

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	<p>(a) High rates of colonization with Extended-spectrum β-lactamase producing <i>Escherichia coli</i> in returning Canadian travellers</p> <hr/> <p>(b) The rate of rectal acquisition of ESBL-producing <i>E. coli</i> in travellers to South Asia</p>
Introduction		
Background/rationale	2	<p>Overseas travel as a risk factor for the acquisition of infections due to AMR <i>E. coli</i> including those with ESBLs</p> <p>It is conceivable that foreign travel to this country potentially play an important role in the spread of AMR, more specifically ESBLs, in Canada.</p>
Objectives	3	<p>Determine the rate of rectal acquisition of ESBL-producing <i>E. coli</i> in travellers to South Asia (i.e. risk of becoming colonized)</p> <p>Identify the different behaviours that put them at a high risk for acquiring ESBL-producing <i>E. coli</i>.</p>
Methods		
Study design	4	<p>Travellers who agreed to participate completed a detailed travel itinerary and a rectal swab specimen was collected prior to travel.</p> <p>Study participants were requested to return to the travel clinics within 7 days after their return to Canada and completed a detailed questionnaire regarding their behaviors during the visit. They also provided a second rectal swab</p>
Setting	5	<p>The study was performed from January 2012 – July 2014 at a travel clinic in Calgary, Alberta, Canada.</p>
Participants	6	<p>Potential travellers older than 18 years that were planning to visit South Asia (i.e. Afghanistan, Bangladesh, Bhutan, India, Iran, Maldives, Nepal, Pakistan, Sri Lanka) for a period of at least 5 days, were approached to participate in the study.</p>
Variables	7	<p>The rate of rectal acquisition of ESBL-producing <i>E. coli</i> in travellers to</p>

South Asia (i.e. risk of becoming colonized). Identify the different behaviours that put them at a high risk for acquiring ESBL-producing E. coli

Data sources/ measurement	8*	Information obtained included the following: main reason (s) for visiting South Asia, tour group, visiting remote/rural/urban/city areas, camping, swimming in open water/sea, using public transport, cost/types of accommodation, consumption of food/beverages; diarrhea; consumption of antibiotics and the seeking of medical care
Bias	9	All volunteers that visited the Odessy Travel clinic and travelled to South Asia were included in the study
Study size	10	No of volunteers that travelled to South Asia during the study period
Quantitative variables	11	Not applicable
Statistical methods	12	Statistical analysis was performed using Analyse-It for Excel (Leeds, UK). Univariate analysis for the acquisition of ESBL producing E. coli was done using Odds ratios with Niettinen-Nurminen 95% confidence intervals. Advanced regression was done using the Fit Model testing for Odds ratios with confidence intervals calculated by the Wald method. Exposure events were only considered significant if the confidence intervals did not cross 1. For all statistical comparisons, a p-value <0.05 was deemed to represent statistical significance.

Results

Participants	13*	<p>Overall 149 travelers were enrolled in our study between January 2012 – July 2014; 116 (78%) provided rectal swabs on their return to Canada and completed both pre- and post-travel questionnaires. The remaining 33 travelers either cancelled their travel plans (n=8) or did not provide a 2nd rectal swab on their return to Canada and/or did not complete a post-travel questionnaire (n=25). They were excluded from further analysis.</p> <p>Of the 116 travelers that provided a 2nd rectal swab on their return to Canada and completed both pre- and post-travel questionnaires, 7 (6%) were colonized with ESBL-producing E. coli prior to leaving Canada. Six of seven were colonized with E. coli producing CTX-M-15, the remaining isolate was positive for TEM-52. These patients were excluded from the analysis of travel activity associated with acquisition of ESBL producing Enterobacteriaceae.</p>
Descriptive data	14*	The mean age \pm SD of the remaining 109 travellers was 34.7 ± 19.4 ; 71 (65%) were females, 106 had post-secondary education, 89 were born within Canada, 3 lived

on a rural property/farm, 6 had a prior history of UTI within 1 year of travel, 12 had been on antibiotics in the 6 months prior to travel, 21 had contact with a health care facility in the 6 months prior to travel and 35 had pets. None had been hospitalized in the 6 months prior to enrollment in the study. The majority of people (n=90 [82%]) travelled to India, while the remaining travellers (n=19) visited Nepal (n=9), Pakistan (n=1), Bangladesh (n=1) and Sri Lanka (n=8)

Outcome data	15*	Of the 109 travelers not colonized with ESBL-producing E. coli on enrolment, 70 (64%) acquired ESBL-producing E. coli during travel
Main results	16	Travellers that visited India, consumed some meals with the local population, took antimalarial or antibiotics and used the public transit system, were likely to be colonized by ESBL producing E. coli on their return to Canada. On regression analysis, only those travellers that visited India, those that consumed meals with the local population, and took any type of antibiotic were significantly more likely to be colonized by ESBL-producing E. coli on their return to Canada, when compared to those that did not participate in such behaviours
Other analyses	17	None
Discussion		
Key results	18	Our study showed that 70 (64%) people acquired MDR ESBL-producing E. coli during travel. Interestingly, of the travellers that visited India, 66/90 (73%) were positive for ESBL-producing E. coli on their return to Calgary; mainly due to CTX-M-15 (58/66 [88%]). The behaviours that were associated with statistically significant risk of acquiring ESBL-producing E. coli, included visiting specifically India (OD 71.5 [95% CI 5.5 – 930.6]), consuming meals with the local population (OD 978.8, CI 19.9 - 56654) and the taking of any type of antibiotic during travel (OD 8.2, CI 1.1 – 63.2)
Limitations	19	The limitations of our study are as follows: 1) we only included travelers to South Asia and we might have missed other “high-risk” destinations. The reason for

choosing South Asia was that a previous Calgary study identified visiting India as a risk factor for patients with infections due to ESBL-producing E. coli. II) The majority of travelers that participated in our study visited India and this might have influenced the high rate of rectal colonization in returning travelers. However, India is an important overseas destination for Canadians because of migration patterns and vacation port of call.

Interpretation	20	Our study showed that a significant number of Canadian travellers acquired MDR ESBL-producing E. coli when visiting India. A previous Calgary study demonstrated that travel to India was associated with high risks of community infections with ESBL-producing E. coli in returning travellers (7). Therefore, Canadian primary care, emergency and infectious disease physicians should be aware that returning travellers from designations such as India, are most likely to be colonized with MDR E. coli, especially if they consumed any type of antibiotics while traveling. When such travellers present with bloodstream and urinary tract infections due to Gram negative bacteria, treatment with the cephalosporins and fluoroquinolones might not be effective.
Generalisability	21	It is important to point out that implications for the traveller, the immediate household, and the local community, are not well defined at this stage but the spread of ESBL-producing E. coli (especially those with CTX-M-15) to the local healthcare and community settings is a distinct possibility. Our results suggest that returning travelers have contributed to the emergence and spread of CTX-M-producing E. coli within Calgary.

Other information

Funding	22	This study was funded by Merck & Co., Inc. Canada (grant number RT630190) but they had no role in the planning the study or interpretation of results.
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.