Antibiotic resistant nontyphoidal *Salmonella* infection following international travel — United States, 2018–2019

Supplementary Materials

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a The Foodborne Disease Active Surveillance Network (FoodNet) conducts surveillance for nontyphoidal *Salmonella* in Connecticut, Georgia, Maryland, Minnesota, New Mexico, Oregon, Tennessee, and selected counties in California, Colorado, and New York.

Supplementary Table 1: Demographic and clinical characteristics of patients with non-typhoidal *Salmonella* infections among patients who did not travel in the 7 days before illness began, United States a, 2018–2019

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristics** | **Travel in the 6 months before illness began**  **N=404** | | **Unknown if travel in the 6 months before illness began N=1866** | **No travel in the 6 months before illness began N=5872** | **Total N=8142** |
|  |  |
| Sex (n=8138)b |  |
| Female | 204 (50%) | | 1044 (56%) | 3164 (54%) | 4412 (54%) |
| Male | 200 (50%) | | 820 (44%) | 2706 (46%) | 3726 (46%) |
| Age (n=8142) |  |
| 0–4 years | 44 (11%) | | 248 (13%) | 1278 (22%) | 1570 (19%) |
| 5–17 years | 57 (14%) | | 201 (11%) | 726 (12%) | 984 (12%) |
| 18–29 years | 60 (15%) | | 273 (15%) | 630 (11%) | 963 (12%) |
| 30–44 years | 69 (17%) | | 277 (15%) | 835 (14%) | 1181 (15%) |
| 45–64 years | 116 (29%) | | 489 (26%) | 1345 (23%) | 1950 (24%) |
| ≥65 years | 58 (14%) | | 378 (20%) | 1058 (18%) | 1494 (18%) |
| Race/ethnicity (n=7605)b |  |
| White, non-Hispanic | 229 (61%) | | 1063 (62%) | 3851 (70%) | 5143 (68%) |
| Hispanic or Latino | 69 (18%) | | 333 (19%) | 641 (12%) | 1043 (14%) |
| Black, non-Hispanic | 28 (8%) | | 167 (10%) | 693 (13%) | 888 (12%) |
| Asian, non-Hispanic | 41 (11%) | | 57 (3%) | 214 (4%) | 312 (4%) |
| AI/AN, non-Hispanic | 1 (<1%) | | 60 (4%) | 23 (<1%) | 84 (1%) |
| Native Hawaiian or Pacific Islander | 1 (<1%) | | 2 (<1%) | 12 (<1%) | 15 (<1%) |
| Multiple or other races, non-Hispanic | 4 (1%) | | 27 (2%) | 89 (2%) | 120 (2%) |
| Severity (n=8121)b |  |
| Not hospitalized | 306 (76%) | | 1280 (69%) | 4077 (70%) | 5663 (70%) |
| Hospitalized | 98 (24%) | | 576 (31%) | 1784 (30%) | 2458 (30%) |
| Intensive care unitc | 9 (13%) | | 15 (18%) | 152 (11%) | 176 (12%) |
| Source (n=8140)b |  |
| Stool | 342 (85%) | | 1464 (78%) | 4897 (83%) | 6703 (82%) |
| Blood | 26 (6%) | | 128 (7%) | 315 (5%) | 469 (6%) |
| Other | 36 (9%) | | 273 (15%) | 659 (11%) | 968 (12%) |
| Resistance determinants (n=8142) |  | |  |  |  |
| Any resistanced | 107 (26%) | | 399 (21%) | 1090 (19%) | 1596 (20%) |
| First-line resistancee | 66 (16%) | | 234 (13%) | 554 (9%) | 854 (10%) |

AI/AN: American Indian or Alaska Native

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 (NARMS) surveillance

b Percent does not include missing characteristics: 4 missing sex, 537 missing race/ethnicity, 21 missing hospitalization, and 2 missing source data.

c Denominator is number hospitalized and intensive care unit admission was not unknown.

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.

e 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

Supplementary Table 2**:** Characteristicsa among *Salmonella* infections associated with resistance to anyb antibiotics, United States, 2018–2019

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Any resistance**  **(N=2071)** | **No resistance**  **(N=7225)** | **Univariable OR (95% CI)** | **Multivariable**c **OR (95% CI)** |
| International travel in the 7 days before illness began | | | | |
| No travel | 1595 (77%) | 6543 (91%) | Ref | Ref |
| Travel | 476 (23%) | 682 (9%) | 2.9 (2.5–3.3) | 2.7 (2.4–3.1) |
| International travel region in the 7 days before illness began | |  |  |  |
| No travel | 1595 (77%) | 6543 (91%) | Ref | Ref |
| Travel to Latin America and the Caribbean | 304 (15%) | 444 (6%) | 2.8 (2.4–3.3) | 2.6 (2.2–3.1) |
| Travel to Asia | 126 (6%) | 88 (1%) | 5.9 (4.4–7.8) | 5.8 (4.4–7.6) |
| Travel to Europe | 17 (1%) | 46 (1%) | 1.5 (0.9–2.7) | 1.6 (0.9–2.8) |
| Travel to Africa | 12 (1%) | 50 (1%) | 1.0 (0.5–1.9) | 0.9 (0.5–1.8) |
| Travel to North America | 7 (<1%) | 32 (<1%) | 0.9 (0.4–2.0) | 0.9 (0.4–2.1) |
| Travel to Multiple regions | 7 (<1%) | 15 (<1%) | 1.9 (0.8–4.7) | 1.8 (0.7–4.5) |
| Travel to Oceania | 0 (0%) | 6 (<1%) | d | d |
| Travel to Unknown region | 3 (<1%) | 1 (<1%) | d | d |

Ref: referent

a Excluding patients with missing sex (n=5)

b 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.

c Each model (travel and travel region) adjusted for age, sex, and season

d Odds ratios not calculated for cells with <5

Supplementary Table 3: Incidence of resistant nontyphoidal *Salmonella* infection among travelers aged 18 years and over within seven days of travel, by travel regiona, United States, 2018–2019

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Africa  n=42 | Asia  n=153 | Europe  n=52 | Latin America and Caribbeanb  n=586 | Oceania  n=5 | Travel, all regionsc  n=886 | No Travel  N=5586 |
| **Total travelers (NTTO)** | 505,329 | 2,842,065 | 5,348,308 | 6,320,119 | 270,719 | 15,621,138 | – |
| **Ciprofloxacin resistant** |  |  |  |  |  |  |  |
| No (%) | 5 (12%) | 66 (43%) | 9 (17%) | 181 (31%) | 0 (0%) | 269 (30%) | 507 (9%) |
| Incidence per 100,000 travelers (95% CI) | 1.0 (0.3–2.3) | 2.3 (1.8–3.0) | 0.2 (0.1–0.3) | 2.9 (2.5–3.3) | 0 | 1.7 (1.5–1.9) |  |
| aORd (95% CI) | 1.2 (0.5–3.2) | **7.3 (5.2–10.3)** | **2.2 (1.1–4.6)** | **4.2 (3.5–5.2)** | – | **4.2 (3.5–5.0)** | Ref |
| **Ceftriaxone resistant** |  |  |  |  |  |
| No (%) | 0 (0%) | 2 (1%) | 0 (0%) | 15 (3%) | 0 (0%) | 20 (2%) | 215 (4%) |
| Incidence per 100,000 travelers (95% CI) | 0 | 0.1 (0.01–0.3) | 0 | 0.2 (0.1–0.4) | 0 | 0.1 (0.1–0.2) |  |
| aORd (95% CI) | – | – | – | 0.6 (0.4–1.1) | – | **0.6 (0.4–0.9)** | Ref |
| **Azithromycin resistant** |  |  |  |  |  |
| No (%) | 0 (0%) | 5 (3%) | 0 (0%) | 20 (3%) | 0 (0%) | 25 (3%) | 34 (1%) |
| Incidence per 100,000 travelers (95% CI) | 0 | 0.2 (0.1–0.4) | 0 | 0.3 (0.2–0.5) | 0 | 0.2 (0.1–0.2) |  |
| aORd (95% CI) | – | **4.9 (1.9–12.7)** | – | **5.9 (3.3–10.5)** | – | **4.6 (2.7–7.9)** | Ref |
| **First-line antibiotic resistante** |  |  |  |  |  |  |  |
| No (%) | 5 (12%) | 69 (45%) | 9 (17%) | 187 (32%) | 0 (0%) | 280 (32%) | 636 (11%) |
| Incidence per 100,000 travelers (95% CI) | 1.0 (0.3–2.3) | 2.4 (1.9–3.1) | 0.2 (0.1–0.3) | 3.0 (2.6–3.4) | 0 | 1.8 (1.6–2.0) |  |
| aORd (95% CI) | 1.0 (0.4–2.5) | **6.2 (4.5–8.7)** | 1.7 (0.8–3.6) | **3.5 (2.8–4.2)** | – | **3.5 (2.9–4.1)** | Ref |
| **Ampicillin resistant** |  |  |  |  |  |  |  |
| No (%) | 3 (7%) | 54 (35%) | 6 (12%) | 55 (9%) | 0 (0%) | 123 (14%) | 544 (10%) |
| Incidence per 100,000 travelers (95% CI) | 0.6 (0.1–1.7) | 1.9 (1.4–2.5) | 0.1 (0.04–0.2) | 0.9 (0.7–1.1) | 0 | 0.8 (0.7–0.9) |  |
| aORd (95% CI) | – | **5.0 (3.6–7.1)** | 1.3 (0.5–3.0) | 0.9 (0.7–1.3) | – | **1.5 (1.2–1.8)** | Ref |
| **Trimethoprim–sulfamethoxazole resistant** | |  |  |  |  |  |  |
| No (%) | 4 (10%) | 24 (16%) | 0 (0%) | 48 (8%) | 0 (0%) | 77 (9%) | 159 (3%) |
| Incidence per 100,000 travelers (95% CI) | 0.8 (0.2–2.0) | 0.8 (0.5–1.3) | 0 | 0.8 (0.6–1.0) | 0 | 0.5 (0.4–0.6) |  |
| aORd (95% CI) | – | **6.3 (3.8–10.4)** | – | **3.1 (2.1–4.4)** | – | **3.3 (2.4–4.4)** | Ref |
| **Any clinical resistancef** |  |  |  |  |  |  |  |
| No (%) | 8 (19%) | 90 (59%) | 13 (25%) | 234 (40%) | 0 (0%) | 358 (40%) | 1127 (20%) |
| Incidence per 100,000 travelers (95% CI) | 1.6 (0.7–3.1) | 3.2 (2.6–3.9) | 0.2 (0.1–0.4) | 3.7 (3.2–4.2) | 0 | 2.2 (2.1–2.5) |  |
| aORd (95% CI) | 0.9 (0.4–1.9) | **5.6 (4.0–7.7)** | 1.4 (0.8–2.7) | **2.5 (2.1–3.0)** | – | **2.6 (2.2–3.0)** | Ref |

a United Nations statistical region. Excluding cases with missing sex (n=3). Not showing North America, Antarctica, and multiple regions

b Including Mexico

c Also includes 4 cases with unknown travel region, 29 who traveled to North America, and 15 who traveled to multiple regions

d Adjusted odds ratio compared to non-travelers. Adjusted for age, sex, and season. Not calculated for cells with <5 travelers

e 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

f 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.

Supplementary Table 4: Resistance determinants in nontyphoidal *Salmonella* isolates, United States, 2018–2019

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Resistance gene or mutation | **All travelers**a  **(n=1159)** | **Non–travelers**  **(n=8142)** | **Chi-squared P–value** | **Odds ratio**  **(95% CI)** |
| **Quinolone resistance determinants** | | |  |  |
| *gyr*A(87) | 203 (17.5%) | 470 (5.8%) | <0.01 | 3.5 (2.9–4.1) |
| *gyr*A(83) | 45 (3.9%) | 41 (0.5%) | <0.01 | 8.0 (5.2–12.2) |
| *qnrB19* | 60 (5.2%) | 109 (1.3%) | <0.01 | 4.0 (2.9–5.5) |
| *qnrS1* | 35 (3.0%) | 25 (0.3%) | <0.01 | 10.1 (6.0–17.0) |
| *qnrA1* | 19 (1.6%) | 24 (0.3%) | <0.01 | 5.6 (3.1–10.3) |
| *oqxB* | 4 (0.4%) | 1 (0.01%) | <0.01 | 28.2 (2.8–1388.6)b |
| *qnrS13* | 1 (0.1%) | 2 (0.02%) | 0.33b | 3.5 (0.1–67.5)b |
| *qnrB2* | 1 (0.1%) | 2 (0.02%) | 0.33b | 3.5 (0.1–67.5)b |
| *qnrS2* | 1 (0.1%) | 2 (0.02%) | 0.33b | 3.5 (0.1–67.5)b |
| *oqxA* | 4 (0.4%) | 0 (0%) | <0.01 | – |
| *qepA2* | 1 (0.1%) | 0 (0%) | 0.13b | – |
| *qnrB9* | 1 (0.1%) | 0 (0%) | 0.13b | – |
| *aac (6’)–Ib–cr* | 0 (0%) | 7 (0.1%) | 1.00b | – |
| *qnrB1* | 0 (0%) | 2 (0.02%) | 1.00b | – |
| *qnrB6* | 0 (0%) | 2 (0.02%) | 1.00b | – |
| *gyr*B(E466D) | 0 (0%) | 1 (0.01%) | 1.00b | – |
| *qnrB81* | 0 (0%) | 1 (0.01%) | 1.00b | – |
| *qnrD1* | 0 (0%) | 1 (0.01%) | 1.00b | – |
| *qnrE1* | 0 (0%) | 1 (0.01%) | 1.00b | – |
| **Ceftriaxone resistance determinants** | | |  |  |
| *bla*CTX–M–65 | 16 (1.4%) | 92 (1.1%) | 0.46 | 1.2 (0.7–2.1) |
| *bla*CMY-2 | 7 (0.6%) | 176 (2.2%) | <0.01 | 0.3 (0.1–0.6) |
| *bla*SHV-12 | 1 (0.1%) | 6 (0.1%) | 0.61b | 1.2 (0.03–9.7)b |
| *bla*CTX–M–15 | 1 (0.1%) | 3 (0.04%) | 0.41b | 2.3 (0.04–29.2)b |
| *bla*CTX–M–55 | 1 (0.1%) | 1 (0.01%) | 0.23b | 7.0 (0.1–551.9)b |
| *bla*CTX–M–124 | 1 (0.1%) | 0 (0%) | 0.13b | – |
| *bla*CMY-61 | 0 (0%) | 2 (0.02%) | 1.00b | – |
| *bla*CMY-4 | 0 (0%) | 1 (0.01%) | 1.00b | – |
| *bla*CMY-54 | 0 (0%) | 1 (0.01%) | 1.00b | – |
| *bla*SHV-30 | 0 (0%) | 1 (0.01%) | 1.00b | – |
| **Azithromycin resistance determinants** | | |  |  |
| *mph*(A) | 27 (2.3%) | 47 (0.6%) | <0.01 | 4.1 (2.5–6.6) |
| *erm(42)* | 1 (0.1%) | 1 (0.01%) | 0.23b | 7.0 (0.1–551.9)b |
| *erm(B)* | 1 (0.1%) | 1 (0.01%) | 0.23b | 7.0 (0.1–551.9)b |
| *mef(B)* | 2 (0.2%) | 0 (0%) | 0.02b | – |
| *mph(B)* | 0 (0%) | 2 (0.02%) | 1.00b | – |

a Travel within seven days before illness began

b Fisher’s exact p-value and exact logistic regression

Supplementary Table 5: Expanded demographic and clinical characteristics of infections linked to travel, United States, 2018–2019

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristics** | **Travel in the 7 days before illness began**  **N=1159** | **No travel in the 7 days before illness began (n=8142)** | | | **Total**  **n=9301** |
| **Travel in the 6 months before illness began**  **n=404** | **No travel in the 6 months before illness began n=5872** | **Unknown if travel in the 6 months before illness began n=1866** |
| Season (n=9301) | | | | | | |
| Summer | 360 (31%) | 163 (40%) | 2325 (40%) | 687 (37%) | 3535 (38%) |
| Fall | 253 (22%) | 110 (27%) | 1661 (28%) | 554 (30%) | 2578 (28%) |
| Winter | 249 (21%) | 57 (14%) | 731 (12%) | 253 (14%) | 1290 (14%) |
| Spring | 297 (26%) | 74 (18%) | 1155 (20%) | 372 (20%) | 1898 (20%) |
| Diarrhea (n=9062)a |  |  |  |  |  |
| Yes | 1093 (98%) | 369 (92%) | 5439 (94%) | 1543 (89%) | 8444 (93%) |
| No | 28 (3%) | 30 (8%) | 371 (6%) | 189 (11%) | 618 (7%) |
| Bloody diarrhea (n=8781)a |  |  |  |  |  |
| Yes | 286 (26%) | 124 (32%) | 2015 (36%) | 512 (31%) | 2937 (33%) |
| No | 800 (74%) | 265 (68%) | 3656 (64%) | 1123 (69%) | 5844 (67%) |
| Fever (n=8846)a |  |  |  |  |  |
| Yes | 697 (64%) | 263 (68%) | 3652 (64%) | 984 (59%) | 5596 (63%) |
| No | 390 (36%) | 124 (32%) | 2058 (36%) | 678 (41%) | 3250 (37%) |
| Duration of illness (n=4602)a |  |  |  |  |  |
| <7 days | 197 (31%) | 104 (43%) | 1184 (34%) | 78 (34%) | 1563 (34%) |
| 7–13 days | 273 (43%) | 95 (39%) | 1608 (46%) | 101 (44%) | 2077 (45%) |
| ≥14 days | 171 (27%) | 45 (18%) | 693 (20%) | 53 (23%) | 962 (21%) |
| Took any antibiotics (n=7312)a | 625 (65%) | 251 (65%) | 3468 (62%) | 265 (71%) | 4609 (63%) |
| Antibiotic treatment (n=4609) |  |  |  |  |  |
| Ciprofloxacin | 279 (45%) | 105 (42%) | 1167 (34%) | 112 (42%) | 1663 (36%) |
| Other fluoroquinolones | 41 (7%) | 23 (9%) | 274 (8%) | 31 (12%) | 369 (8%) |
| Ceftriaxone | 16 (3%) | 8 (3%) | 144 (4%) | 9 (3%) | 177 (4%) |
| Other third generation cephalosporin | 0 (0%) | 1 (0.4%) | 13 (0.4%) | 0 (0%) | 14 (0.3%) |
| Azithromycin | 125 (20%) | 18 (7%) | 275 (8%) | 16 (6%) | 434 (9%) |
| Ampicillin | 22 (4%) | 10 (4%) | 196 (6%) | 9 (3%) | 237 (5%) |
| Penicillin | 1 (0.2%) | 0 (0%) | 10 (0.3%) | 0 (0%) | 11 (0.2%) |
| Augmentin | 4 (1%) | 5 (2%) | 53 (2%) | 6 (2%) | 68 (1%) |
| Tetracycline | 3 (0.5%) | 1 (0.4%) | 23 (1%) | 2 (1%) | 29 (1%) |
| Trimethoprim-Sulfamethoxazole | 40 (6%) | 16 (6%) | 273 (8%) | 28 (11%) | 357 (8%) |
| Pediazole | 0 (0%) | 0 (0%) | 7 (0.2%) | 0 (0%) | 7 (0.2%) |
| First generation cephalosporin | 4 (1%) | 3 (1%) | 53 (2%) | 5 (2%) | 65 (1%) |
| Second generation cephalosporin | 2 (0.3%) | 1 (0.4%) | 28 (1%) | 3 (1%) | 34 (1%) |
| Clarithromycin | 1 (0.2%) | 1 (0.4%) | 3 (0.1%) | 0 (0%) | 5 (0.1%) |
| Erythromycin | 1 (0.2%) | 1 (0.4%) | 5 (0.1%) | 0 (0%) | 7 (0.2%) |
| Dapsone | 0 (0%) | 0 (0%) | 1 (0.03%) | 0 (0%) | 1 (0.02%) |
| Metronidazole | 57 (9%) | 36 (14%) | 401 (12%) | 31 (12%) | 525 (11%) |
| Vancomycin | 0 (0%) | 0 (0%) | 1 (0.03%) | 0 (0%) | 1 (0.02%) |
| Other | 40 (6%) | 22 (9%) | 304 (9%) | 37 (14%) | 403 (9%) |
| Unknown | 90 (14%) | 50 (20%) | 827 (24%) | 27 (10%) | 994 (22%) |

a  Percent does not include missing characteristics: 239 diarrhea (bloody or not bloody) unknown; 520 bloody diarrhea unknown; 455 fever unknown; 4699 duration of illness unknown; 1989 unknown if antibiotics taken