began. Travel destinations were grouped into 6 geographic regions using the United Nations standard country or area codes for statistical use [18]: Africa, Asia, Europe, Latin America and the Caribbean (including Mexico), North America, and Oceania. Travelers who visited >1 region were included only in "multiple regions," and those with an unknown travel destination were included in "unknown region."

We compared demographic and clinical characteristics by travel history, summarized the proportion of infections with predicted antimicrobial resistance by travel region, and compared odds of predicted resistance by travel status. We used multivariable logistic regression to assess associations between resistance and travel region (compared with no travel) among reported NTS infections. We adjusted estimates for age, sex, and season of infection.

To estimate the incidence of antimicrobial-resistant NTS infection per 100 000 travelers, we divided the number of travel-associated antimicrobial-resistant infections by the US Department of Commerce's National Travel and Tourism Office survey of outgoing international passenger data from FoodNet sites in 2018 and 2019. We calculated confidence intervals (CIs) using the exact binomial method. Because travel data were limited to passengers ≥18 years, we restricted estimates of incidence to adults. We did not estimate incidence for travel to North America or to multiple regions or if the travel destination was not reported. To estimate the proportion of antimicrobial-resistant infections attributable to international travel, we calculated adjusted population-attributable fractions, reflecting both the association between travel and resistance and the proportion of infections occurring after travel [19].

We reviewed antimicrobials that patients reported taking for infections and whether patient isolates had resistance determinants to those antimicrobials. We used χ^2 tests to compare the use of antimicrobials recommended to treat *Salmonella* by travel status. We considered several antimicrobials as recommended treatment for *Salmonella* infection: ciprofloxacin or other fluoroquinolones, ceftriaxone or other third-generation cephalosporins, azithromycin, ampicillin or other penicillin, and trimethoprim-sulfamethoxazole [20, 21]. This activity was reviewed by the Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy (45 CFR part 46.102(I)(2); 21 CFR part 56; 42 USC §241(d); 5 USC §552a; 44 USC §3501 et seq).

RESULTS

Study Population

Among 17 508 NTS infections reported by FoodNet sites during 2018–2019, 10 723 (61%) were sequenced and screened for resistance determinants. We excluded 1422 of (13%) NTS isolates with missing travel data (Supplementary Figure). Among the 9301 NTS infections with sequenced isolates and known travel status, 6475 (70%) were in adults (aged ≥18 years), 5060 (54%) were in females, and 5886 (68%) were in non-Hispanic white persons (Table 1).

Travel and Antimicrobial-Resistant Infection

Travel was reported during the 7 days before illness began for 1159 infections (12%), and in the 8 days to 6 months before illness began for 404 (4%) (Table 1 and Supplementary Table 1). Antimicrobial resistance determinants were present in 2073 (22%) of the 9301 infections. By travel status, resistance determinants were present in 477 of 1159 (41%) with travel in the 7 days before illness began, 107 of 404 (26%) with travel between 8 days and 6 months before illness began, 399/1866 (21%) with unknown travel between 8 days and 6 months before illness began, and 1090 of 5872 (19%) among nontravelers. Resistance determinants to first-line antimicrobials were present in 1220 (13%) of the 9301 infections—366 of 1159 (32%) with travel in the 7 days before illness began, 66 of 404 (16%) with travel between 8 days and 6 months before illness began, 234 of 1866 (13%) with no travel in the 7 days and unknown travel between 8 days and 6 months before illness began, and 554 of 5872 (9%) among nontravelers.

Odds of Antimicrobial-Resistant Infections

Predicted resistance to first-line antimicrobials was more likely among children >5 years old and adults than in children <5 years old, more likely for infections in the winter and spring than for infections in the summer, and more likely among persons who had traveled to Asia, Latin America and the Caribbean, or Europe during the 7 days before illness began than among nontravelers (Table 2). Adjusted for age, sex, and season, NTS infections following recent travel were more likely than infections in nontravelers to have predicted resistance to first-line antimicrobials (adjusted odds ratio [aOR], 3.7 [95% CI, 3.2–4.3]). Travelers to any international destination, to Asia, and to Latin America and the Caribbean had increased odds of predicted resistance to any antimicrobials compared with nontravelers (Supplementary Table 2). Travel to any international destination during the 8

days to 6 months before illness began and international travel by a household member in the 6 months before illness began were not associated with higher odds of predicted resistance to first-line antimicrobials (aOR [95% CI], 1.3 [1.0–1.7] and 0.6 [.3–1.0], respectively) or to any antimicrobials (1.2 [1.0–1.6] and 0.6 [.4–.9]), when adjusted for age, sex, and season.

Among adults, findings were similar to those from the overall analysis; the odds of predicted first-line antimicrobial resistant infection were highest among travelers to Asia (aOR, 6.2 [95% CI, 4.5–8.7]) and Latin America and Caribbean (3.5 [2.8–4.2]) compared with nontravelers (Supplementary Table 3). The incidence rate per 100 000 adult travelers was 2.2 infections (95% CI, 2.1–2.5) that had predicted resistance to any antimicrobials and 1.8 per 100 000 (1.6–2.0) with predicted first-line resistance. Incidence rates of infections resistant to first-line antimicrobials per 100 000 adults travelers (≥18 years old) ranged from 0.2 (95% CI, .1–.3) among travelers to Europe to 3.0 (.6–3.4) among travelers to Latin America and the Caribbean (Figure 1).

Resistance Mechanisms Associated With Travel

Overall, 34 resistance determinants detected in NTS isolates conferred resistance to first-line antimicrobials, varying by travel region (Table 3). Twelve resistance determinants (35%) were unique to or more frequently represented in travelers: *gyr*A(83), *gyr*A(87), *oqxA*, *oqxB*, *qepA2*, *qnrA1*, *qnr*B9, *qnrB19*, *qnrS1*, $bla_{\text{CTX-M-124}}$, *mef*(B), and *mph*(A)]. Thirteen (38%) were unique to or more frequently represented in nontravelers: *aac(6')–Ib–cr*, *gyr*B(E466D), *qnrB1, qnrB6, qnrB81, qnrD1, qnrE1,* $bla_{\text{CMY-2}}$, $bla_{\text{CMY-4}}$, $bla_{\text{CMY-54}}$, $bla_{\text{CMY-61}}$, $bla_{\text{SHV-30}}$, and *mph(B)*. There was no significant difference between travelers and nontravelers for 9 resistance determinants (26%): *qnrB2, qnrS2, qnrS13,* $bla_{\text{CTX-M-15}}$, $bla_{\text{CTX-M-55}}$, $bla_{\text{CTX-M-65}}$, $bla_{\text{SHV-12}}$, *erm(42),* and *erm(B)* (Supplementary Table 4). Among the 366 infections resistant to first-line antimicrobials reported after travel in the previous 7 days, 350 (96%) had predicted resistance to fluoroquinolones. Of these, 227 (65%) followed travel to Latin America and the Caribbean, 95 (27%) followed travel to Asia, and 28 (8%) followed travel to other or multiple regions. Of the 350 infections with ciprofloxacin resistance, 6% also had resistance determinants for azithromycin, 5% for ceftriaxone, and none for all 3 antimicrobials.

Resistant NTS Infections Attributable to Travel

Among 1220 infections with predicted resistance to first-line antimicrobials, 30% were among travelers, and 19% (95% CI, 17%–22%) were estimated to be attributable to international travel during the 7 days before illness began. Among 2073 infections with predicted resistance to any antimicrobials, 23% were among travelers and 12% (95% CI, 10%–13%) were estimated to be attributable to international travel during the 7 days before illness began.

Antimicrobial Use for NTS Infection

Among patients with data, 4609 of 7312 (63%) reported taking antimicrobials to treat the infection; 3071 of 4609 (67%) took antimicrobials recommended to treat *Salmonella*, most frequently ciprofloxacin (1663 of 4609 [36%]) (Supplementary Table 5). More patients who had traveled during the 7 days before illness began reported taking antimicrobials

recommended to treat *Salmonella* (489 of 955 [51%]) than those who had not traveled (2582 of 6357 [41%]; $P < .01$). A higher proportion of travelers with NTS infections compared with non-travelers reported taking ciprofloxacin or other fluoroquinolones (33% vs 27%; $P < .01$) (Figure 2) or azithromycin (13% vs 5%; $P < .01$). More nontravelers than travelers reported taking ceftriaxone or other third-generation cephalosporins (3% vs 2%; $P = .04$)

Overall, 308 of 3071 patients (10%) taking recommended antimicrobials had isolates with resistance determinants to those antimicrobials; for patients taking ciprofloxacin or other fluoroquinolones, 238 of 2014 (12%) had predicted resistance determinants to antimicrobials taken. More travelers than nontravelers who took recommended antimicrobials had resistance determinants to those antimicrobials (22% vs 8%; $P < .01$). Among patients who received ciprofloxacin or other fluoroquinolones, 29% of infections after travel had predicted resistance to those agents compared to 9% of infections without recent travel ($P < .01$). The proportion of those receiving azithromycin who had predicted decreased susceptibility was low, irrespective of travel status (2% vs 1%; $P = .81$), and no travelers taking third-generation cephalosporins had infections with decreased susceptibility to ceftriaxone.

DISCUSSION

Our findings demonstrate that international travel contributes substantially to antimicrobial-resistant NTS infections in the United States. Overall, international travel during the 7 days before illness began was associated with 4-fold increased odds of predicted resistance to first-line antimicrobials, with varying risks by travel region. Approximately one-fifth of NTS infections with predicted resistance to first-line antimicrobials and one-eighth of NTS infections with predicted resistance to any antimicrobials were attributable to international travel. The contribution of recent travel to antimicrobial resistance reflected the presence of several genetic resistance determinants, particularly those conferring resistance to fluoroquinolones.

Risks of acquiring a resistant NTS infection varied by travel region. Although infections after travel to Asia had the highest risk of predicted resistance to first-line antimicrobials, the highest incidence of these infections was among travelers to Latin America and the Caribbean. By contrast, the incidence of infections with predicted first-line resistance was lowest after travel to Oceania and Europe. Overall, our other observations are broadly consistent with previous studies [7, 22–24]. The incidence of resistant infection in travelers depends on the risk of any NTS infection being resistant and on the underlying risk of any NTS infection after travel [25]; within a particular region these risks might be independent. The relative incidence of resistant NTS infections by region presented in this study can provide information on the risks of a resistant infection among patients who have recently traveled. If NTS infection is suspected, a history of travel to Latin America, the Caribbean, or Asia indicates an elevated risk of resistance, particularly to ciprofloxacin.

We found that international travel was also associated with differences in antibiotic prescribing that might lead to unnecessary or ineffective treatment. Travel was associated with increased prescribing, and approximately 1 in 3 travelers with NTS infection received

ciprofloxacin or another fluoroquinolone. When first-line antibiotics were prescribed, travelers with NTS infection were more likely to have genetic resistance to those agents; 29% of those prescribed fluoroquinolones had isolates carrying genetic resistance determinants to that class of antibiotics. For patients with invasive NTS infection or other indications for antimicrobials, care should be taken to limit inappropriate use of antimicrobials, and antimicrobial susceptibility testing is particularly important to guide antimicrobial treatment. Appropriate prescribing of drugs not recommended for treatment of *Salmonella* is also important because of potential coselection of resistance to treatment drugs and possible association between virulence and resistance genes [6, 26].

The association between travel and antimicrobial resistance could be related to increased selection pressure in particular regions from treatment for human illness, or from other sources, including the use of antimicrobial classes in animals that select for resistance determinants to these agents in humans [27, 28]. We found that 13 resistance determinants (35% of all antimicrobial resistance determinants detected in these NTS isolates) conferring resistance to first-line antimicrobials were frequently detected among travelers. Surveillance of NTS using WGS can help track resistance strains [29]; improved global surveillance could help determine which resistance genes are prevalent in infections in other countries.

Consistent with the usual incubation period for NTS [30, 31], we found evidence that the strongest association between antimicrobial-resistant infection and international travel was when travel occurred during 7 days before illness began. There was also an increased association (although not significant) with travel occurring in the 8 days to 6 months preceding illness onset. Since the incubation period has a substantial “tail” beyond 7 days [30, 32], it is likely that the association with travel in the 6 months before illness began was a result of travel just outside the 7-day window, although this information was not collected. Earlier travel might also contribute to this association via changes in carriage of resistance genes [33]. Although resistance genes in NTS infection among household members might be a risk [33], we did not find this to be a risk factor for a resistant infection. This might be a result of limited person-to-person transmission of NTS infection or transmission of resistance genes independently from resistant NTS. Collecting data over a longer time frame or collecting data on travel dates within the 6 months before symptom onset might help in our understanding of risk.

Our analysis had several limitations. First, while FoodNet sites are broadly representative of the United States population [9, 34], they might be less representative for travel or resistance patterns. Second, only 61% of infections reported to FoodNet were sequenced and screened, and 13% were missing travel data and excluded from this analysis, which might introduce selection bias. Third, predicted resistance from WGS data was used instead of antimicrobial susceptibility testing data; however, a high correlation of predicted resistance with phenotypic testing has been demonstrated [35]. Fourth, our estimation of the contribution of travel to first-line resistance among NTS assumed that the odds of resistance by travel status reflected the causal contribution of travel to resistance. Fifth, our analysis was limited to symptomatic NTS infections that were identified as part of public health surveillance, and incidence of infection was limited to adults. Overall infections in the community are likely to be underestimated, since approximately 29 undiagnosed infections

have been estimated to occur for each culture-confirmed infection [4, 36]. In addition, we did not assess the potential for asymptomatic NTS carriage from imported resistance genes; asymptomatic carriage of NTS has been reported elsewhere [37, 38]. Although underdiagnosis might vary by travel status, it is unlikely to affect comparative assessments, and our findings directly inform understanding of infections leading to symptomatic illness. Finally, our analysis was restricted to a 2-year period before the COVID-19 pandemic. Data availability was limited for some travel regions, and travel patterns might be altered by the COVID-19 pandemic.

In conclusion, we found that a high proportion of resistant NTS infections in the United States are attributable to international travel, especially those with predicted resistance to first-line agents. It is important to continue to conduct surveillance for emerging imported strains using WGS, because it provides important data on pathogens with new resistance patterns, how selection differs in other countries, and how resistance determinants are spread. Identification of new genes using widely available databases such as the National Center for Biotechnology Information could inform the development of targeted interventions to limit their spread. Providers can help these efforts by obtaining stool or blood samples for patients, requesting isolation of the organism and susceptibility testing, prescribing antimicrobials only if indicated, and, for travelers, considering differences in region-specific risks of a resistant pathogen when prescribing antibiotics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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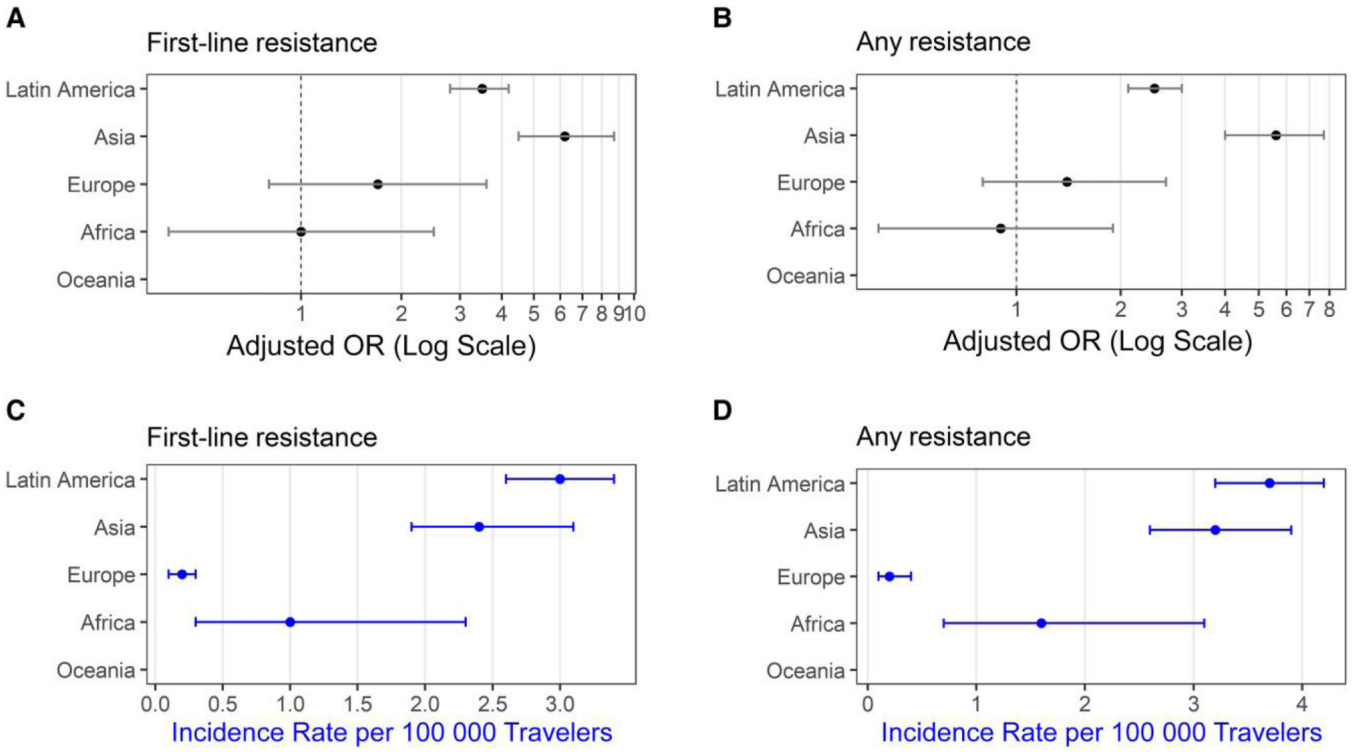

Figure 1.

Odds of resistance in nontyphoidal *Salmonella* infections in adults (*A, B*) and incidence rate per 100 000 adult travelers (*C, D*), by region of travel in the 7 days before illness began in 2018–2019. Note: Latin America includes the Caribbean and Mexico. Resistance to first-line antibiotics ("first-line resistance") is defined as the presence of a resistance gene or mutation conferring decreased susceptibility to ciprofloxacin, ceftriaxone, or azithromycin; resistance to any antibiotics ("any resistance"), as the presence of a resistance gene or mutation conferring decreased susceptibility to amikacin, gentamicin, kanamycin, streptomycin, amoxicillin–clavulanic acid, cefoxitin, ceftriaxone, sulfisoxazole, trimethoprim-sulfamethoxazole, azithromycin, ampicillin, chloramphenicol, ciprofloxacin, or tetracycline. Odds ratios (ORs) were adjusted for age, sex, and season of infection, and adjusted ORs were not calculated for first-line or any resistance after travel to Oceania, because cells contained <5 travelers.

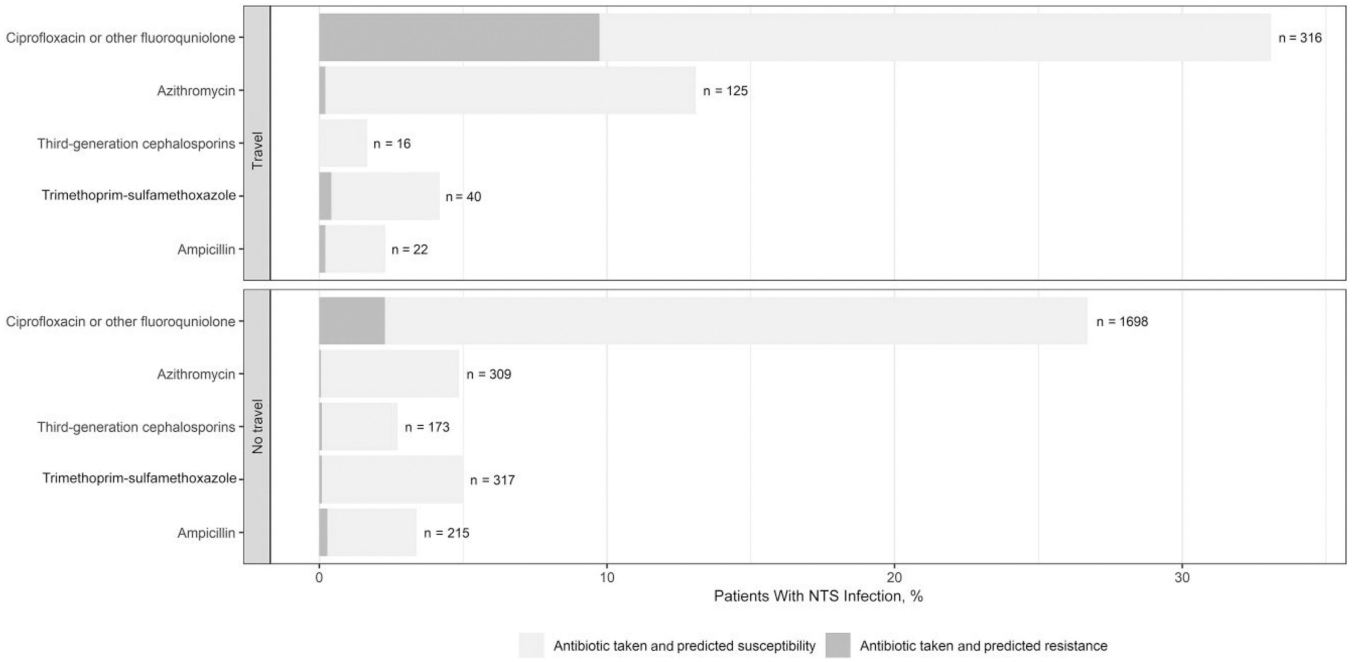

Figure 2.

Percentage of patients with nontyphoidal *Salmonella* (NTS) infection reporting taking select antimicrobials (numbers displayed at ends of bars), by predicted susceptibility and international travel within 7 days before illness began in 2018–2019. Predicted resistance to an antibiotic is defined as the presence of a resistance gene or mutation conferring decreased susceptibility to that antibiotic. Third-generation cephalosporins include ceftriaxone.

Table 1.

Demographic and Clinical Characteristics of Patients With Nontyphoidal *Salmonella* Infections Linked or Not Linked to Travel, United States, 2018–2019[a]

Characteristic	Patients, No. (%)		
	Travel in 7 d Before Illness Began (n = 1159)	No Travel in 7 d Before Illness Began (n = 8142)	Total (N = 9301)
Sex (n = 9296)[b]			
Female	648 (56)	4412 (54)	5060 (54)
Male	510 (44)	3726 (46)	4236 (46)
Age (n = 9301)			
0–4 y	122 (11)	1570 (19)	1692 (18)
5–17 y	150 (13)	984 (12)	1134 (12)
18–29 y	219 (19)	963 (12)	1182 (13)
30–44 y	244 (21)	1181 (15)	1425 (15)
45–64 y	303 (26)	1950 (24)	2253 (24)
≥65 y	121 (10)	1494 (18)	1615 (17)
Race/ethnicity (n = 8676)[b]			
White, non-Hispanic	743 (69)	5143 (68)	5886 (68)
Hispanic or Latino	152 (14)	1043 (14)	1195 (14)
Black, non-Hispanic	76 (7)	888 (12)	964 (11)
Asian, non-Hispanic	69 (6)	312 (4)	381 (4)
American Indian or Alaska Native, non-Hispanic	1 (<1)	84 (1)	85 (1)
Native Hawaiian or Other Pacific Islander, non-Hispanic	4 (<1)	15 (<1)	19 (<1)
Multiple or other races, non-Hispanic	26 (2)	120 (2)	146 (2)
Severity (n = 9275)[b]			
Not hospitalized	976 (85)	5663 (70)	6639 (72)
Hospitalized	178 (15)	2458 (30)	2636 (28)
Intensive care unit admission[c]	12 (12)	176 (12)	188 (12)
Isolate source (n = 9298)[b]			
Stool sample	1037 (90)	6703 (82)	7740 (83)
Blood sample	59 (5)	469 (6)	528 (6)
Other	62 (5)	968 (12)	1030 (11)
Resistance determinants (n = 9301)[d]			
Any resistance	477 (41)	1596 (20)	2073 (22)
First-line resistance	366 (32)	854 (10)	1220 (13)

[a] Isolates with Foodborne Diseases Active Surveillance Network (FoodNet) data were linked with whole-genome sequencing results in PulseNet, and predicted resistance was assigned as part of National Antimicrobial Resistance Monitoring System surveillance.

[b] Denominators for percentages do not include patients with missing data: 5 missing for sex, 625 for race and/or ethnicity, 26 for hospitalization, and 3 for source data.

[c] The denominator for intensive care unit admission is the number hospitalized for whom intensive care unit admission status was known.

[d] Resistance to any antibiotics ("any resistance") is defined as the presence of a resistance gene or mutation conferring decreased susceptibility to amikacin, gentamicin, kanamycin, streptomycin, amoxicillin–clavulanic acid, cefoxitin, ceftriaxone, sulfisoxazole, trimethoprim-sulfamethoxazole, azithromycin, ampicillin, chloramphenicol, ciprofloxacin, or tetracycline; resistance to first-line antibiotics ("first-line resistance"), the presence of a resistance gene or mutation conferring decreased susceptibility to ciprofloxacin, ceftriaxone, or azithromycin.

Table 2.

Characteristics of Patients With Nontyphoidal *Salmonella* Infections Associated With Resistance to First-Line Antimicrobials, United States, 2018–2019[a]

Characteristic	Patients, No. (%)		Univariable OR (95% CI)	Multivariable OR (95% CI)
	First-Line Resistance (n = 1219)	No First-Line Resistance (n = 8077)		
Age				
<5 y	158 (13)	1533 (19)	Referent	Referent
5–17 y	145 (12)	988 (12)	1.4 (1.1–1.8)	1.3 (1.0–1.7)
18–29 y	177 (15)	1005 (12)	1.7 (1.4–2.1)	1.4 (1.1–1.8)
30–44 y	217 (18)	1207 (15)	1.7 (1.4–2.2)	1.5 (1.2–1.8)
45–64 y	310 (25)	1941 (24)	1.5 (1.3–1.9)	1.4 (1.1–1.7)
≥65 y	212 (17)	1403 (17)	1.5 (1.2–1.8)	1.5 (1.2–1.9)
Sex				
Female	655 (54)	4405 (55)	Referent	Referent
Male	564 (46)	3672 (45)	1.0 (.9–1.2)	1.1 (.9–1.2)
International travel in the 7 d before illness began				
No travel	854 (70)	7284 (90)	Referent	Referent
Travel to Latin America and the Caribbean	235 (19)	513 (6)	3.9 (3.3–4.6)	3.6 (3.0–4.3)
Travel to Asia	98 (8)	116 (1)	7.2 (5.5–9.5)	7.0 (5.3–9.3)
Travel to Europe	12 (1)	51 (1)	2.0 (1.1–3.8)	2.0 (1.1–3.8)
Travel to Africa	8 (1)	54 (1)	1.3 (.6–2.7)	1.2 (.6–2.5)
Travel to North America	5 (<1)	34 (<1)	1.3 (.5–3.2)	1.3 (.5–3.3)
Travel to multiple regions	4 (<1)	18 (<1)	…[b]	…[b]
Travel to Oceania	0 (0)	6 (<1)	…[b]	…[b]
Travel to unknown region	3 (<1)	1 (<1)	…[b]	…[b]
Season				
Summer	408 (33)	3126 (39)	Referent	Referent
Fall	288 (24)	2287 (28)	1.0 (.8–1.1)	1.0 (.8–1.1)
Winter	219 (18)	1071 (13)	1.6 (1.3–1.9)	1.3 (1.1–1.6)
Spring	304 (25)	1593 (20)	1.5 (1.2–1.7)	1.3 (1.1–1.6)

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

[a] Excluding patients with missing sex (n = 5). Resistance to first-line antibiotics ("first-line resistance") is defined as the presence of a resistance gene or mutation conferring decreased susceptibility to ciprofloxacin, ceftriaxone, or azithromycin

[b] ORs were not calculated for cells including <5 patients.

Table 3.

First-line Antimicrobial Resistance Determinants Detected in Nontyphoidal *Salmonella* Isolates, by Travel Region and Status, 2018– 2019

			Isolates by Patient Travel Status, No. (%)						
			Travel Within 7 d Before Illness Began, by Region[a]						
Resistance Gene or Mutation	**Latin America and Caribbean[b] (n = 748)**	**Asia (n = 215)**	**Africa (n = 62)**	**Europe (n = 63)**	**North America (n = 39)**	**Multiple Regions[c] (n = 22)**	**Oceania (n = 6)**	**Any Travel (n = 1159)**	**No Travel (n = 8142)**
Ciprofloxacin									
*gyr*A(87)	141 (19)	51 (24)	2 (3)	4 (6)	2 (5)	2 (9)	0 (0)	203 (18)	470 (6)
*gyr*A(83)	12 (2)	25 (12)	2 (3)	6 (10)	0 (0)	0 (0)	0 (0)	45 (4)	41 (0.5)
qnrB19	54 (7)	1 (0.5)	0 (0)	1 (2)	1 (3)	1 (5)	0 (0)	60 (5)	109 (1)
qnrS1	2 (0.3)	29 (13)	3 (5)	0 (0)	0 (0)	1 (5)	0 (0)	35 (3)	25 (0.3)
qnrAI	18 (2)	1 (0.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	19 (2)	24 (0.3)
Other genes[d]	7 (1)	6 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	13 (1)	7 (0.1)
Ceftriaxone									
$bla_{\text{CTX-M-65}}$	14 (2)	1 (0.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	16 (1)	92 (1)
$bla_{\text{CMY-2}}$	3 (0.4)	1 (0.5)	0 (0)	1 (2)	2 (5)	0 (0)	0 (0)	7 (0.6)	176 (2)
$bla_{\text{SHV-12}}$	1 (0.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	6 (0.1)
Other genes[e]	1 (0.1)	1 (1)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.3)	4 (0.05)
Azithromycin									
mph(A)	22 (3)	5 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	27 (2)	47 (0.6)
Other genes[f]	1 (0.1)	2 (1)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	4 (0.3)	2 (0.02)

[a] United Nations statistical regions. Travelers to unknown regions were not included in these regions but were included in "any travel."

[b] Including Mexico.

[c] Travel to >1 region. Not included in individual regions.

[d] Includes *qnrB2* (1 traveler to Latin America and the Caribbean and 2 nontravelers), *qnrB9* (1 traveler to Asia), *qnrS2* (1 traveler to Asia and 2 nontravelers), *qnrS13* (1 traveler to Asia and 2 nontravelers), *oqxA* (3 travelers to Latin America and the Caribbean and 1 to Asia), *oqxB* (3 travelers to Latin America and the Caribbean, 1 to Asia, and 1 nontraveler), and *qepA2* (1 traveler to Asia).

[e] Includes $bla_{\text{CTX-M-15}}$ (1 traveler to Africa and 3 nontravelers), $bla_{\text{CTX–M–55}}$ (1 traveler to Asia and 1 nontraveler), and $bla_{\text{CTX-M-124}}$ (1 traveler to Latin America and the Caribbean).

[f] Includes *mef*(B) (1 traveler to Latin America and the Caribbean and 1 to Africa), *erm*(42) (1 traveler to Asia and 1 nontraveler), and *erm*(B) (1 traveler to Asia and 1 nontraveler).