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Travel-Associated *Salmonella* and *Campylobacter* Gastroenteritis in England: Estimation of Under-Ascertainment Through National Laboratory Surveillance

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Increased international travel raises the importance of accurate surveillance of travel-associated gastroenteric pathogens to improve treatment and the investigation of cross-border outbreaks. This study found that 45% of *Salmonella* and 17% of *Campylobacter* infections in England were travel-associated, but only 29 and 3% of travel histories were accurately identified by national laboratory surveillance. More structured data collection forms and staff training may be needed to address this.

Campylobacter and *Salmonella* species are major causes of diarrheal disease in the UK with 50,000 and 10,000 confirmed cases per year, respectively.[1] Both pathogens can lead to serious complications with associated excess morbidity and mortality,[2,3] particularly in vulnerable population groups. Increasing resistance to antibiotics[4] and chronic *Salmonella* carriage[3] are additional problems.

Accurate travel information is necessary to monitor emerging subtypes or antibiotic resistance patterns, to correctly interpret output from national laboratory exceedance reporting tools[5] (in order to direct further investigations into putative clusters) and to help identify and remove relevant exposures. It is also necessary for the surveillance and investigation of clusters in returning travelers and to distinguish these from infections acquired in the UK. Cases' travel status is currently ascertained through laboratory surveillance, but the predictive value of this information has never been estimated.

The aim of this study was to quantify the proportion of travel under-ascertainment for *Salmonella* and *Campylobacter* cases in the national laboratory surveillance system in England. In addition the proportion of foreign travel-associated salmonellosis and campylobacteriosis was estimated and characteristics of illness related to these pathogens described.

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Methods

We used data from the Coordinated Local Authority Sentinel Surveillance of Pathogens (CLASSP) study,[6] a large, active population-based surveillance system in England. Detailed standardized questionnaires were administered to all the cases of laboratory-confirmed *Campylobacter* and non-typhoidal *Salmonella* infections in sentinel areas, and 11,523 questionnaires were returned from individuals with a recent history of campylobacteriosis and 2,393 from people with a recent history of salmonellosis (about 10 and 7% of all cases in England). The information on travel from these questionnaires was almost complete and foreign travel was defined as any nights outside the UK in the 5 days before the onset of illness.

Travel information from CLASSP was compared with travel information from the national surveillance system of gastrointestinal pathogens in England and Wales, coordinated by the Health Protection Agency (HPA).[1] This information was derived from the initial laboratory request forms completed by the attending clinician. We confirmed with laboratories that subsequent information loss is negligible. Both surveillance systems do not collect denominator data, which would allow the calculation of response rates.

The extent of travel under-ascertainment was analyzed by comparing information provided on the initial laboratory request form with information obtained through patient questionnaires (gold standard). Travel information reported through the national surveillance system (based on laboratory forms) was assessed by calculating its test properties, treating this information as a "diagnostic test." The laboratory forms are

arranged so that travel information will be recorded in a text field and non-recording of travel will be interpreted as non-travel from the laboratory side. In order to estimate travel under-ascertainment, two estimates of test properties are given—one assuming random distribution and thus excluding missing data from the laboratory forms and one assuming that interpreting the missing information is more likely to represent non-travel and thus including these data as non-recorded travel. Statistical analysis was by χ^2-TESTS and Mann–Whitney rank sum tests for not-normally distributed data.

Results

Previous foreign travel was reported by 3,129 (22.5%) CLASSP study participants. A history of travel was more common among the patients with *Salmonella* (45.1%) than those with *Campylobacter* (17.8%, $p < 0.001$). Travelers were less likely infected with *S typhimurium* compared to non-travelers (11% vs 16%, $p < 0.001$) but proportions of *S enteritidis* were similar. About half of the cases were male, both among travelers and non-travelers. The median age of travelers infected with *Salmonella* (39 y) was younger than those with *Campylobacter* (47 y, $p < 0.001$), and they tended to be older than those who did not travel (35 and 46 y).

A total of 1,365 (10.4%) of CLASSP respondents were admitted to a UK hospital; those with a travel history were less commonly hospitalized compared with those without (7.1% vs 11.3%, $p < 0.0001$). Patients with *Salmonella* were more likely to be hospitalized, both among travelers (10.9% vs 5.0%, $p < 0.0001$) and non-travelers (20.3% vs 10.1%, $p < 0.0001$). This analysis excludes hospitalization overseas and is confounded by the effect of age, because patients aged under 10 and over 60 years were less likely to travel ($p < 0.0001$) and more likely to be admitted to hospital ($p < 0.0001$). The median length of hospital stay for patients with campylobacteriosis was shorter in travelers compared with non-travelers (2 vs 3 d ($p = 0.0007$), while for patients with salmonellosis there was no difference (3 d, Table 1).

Respondents spent a median of 9 days abroad, longer among patients with *Salmonella* than those with *Campylobacter* (12 vs 8 d, $p < 0.0001$). The median time between return and illness onset was 2 days. Most travelers had returned from Western Europe and North America (53.7%), Africa and the Middle East (20.8%), and South Asia (11.6%). A history of travel to Africa and the Middle East was more common among patients with *Salmonella* than those with *Campylobacter* (26.2% vs 17.9%, respectively, $p < 0.0001$), and of these *Salmonella* cases, most had returned from Turkey (25.4%), Egypt (24.8%), or Tunisia (17.1%). Patients with *Campylobacter* were more often returnees from Europe or North America (46.7% vs 57.4%, $p < 0.0001$).

Comparing foreign travel information from the national laboratory surveillance with travel information from CLASSP, laboratory form information was highly predictive for "true" travel for both pathogens (>90%, Table 2). Conversely, the proportion of travelers correctly identified through laboratory forms (sensitivity) was very low in both estimates. Including missing information as non-travel, sensitivity estimates were 45.1% (CI 43.1%–47.2%) for *Salmonella* and 3.0% (CI 2.7%–3.3%) for *Campylobacter*. Even excluding cases with missing travel information, sensitivity was estimated with 73.1% (CI 70.5%–75.7%) and 29.1% (CI 26.2%–31.9%) for *Salmonella* and *Campylobacter* cases, respectively. The difference in travel-ascertainment was significantly higher for patients with *Salmonella* compared with *Campylobacter* ($p < 0.0001$, Table 2).

Discussion

Almost one quarter of all patients with reported *Salmonella* or *Campylobacter* had a travel history, but travel histories were more common in *Salmonella* cases. Current levels of travel history under-ascertainment and misclassification within laboratory surveillance in England are very high, particularly in patients with *Campylobacter*. Missing travel information will be routinely interpreted by laboratories as non-travel; we therefore calculated two estimates. However, even excluding cases with missing data (assuming random distribution), travel ascertainment within laboratory surveillance remains low.

The burden of travel-associated gastrointestinal illness in the UK is significant. Using suggested adjustment factors[7] for underreporting, we estimate 29,053 *Salmonella* and 439,067 *Campylobacter* cases in England and Wales in 2009.[1] Including missing travel information as non-travel, a total of 13,103 *Salmonella* and 78,154 *Campylobacter* cases would have been travel-associated, with unknown travel histories in more than half (7,194) of *Salmonella* cases and more than 97% (75,809) of *Campylobacter* cases.

Pathogens causing travelers' diarrhea vary between world regions[8] and accurate travel histories provide valuable information for laboratory services to facilitate diagnosis and, allowing expanded routine testing, facilitate appropriate treatment. Travel histories are important for gastroenteric pathogen surveillance and antimicrobial resistance monitoring in the UK and overseas and may be helpful for the identification and control of an increasing number of international outbreaks or those involving western tourists.[9]

Our study benefits from the comparison of travel information from a large observational study with the national laboratory surveillance system. The CLASSP study excluded foreign day trips, however, leading to potential inaccuracies if these were deemed clinically

Table 1 Characteristics of travelers and non-travelers

	Salmonella		*Campylobacter*	
History of travel (*n*, %, and CI)				
No history of travel	1,263	52.8% (50.8%–54.8%)	9,294	80.7% (80.0%–81.4%)
Travel in 5 d before illness	1,079	45.1% (43.1%–47.1%)	2,050	17.8% (17.1%–18.5%)
Travel status unknown	51	2.1% (1.6%–2.7%)	179	1.6% (1.3%–1.8%)
Age (median and IQR)				
Travelers	39	(19–54)	47	(30–58)
Non-travelers	35	(11–54)	46	(27–62)
Sex (*n*, %, and CI)				
Male travelers	516	48.0% (45.0%–50.9%)	1,000	48.8% (46.7%–51.0%)
Male non-travelers	618	48.9% (46.2%–51.7%)	4,602	49.5% (48.5%–50.6%)
Hospital admission (*n*, %, and CI)				
Travelers	113	10.9% (9.4%–12.9%)	98	5.0% (4.0%–6.0%)
Non-travelers	249	20.3% (18.1%–22.6%)	905	10.1% (9.4%–10.7%)
Hospital days (median and IQR)				
Travelers	3	(1.25–5)	2	(1–3)
Non-travelers	3	(1–6)	3	(2–5)
Travel details (median and IQR)				
Days abroad	12	(7–15)	8	(7–14)
Days between return and illness	2	(1–5)	2	(1–4)
Region visited (*n*, %, and CI)				
Africa and Middle East	279	26.2 (23.6%–28.8%)	363	17.9% (16.2%–19.6%)
East Asia	65	6.4% (4.9%–7.8%)	79	3.9% (3.1%–4.7%)
South America	51	4.7% (3.5%–6.0%)	71	3.5% (2.7%–4.3%)
South Asia	113	10.7% (8.8%–12.5%	246	12.1% (10.7%–13.6%)
W. Europe & N. America	493	46.7% (43.7%–49.6%)	1163	57.4% (55.2%–59.5%)
E. Europe and C. Asia	54	5.0% (3.7%–6.3%)	90	4.4% (3.5%–5.3%)
Australia and Oceania	4	0.4% (0.0%–0.7%)	15	0.7% (0.4%–1.1%)

Characteristics of Salmonella and Campylobacter in the CLASSP sentinel surveillance study. Rows may exceed 100% because of dual infections. Travel is defined as spending nights outside of the UK in the 5 days prior to onset of illness. CI = 95% confidence intervals; IQR = interquartile range.

Table 2 Test properties for travel information from national surveillance

Excluding unknowns	*Salmonella* ($n = 1,119$)		*Campylobacter* ($n = 949$)	
	%	95% CI	%	95% CI
Sensitivity	73.1	70.5–75.7	29.1	(26.2–31.9)
Specificity	90.3	88.6–92.0	99.5	(99.0–99.9)
Positive predictive	91.7	90.1–93.3	93.9	(92.3–95.4)
Negative predictive	69.6	66.9–72.3	83.1	(80.8–85.5)
Unknowns as "no travel information"	*Salmonella* ($n = 2,342$)		*Campylobacter* ($n = 11,344$)	
Sensitivity	45.1	43.1–47.2	3.0	(2.7–3.3)
Specificity	96.5	95.8–97.3	100.0	(99.9–100.0)
Positive predictive value	91.7	90.6–92.8	93.9	(93.4–94.3)
Negative predictive value	67.3	65.4–69.2	82.4	(81.7–83.1)

Test properties for travel ascertainment on the laboratory form. Test properties are given for the assumption of random misclassification of missing data (ideal case, excluding all cases with missing travel information, $n = 2,068$) and for non-random misclassification of missing data (real case, cases with missing travel information are included as "travel not recorded"). Rows may exceed 100% because of dual infections. Travel is defined as spending nights outside of the UK in the 5 days prior to onset of illness. CI = 95% confidence intervals.

significant and reported through routine laboratory surveillance.

Laboratory surveillance will routinely underestimate those individuals with mild or short-duration illness, and such underestimation will increase for individuals who are ill toward the beginning of their travel period. Such effects will not impact on this study, however, as both sets of cases are identified through laboratory surveillance and are subject to the same bias.

It is possible that data entry or transcription errors led to travel information being lost despite initial recording; however, we confirmed with participating laboratories

that internal auditing and re-check procedures minimize the scope for these errors. It is therefore likely that poor initial recording drives the high proportion of travel under-ascertainment found. This could reflect a lack of clinical history taking or recording, and further studies cross-referencing our findings with the respective clinical notes could determine this. It is possible that clinicians do not perceive travel history as an essential item, particularly in mild diarrheal disease. The findings of higher ascertainment for salmonellosis could indicate that travel recording improves with disease severity, as clinicians will be unaware of the etiology at the time of recording.

The rapid growth of international travel which brings with it the potential to increase travel-associated illness means that accurate travel information is of major importance to the laboratory service and surveillance system and—naturally—to the attending clinician, especially where antimicrobial chemotherapy is indicated.[4] Travel is currently recorded in a free-text field and this may have contributed to current levels of under-ascertainment. Perhaps a more structured collection format (eg, closed questions) and improved staff awareness and training[10] may help to improve ascertainment and hence facilitate treatment and prevention of diarrheal disease.

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Declaration of Interests

The authors state that they have no conflicts of interest to declare.

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