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Changes to human faecal microbiota after international travel

Christian Kampmann [a], Johan Dicksved [b], Lars Engstrand [c], Hilpi Rautelin [a,*]

[a] Clinical Microbiology, Department of Medical Sciences, Uppsala University, Uppsala, Sweden
[b] Department of Animal Nutrition and Management, Swedish University of Agricultural Sciences, Uppsala, Sweden
[c] Centre for Translational Microbiome Research, Department of Microbiology, Tumor and Cell Biology, Karolinska Institute, Stockholm, Sweden

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ABSTRACT

Background: The aim was to investigate whether travelling to less-resourced destinations influences the composition of faecal microbiota in generally healthy adults.
Method: In this prospective observational study, 47 adults (median age, 24 years; 73% females) travelled from Sweden to distant destinations for 1–12 weeks. Five faecal samples, two before and three after travel, were analysed by 16S amplicon massive parallel sequencing. Subjects had taken no antibiotics within three months of each sampling.
Results: The overall composition of faecal microbiota was not affected by travel. However, when looking at the relative abundance of individual bacterial taxa, *Enterobacteriaceae* demonstrated a 10-fold increase immediately after the trip as compared to the samples taken before travelling. Conversely, the relative abundance of *Christensenellaceae* had decreased equally much. Both these changes were reversible within nine weeks.
Conclusions: International travel, even to less-resourced countries, did not appear to alter the overall diversity of human faecal microbiota as studied here after travelling. However, *Enterobacteriaceae* bacteria, often associated with infection, inflammation, and antibiotic resistance, showed dramatically elevated levels, and *Christensenellaceae*, frequently associated with healthy conditions, demonstrated remarkably declined levels in relative abundance as detected immediately after travel. Both these changes returned to original pre-travel levels within nine weeks.

1. Introduction

In 2015, there were 1.2 billion international tourist arrivals globally [1]. Annually, up to 100 million people travel from industrialized countries to resource-limited countries in tropical and semitropical areas. Between 15 and 50% of them develop travellers' diarrhoea [2]. Every one of these travellers contains an internal ecosystem composed of tens of trillions of microbes commonly referred to as the human intestinal microbiota, which has co-evolved with humans through evolution and has a large impact on health [3–5]. Although the microbiota seems to be highly individual and mostly stable, it is significantly affected by many factors, e.g. geography [6] and diet [7]. Thus, it seems reasonable to hypothesize that the microbiota might be affected by international travel.

In a study by Youmans and co-workers [8], the composition of the microbiota in a single faecal sample, collected from travellers after returning to the USA with travellers' diarrhoea, was studied retrospectively with 16S rRNA gene-based sequencing. A high *Firmicutes*: *Bacteroidetes* ratio was detected in all symptomatic travellers, but even in asymptomatic ones. Furthermore, when the faecal microbiota results of the asymptomatic travellers were compared to those of healthy (presumably non-travelling) subjects, whose faecal samples had been collected in the Human Microbiome Project and analysed by the same laboratory, a much higher relative abundance of *Firmicutes* and a lower abundance of *Bacteroidetes* was detected in the samples of the travellers [8].

In another study [9], David and co-workers closely followed one individual who moved from urban USA to a major city in South East Asia for 51 days and showed, in contrast to the results of Youmans [8], a major shift in the faecal microbiota with decreased abundance of *Firmicutes* and increased abundance of *Bacteroidetes*. A fortnight after the subject had returned to the USA the microbiota had shifted back to more or less its original composition [9].

In three very recent studies, focusing on the acquisition of multidrug-

* Corresponding author.
E-mail addresses: christian.kampmann@medsci.uu.se (C. Kampmann), johan.dicksved@slu.se (J. Dicksved), lars.engstrand@ki.se (L. Engstrand), hilpi.rautelin@medsci.uu.se (H. Rautelin).

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resistant bacteria in distant travel destinations, no statistically significant difference in the intra-individual diversity of the faecal microbiota before and after travel could be demonstrated [10–12]. However, in two of the studies, significantly elevated abundances of Enterobacteriaceae were detected after travel [10,12].

Our present, prospective study was designed to investigate if and how international travel to distant destinations for 1–12 weeks could alter the composition of the faecal microbiota of the travellers. For that purpose, we analysed faecal samples of 47 generally healthy adults before and after they travelled from Sweden to mostly tropical destinations. We found no significant changes in the overall diversity of faecal bacterial composition as a result of travelling. However, two significant bacterial families (*Enterobacteriaceae* and *Christensenellaceae*) were dramatically and conversely affected. These changes were reversible within 9 weeks after returning home.

2. Methods

2.1. Participants and sample collection

This was a prospective, observational study in which persons who planned to travel in groups (of at least three individuals) from Sweden to distant destinations were recruited. Some results of these travellers have been published earlier [13]. In the present study, 47 generally healthy people aged 18–64 years (median, 24 years) were included. Eleven tourists attended short trips of 1–2 weeks and 36 volunteers studied and/or worked while abroad for 2–12 weeks (Table 1). The data collection took place between May 2012 and June 2014.

Five faecal samples were available for each participant. The samples were collected with a median of 12 and 2 days before, and 3, 13 and 63 days after the trip, respectively. The sets of the first three samples have been used earlier in a study investigating the composition of faecal microbiota and susceptibility to *Campylobacter* infection. All the faecal samples were cultured for *Campylobacter*, *Salmonella*, *Shigella* and *Yersinia* and analysed with *Campylobacter*-specific PCR [13]. On each sampling occasion, the participants filled in a short questionnaire including information on previous medical conditions, intake of antibiotics and other medicines, dietary habits and intestinal symptoms. None of the included 47 travellers had taken antimicrobials within three months of any sampling. Twelve became infected with *Campylobacter jejuni* and one with *Salmonella enterica* during travelling, whereas 34 remained uninfected.

Written informed consent was obtained from each participant. The regional board of the ethics committee at Uppsala University approved the study.

Table 1
Characteristics of the 47 travellers included in the study.

	Tourists (n = 11)	Volunteers (n = 36)	All (N = 47)
Age: range; median (yrs)	23-64; 28	18-36; 23	18-64; 24
Males (%)	27%	22%	23%
Travel destination (no of travellers)			
Bangladesh	0	17	17
Curaçao	5	0	5
Ecuador	0	18	18
Egypt	3	0	3
Tanzania	0	1	1
Turkey	3	0	3
Duration of travel (no of travellers)			
1 week	6	0	6
2 weeks	5	16	21
8 weeks	0	1	1
11 weeks	0	1	1
12 weeks	0	18	18
Asymptomatic (%)	45%	22%	28%
Smoker (%)	0%	8%	6%
Vegetarian (%)	0%	47%	36%
PPI (%)[a]	36%	8%	15%
BMI[b] range; median (kg/m^2)	18-28; 22	18-33; 22	18-33; 22

[a] Proton pump inhibitor user.
[b] Body Mass Index.

2.2. 16S rRNA gene analysis

Faecal samples were kept at −70 °C for subsequent DNA extraction. DNA was extracted from approximately 200 mg of faeces as described previously [13].

We prepared sequencing libraries by amplifying the V3–V4 region of the 16S rRNA gene using the 341f-805r primers, described by Hugerth et al. [14]. In order to attach Illumina adapters as well as barcodes that allow for multiplexing, a second PCR was performed after the initial amplification. The Illumina MiSeq platform was used to sequence the samples, producing 300 bp reads. Primer sequences were trimmed away. The paired-end reads produced by the sequencing instrument were merged using SEQPREP version 1.1 (https://github.com/jstjohn/SeqPrep) with default parameters. Thereafter, the merged sequences were processed with the QIIME 1.8.0 pipeline (Quantitative Insights Into Microbial Ecology) [15]. A closed reference operational taxonomic unit (OTU) strategy was used to assign sequences to OTUs. Sequences were clustered at 97% identity against the Greengenes reference database [16] by using the UCLUST [17] algorithm built into the QIIME pipeline. This produced a data set with an average of 20 527 reads per sample (range 11 306–24 869). Details on 16S rRNA gene primers, amplification conditions and sample barcodes were as published earlier [18].

2.3. Statistical analysis

Weighted UniFrac distances generated by QIIME were used to monitor changes in beta-diversity within an individual over time. In parallel, a univariate statistical approach was applied to investigate if specific taxa (at genus level) were linked to the travel. In these univariate tests, Wilcoxon tests were first used to identify taxa that differed significantly when comparing samples collected 2 days before and 3 days after the travel. Taxa that differed significantly in the Wilcoxon's test were further evaluated with a Kruskal-Wallis test that included all sampling occasions to monitor the temporal dynamics in relative abundance over time. Mann Whitney's test was used for statistical evaluation of the pairwise comparisons between groups in the Kruskal Wallis test. The statistical software PAST was used for the univariate significance testing between groups [19]. To avoid redundant univariate testing of taxa with low prevalence, only taxa present in at least 50% of the samples were included in the univariate analyses. False discovery rates (FDR) were applied to adjust for multiple univariate testing, with FDR rate of alpha = 0.05 [20].

3. Results

3.1. Influence of travelling on overall composition of faecal microbiota

We wanted to see if the composition of the faecal microbiota was altered by travelling. Using weighted UniFrac distance analysis, we showed in our previous study that there were no significant individual differences in the taxon composition of the microbiota between the two samples taken before travelling [13]. Thus, the second samples taken immediately before travelling were considered representative and used in the further analyses here. We compared these pre-travel samples with the follow-up samples taken on three different occasions after the trip. No significant differences in the overall composition of faecal microbiota were detected after the trip for the whole group of travellers. We then made the same comparisons for the groups of tourists and volunteers separately with no significant differences. Finally (Fig. 1), the comparisons were performed separately in three groups; for the

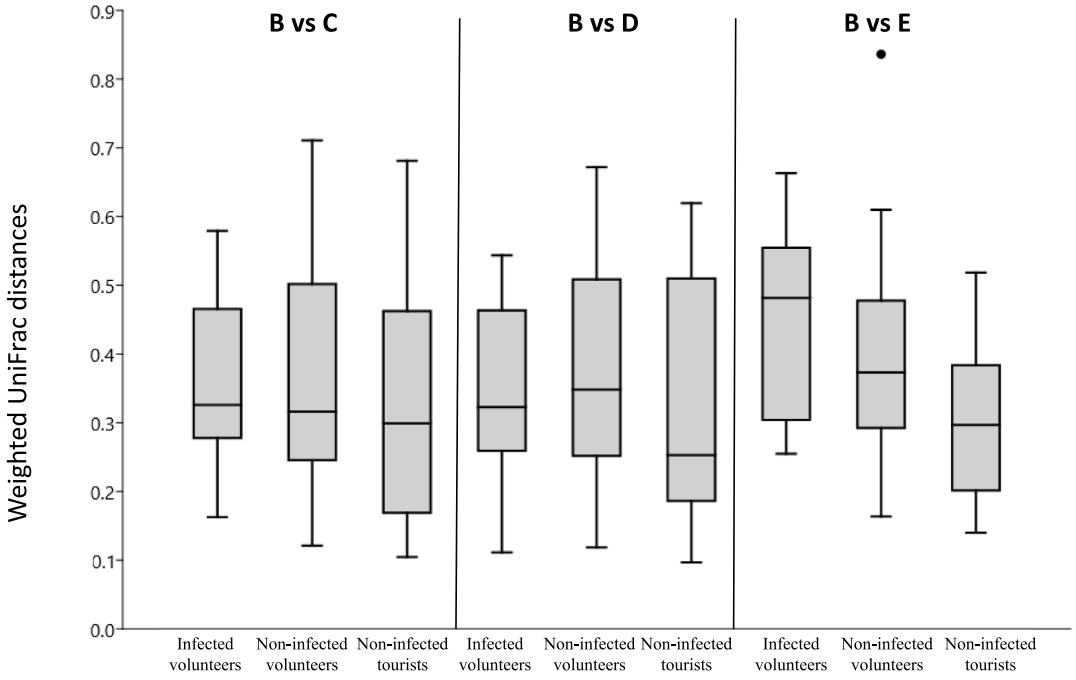

Fig. 1. Intra-individual stability of faecal microbiota composition before and after international travel.
The pre-travel sample (B) was collected a median of 2 days before travel and the post-travel samples were taken a median of 3 (C), 13 (D) and 63 (E) days after return home. Comparisons were performed by weighted UniFrac distance analysis. The results are shown separately for volunteers who became infected during travel, volunteers who remained non-infected and for the non-infected tourists (there were no infected tourists). No significant differences were detected. The horizontal line in the box plot indicates the median value and the box is drawn from 25% to 75% quartiles. Dot represents an outlier value.

volunteers who became infected during travel and the volunteers who remained non-infected as well as for the non-infected tourists (no infected tourists were available). Again, the overall composition of faecal microbiota after the trip did not significantly differ from that of the sample collected immediately before travelling in any of the groups studied.

3.2. Changes in relative abundances of bacterial taxa after travel

In order to detect post-travel changes in the relative abundances of specific bacterial taxa, samples collected before travel were compared to those taken immediately after the trip. Only two bacterial taxa differed significantly in these comparisons; *Enterobacteriaceae* (Wilcoxon's test, FDR adjusted q-value = 0.0008) and *Christensenellaceae* (Wilcoxon's test, FDR adjusted q-value = 0.042). These two taxa that had

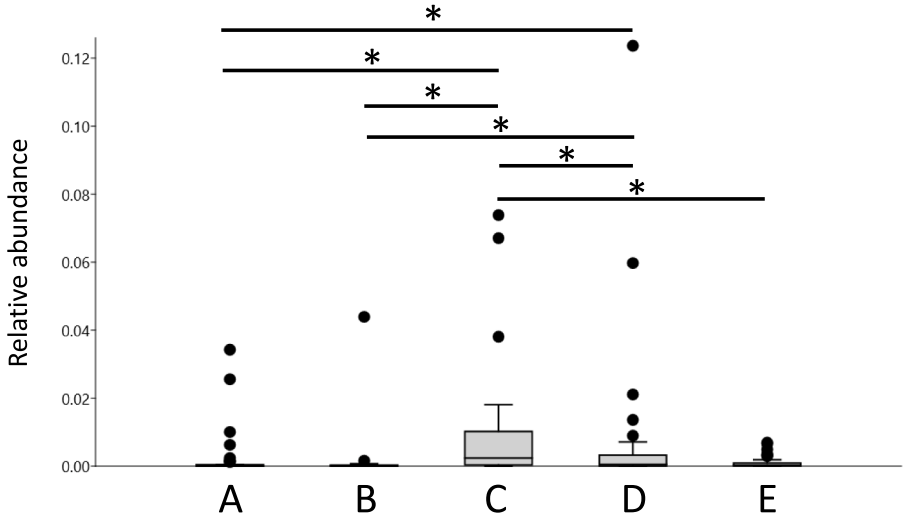

Fig. 2. Relative abundance of *Enterobacteriaceae* in faecal samples collected before and after international travel.
The pre-travel samples were collected median of 12 days (A) and 2 days (B) before travelling and the post-travel samples median of 3 days (C), 13 days (D) and 63 days (E) after return home from travel. Results are shown for the whole group of travellers. The star (*) indicates a significant difference for the comparisons in question. The horizontal line in the box plot indicates the median value and the box is drawn from 25% to 75% quartiles. Dots represent outlier values.

significantly different abundances immediately after returning home were then evaluated further with a Kruskal Wallis test to assess the temporal dynamics in abundance in all sampling occasions.

In the samples collected a median of 3 days after returning home from travelling, the relative abundance of the family *Enterobacteriaceae* was in average at more than a 10-fold higher level as compared to the sample taken just before travelling ($p = 0.000003$ for the whole group of travellers) (Fig. 2). In the second follow-up sample, collected a median of 13 days after returning from travel, the relative abundance of organisms classified as *Enterobacteriaceae* had declined significantly as compared to the first follow-up sample ($p = 0.009$) but was still significantly higher as compared to the pre-travel sample ($p = 0.002$). In the third follow-up sample, collected a median of nine weeks after return from travel, the relative abundance was more or less back to the same level as before the travel (Fig. 2).

When the individuals who became infected during travel and those who remained non-infected were analysed separately, the results were the same; high abundance of *Enterobacteriaceae* in samples collected soon after travel and abundance close to pre-travel levels in the last follow-up sample (Fig. 3). We also separately compared those non-infected individuals who reported gastrointestinal symptoms ($n = 23$) to those who were asymptomatic ($n = 11$), but the pattern was still the

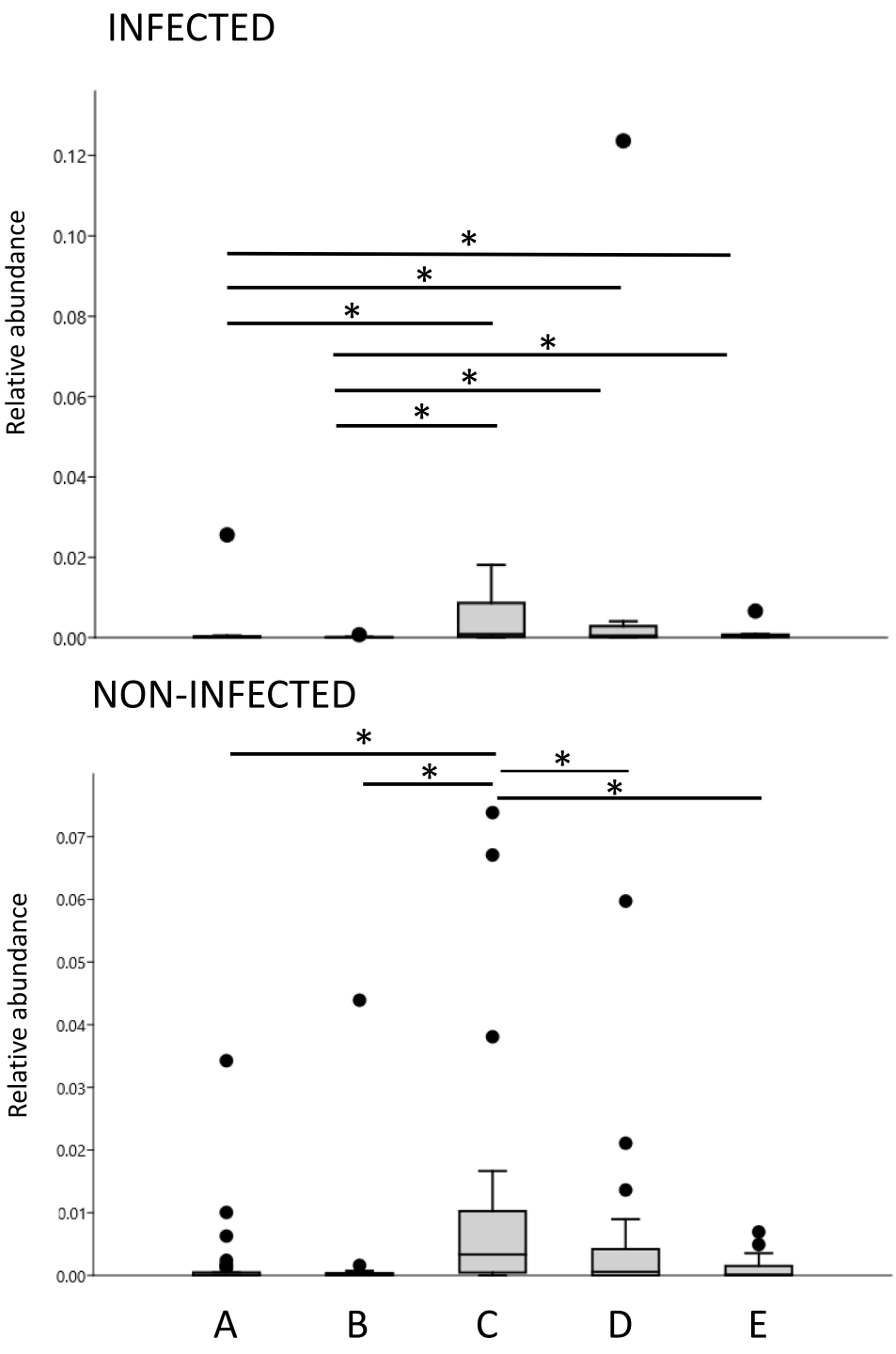

Fig. 3. Relative abundance of *Enterobacteriaceae* in faecal samples collected before and after international travel. The pre-travel samples were collected median of 12 days (A) and 2 days (B) before travelling and the post-travel samples median of 3 days (C), 13 days (D) and 63 days (E) after return home from travel. The results are shown separately for subjects who became infected during travel and those who remained non-infected. The star (*) indicates a significant difference for the comparisons in question. The horizontal line in the box plot indicates the median value and the box is drawn from 25% to 75% quartiles. Dots represent outlier values.

same (data not shown).

The family *Christensenellaceae* showed the opposite pattern with a significantly lower relative abundance in the first post-travel sample as compared to the sample collected immediately before the trip ($p = 0.008$ for all travellers, Fig. 4). The declined level of *Christensenellaceae* then increased in the next two post-travel samples and the relative abundance of *Christensenellaceae* was back to the pre-travel level in the last follow-up sample (Fig. 4). These post-travel changes were significant even when the non-infected individuals were analysed separately (data not shown). However, for those infected ($n = 13$), the results did not reach significance.

4. Discussion

Gastrointestinal disturbances, including travellers' diarrhoea, are a major concern during and after international travel [2]. Presumably, the intestinal microbiota plays an important role in these disorders [21]. Recently, we showed that the composition of pre-travel faecal microbiota was connected with the susceptibility to *Campylobacter* infection during travelling [13]. Here, we studied how international travel to less-resourced destinations changes human faecal microbiota. We could show that the overall composition of faecal microbiota was not affected by travelling but two distinct bacterial families, *Enterobacteriaceae* and *Christensenellaceae,* were reversibly but definitely altered.

Our finding that post-travel changes in microbiota diversity were not detected was true regardless of the length or the purpose of travelling as well as independent of whether enteric infection was obtained abroad or not. Accordingly, travelling to less-resourced countries did not change intestinal species richness of French tourists [10], Swiss travellers [11] or American health care workers [12], as demonstrated in some recent studies. In these particular studies, the length of travelling was up to 9 weeks, and although some of the volunteers in our study stayed abroad for 12 weeks, the results were the same. It might be that more time is needed for the diversity of the microbiota to be clearly changed. However, significant decrease in intestinal microbiota diversity was detected for immigrants within 9 months after moving from Southeast Asia to the United States [22]. Furthermore, in second-generation immigrants, the bacterial and metabolic profile of the microbiota was very similar to the native US control group, even though the diets of the two groups differed considerably [22].

The family *Enterobacteriaceae* includes several bacterial genera that are very important as human pathogens as well as members of the normal microbiota. Many of these bacteria have a high tendency to pick up and pass along genes coding for antimicrobial resistance [23,24]. *Enterobacteriaceae* bacteria are associated with inflammation in the gut and seem to reduce intestinal colonization resistance against other enteropathogens and aggravate several diseases connected with intestinal inflammation, e.g., celiac disease [25–29]. In the present study, a significant post-travel increase in the relative abundance of *Enterobacteriaceae* was demonstrated. The same phenomenon was shown in some [10,12] but not in all [11] studies. Furthermore, in one of these particular studies [10], in addition to ours, the elevated proportion of *Enterobacteriaceae* after travelling was transient and declined to pre-travel levels within weeks. In addition, in an older study, demonstrated for one traveller only, the faecal microbiota changes rapidly returned to the original level after returning home [9].

The organisms belonging to the family *Christensenellaceae*, in contrast, seem to play a beneficial role for human health. This novel bacterial family, of the order *Clostridiales*, was first named in 2012 [30]. These bacteria seem to be present from birth and not to be associated with diet [31]. Their presence has repeatedly been associated with a lean body type in humans [31–33] and faecal transplants containing these bacteria have prevented induced obesity in germ-free mice [31]. In some studies, organisms of the family *Christensenellaceae* have been negatively associated with inflammatory bowel disease [34] and positively associated with extreme longevity as showing high relative abundance and prevalence in persons 99–109 years of age [35]. We previously showed a possible beneficial effect of *Clostridiales* on colonization resistance against *Campylobacter* in highly exposed poultry abattoir-workers [26]. It remains to be studied which factors during travel might decrease the relative abundance of *Christensenellaceae*, a novel and reversible finding shown in the present study.

In the present study, significant changes in the composition of faecal microbiota could be demonstrated for *Enterobacteriaceae* and *Christensenellaceae*. It is striking how uniform the observed changes in relative abundances were. No matter if the individuals had stayed for two weeks at all-inclusive hotels in Curaçao, or if they had spent 12 weeks living with the locals in the Ecuadorian countryside or two weeks in urban

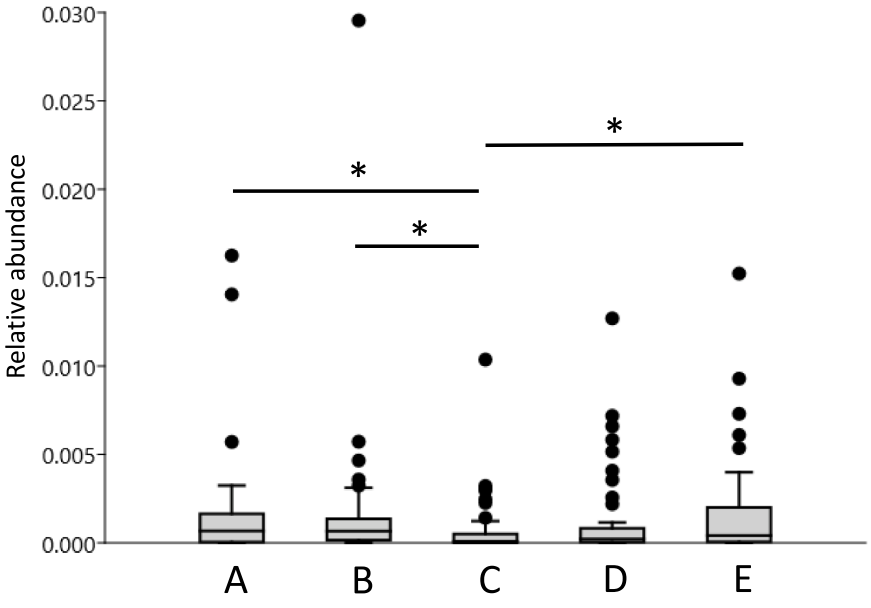

Fig. 4. Relative abundance of *Christensenellaceae* in faecal samples collected before and after travel.
The pre-travel samples were collected median of 12 days (A) and 2 days (B) before travelling and the post-travel samples median of 3 days (C), 13 days (D) and 63 days (E) after return home from travel. Results are shown for the whole group of travellers. The star (*) indicates a significant difference for the comparisons in question. The horizontal line in the box plot indicates the median value and the box is drawn from 25% to 75% quartiles. Dots represent outlier values.

Bangladesh – the pattern of changes was the same. This was also true whether or not the travellers became infected with *Campylobacter* or *Salmonella*. Our study material was also heterogeneous as far as e.g. diet and body mass index were considered (Table 1), although this might also be seen as a weakness. The prospective design and prolonged follow-up with sequential samples made it possible to detect the reversibility of the post-travel changes in the relative abundances.

What is the significance of the considerable increase in the faecal ratio of *Enterobacteriaceae/Christensenellaceae* demonstrated immediately after travelling? It is tempting to speculate that the transient changes in the faecal microbiota presented here explain intestinal discomfort often experienced by the travellers during and shortly after the trip. After all, most of the travellers in the present study were not diagnosed to be infected with enteropathogens. The high relative abundance of *Enterobacteriaceae,* as demonstrated immediately after travel but likely to be present even earlier during travelling, might actually decrease the colonization resistance to enteropathogens during travel if present early enough. Furthermore, the elevated relative abundance within the *Enterobacteriaceae* family may not only have a role in inflammation in the gut but could even increase the likelihood to acquire antimicrobial resistance genes and thus contribute to the global spread of antimicrobial resistant bacteria. It is worth noting though that the data used in this study was based on relative abundance values, thus this may not reflect if there was a difference in the actual numbers of these bacteria, which is something that should be investigated in future studies.

How could the present study results benefit everyday travel medicine? So far, studies investigating possible relationship between the human intestinal microbiota and specific disease conditions have frequently given results of low concordance [36]. However, in the present study, the question as how much the composition of human gut flora is changed during travelling could at least partly be answered. Although the overall diversity of faecal microbiota did not seem to be changed, striking alterations demonstrated in the ratio of *Enterobacteriaceae/Christensenellaceae* were seen. Furthermore, unlike in most studies on microbiota alterations, where the individual differences are typically much more pronounced than those shown on a group level, the changes demonstrated here for *Enterobacteriaceae/Christensenellaceae* were consistent in all the heterogenous groups of travellers studied. It would be interesting to see whether probiotics could be used to press down high relative abundance of *Enterobacteriaceae* and possible spread of antimicrobial resistance.

In conclusion, the data from our prospective, observational, longitudinal study help to better understand the impact of international travel on the composition of intestinal microbiota and might even contribute to the development of future strategies and probiotic products for preventing health problems connected with travelling.

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CRediT authorship contribution statement

Christian Kampmann: enrolment of participants, Investigation, Funding acquisition, Writing – original draft, approval of final draft. **Johan Dicksved:** Study design, Investigation, Formal analysis, approval of final draft. **Lars Engstrand:** Study design, approval of final draft. **Hilpi Rautelin:** Study design, Supervision, Writing – original draft, approval of final draft.

Declaration of competing interest

We declare no competing interests.

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References

[1] World Tourism Organization. UNWTO Annual Report 2015. Madrid: UNWTO; 2016.
[2] de la Cabada Bauche J, Dupont HL. New developments in traveler's diarrhea. Gastroenterol Hepatol 2011;7:88–95.
[3] Dominguez-Bello MG, Godoy-Vitorino F, Knight R, et al. Role of the microbiome in human development. Gut 2019;68:1108–14.
[4] Sommer F, Bäckhed F. The gut microbiota–masters of host development and physiology. Nat Rev Microbiol 2013;11:227–38.
[5] Lynch SV, Pedersen O. The human intestinal microbiome in health and disease. N Engl J Med 2016;375:2369–79.
[6] Yatsunenko T, Rey FE, Manary MJ, et al. Human gut microbiome viewed across age and geography. Nature 2012;486:222–7.
[7] Albenberg LG, Wu GD. Diet and the intestinal microbiome: associations, functions, and implications for health and disease. Gastroenterology 2014;146:1564–72.
[8] Youmans BP, Ajami NJ, Jiang ZD, et al. Characterization of the human gut microbiome during travelers' diarrhea. Gut Microb 2015;6:110–9.
[9] David LA, Materna AC, Friedman J, Campos-Baptista MI, Blackburn MC, Perrotta A, Erdman SE, Alm EJ. Host lifestyle affects human microbiota on daily timescales. Genome Biol 2014;15:R89.
[10] Leo S, Lazarevic V, Gaia N, et al. The intestinal microbiota predisposes to traveler's diarrhea and to the carriage of multidrug-resistant Enterobacteriaceae after traveling to tropical regions. Gut Microb 2019;10:631–41.
[11] Pires J, Kraemer JG, Kuenzli E, et al. Gut microbiota dynamics in travelers returning from India colonized with extended-spectrum cephalosporin-resistant Enterobacteriaceae: a longitudinal study. Trav Med Infect Dis 2019;27:72–80.
[12] Langelier C, Graves M, Kalantar K, et al. Microbiome and antimicrobial resistance gene dynamics in international travelers. Emerg Infect Dis 2019;25:1380–3.
[13] Kampmann C, Dicksved J, Engstrand L, et al. Composition of human faecal microbiota in resistance to Campylobacter infection. Clin Microbiol Infect 2016;22. 61.e1-e8.
[14] Hugerth LW, Wefer HA, Lundin S, et al. DegePrime, a program for degenerate primer design for broad-taxonomic-range PCR in microbial ecology studies. Appl Environ Microbiol 2014;80:5116–23.
[15] Caporaso JG, Kuczynski J, Stombaugh J, et al. QIIME allows analysis of high-throughput community sequencing data. Nat Methods 2010;7:335–6.
[16] Caporaso JG, Bittinger K, Bushman FD, et al. PyNAST: a flexible tool for aligning sequences to a template alignment. Bioinformatics 2010;26:266–7.
[17] Edgar RC. Search and clustering orders of magnitude faster than BLAST. Bioinformatics 2010;26:2460–1.
[18] Engstrand Lilja H, Wefer HA, Nyström N, et al. Intestinal dysbiosis in children with short bowel syndrome is associated with impaired outcome. Microbiome 2015;3:18.
[19] Hammer O, Harper DAT, Ryan PD. PAST: paleontological statistics software package for education and data analysis. Palaeontol Electron 2001;4:1–9.
[20] Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J Roy Stat Soc B 1995;57:289–300.
[21] Rasko DA. Changes in microbiome during and after travellers' diarrhea: what we know and what we do not. J Trav Med 2017;24:S52–6.
[22] Vangay P, Johnson AJ, Ward TL, et al. US immigration westernizes the human gut microbiome. Cell 2018;175:962–72. e10.
[23] Ruppe E, Andremont A, Armand-Lefevre L. Digestive tract colonization by multidrug-resistant Enterobacteriaceae in travellers: an update. Trav Med Infect Dis 2018;21:28–35.
[24] Bengtsson-Palme J, Angelin M, Huss M, et al. The human gut microbiome as a transporter of antibiotic resistance genes between continents. Antimicrob Agents Chemother 2015;59:6551–60.
[25] Zeng MY, Inohara N, Nunez G. Mechanisms of inflammation-driven bacterial dysbiosis in the gut. Mucosal Immunol 2017;10:18–26.
[26] Dicksved J, Ellstrom P, Engstrand L, et al. Susceptibility to Campylobacter infection is associated with the species composition of the human fecal microbiota. mBio 2014;5:e01212–4.
[27] Chander AM, Yadav H, Jain S, et al. Cross-talk between gluten, intestinal microbiota and intestinal mucosa in celiac disease: recent advances and basis of autoimmunity. Front Microbiol 2018;9:2597.
[28] Winter SE, Baumler AJ. Why related bacterial species bloom simultaneously in the gut: principles underlying the 'Like will to like' concept. Cell Microbiol 2014;16:179–84.
[29] Mirsepasi-Lauridsen HC, Vallance BA, Krogfelt KA, et al. Escherichia coli pathobionts associated with inflammatory bowel disease. Clin Microbiol Rev 2019;32. e00060-18.
[30] Morotomi M, Nagai F, Watanabe Y. Description of Christensenella minuta gen. nov., sp. nov., isolated from human faeces, which forms a distinct branch in the order Clostridiales, and proposal of Christensenellaceae fam. nov. Int J Syst Evol Microbiol 2012;62:144–9.

[31] Goodrich JK, Waters JL, Poole AC, et al. Human genetics shape the gut microbiome. Cell 2014;159:789–99.
[32] Beaumont M, Goodrich JK, Jackson MA, et al. Heritable components of the human fecal microbiome are associated with visceral fat. Genome Biol 2016;17:189.
[33] Oki K, Toyama M, Banno T, et al. Comprehensive analysis of the fecal microbiota of healthy Japanese adults reveals a new bacterial lineage associated with a phenotype characterized by a high frequency of bowel movements and a lean body type. BMC Microbiol 2016;16:284.
[34] Papa E, Docktor M, Smillie C, et al. Non-invasive mapping of the gastrointestinal microbiota identifies children with inflammatory bowel disease. PLoS One 2012;7:e39242.
[35] Biagi E, Franceschi C, Rampelli S, et al. Gut microbiota and extreme longevity. Curr Biol 2016;26:1480–5.
[36] Vujkovic-Cvijin, Sklar J, Jiang L, et al. Host variables confound gut microbiota studies of human disease. Nature 2020;587:448–54.