

### Risk of acquisition of diarrhoeagenic *Escherichia coli* virulence genes in a cohort of healthy travellers

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#### Introduction

Incidental acquisition of genes encoding virulence factors (VFs) associated with different pathotypes can augment virulence of *E. coli* as seen during the *E. coli* O104:H4 outbreak in Germany 2011.

#### Objectives

To study the acquisition of genes encoding VFs of diarrhoeagenic *E. coli* in travellers and the association of acquisition with travel destination and travellers' diarrhoea (TD).

#### Methods

The COMBAT-study is a multicenter longitudinal cohort study, following 2,001 healthy Dutch adults travelling abroad for 1-12 weeks. Fecal samples and questionnaires were collected directly before and after travel.

From 98 randomly selected travellers, qPCR on fecal DNA was done to detect *stx1*, *stx2*, *eae*, *ehxA*, *est*, *elt*, *aggR*, *bfpA* and *invA* genes. Acquisition rates were calculated for travellers with a negative pre-travel test. TD was defined as at least one day three or more stools and any loose or liquid stool during travel. Univariable logistic regression analysis was done to investigate the association between acquisition of virulence genes and travel destination or history of travellers' diarrhoea (TD).

#### Results

The median age was 48 years (range 19-75) and 52% was female. Mean travel duration was 22 (7-72) days. Most frequently visited sub-regions were South-Eastern Asia (n=30), South America (n=13) and Eastern Africa (n=10). These distributions in the sub-sample were similar to the distributions for the entire cohort, except for destination Southern Asia, which was significantly underrepresented compared to the total population.

Nine percent (9/98) of travellers carried one or more virulence genes before travel (7 *eae*, 3 *aggR*, 2 *ehxA*, 1 *stx1*, 2 *bfpA*, 1 *est*). Thirty-four travellers acquired a total of 54 genes: 24/90 travellers at risk acquired the *eae* gene (acquisition rate 27%), 10/95 *aggR* (11%), 6/96 *ehxA* (6%), 5/97 *stx1* (5%), 3/98 *stx2* (3%), 3/97 *est* (3%), 2/98 *elt* (2%) and 1/98 *invA* (1%). Five travellers acquired a combination of *ehxA* with *stx1*, *stx2* or *eae* genes.

Acquisition of *aggR* was significantly associated with a travel destination in Northern Africa (OR 13.3; p=0.002) and Central America (OR 20.8; p=0.018). Two travellers to North Africa acquired a combination of *aggR* and *elt*. Acquisition of *aggR* combined with *stx2* or with *stx1* was not observed. Acquisition of *eae* was not associated with travel to any of the sub-regions.

Thirty-five percent of travellers (34/98) reported TD. TD was not significantly associated with acquisition of any of the genes tested.

#### Conclusion and discussion

We found high acquisition rates of *eae* and *aggR* *E. coli* virulence genes in healthy travellers. Travel to destinations in Africa poses a high risk of acquiring *aggR*. Healthy travellers visiting these regions may introduce and spread these genes upon return.