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1 **Risk factors for symptoms of infection and microbial carriage among French medical students**
2 **abroad**

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20 **Abstract**

21 **Objectives:** To investigate symptoms of infections and their risk factors among French medical
22 students undertaking an internship abroad.

23 **Methods:** Clinical follow up and qPCR-based respiratory, gastrointestinal, and vaginal pathogen
24 carriage were prospectively assessed pre-travel and post-travel, in a cohort of medical students
25 departing from Marseille, France.

26 **Results:** 293 students were included. 63.5%, 35.8% and 3.6% of students reported gastrointestinal,
27 respiratory, and vaginal symptoms, respectively. The acquisition rate of Enteroaggregative
28 *Escherichia coli* and Enteropathogenic *E. coli* was 40.9% and 18.6%, respectively. A significant
29 increase was observed for rhinovirus and *Streptococcus pneumoniae* by comparing the prevalence of
30 pathogens in pre-travel and post-travel samples. *Gardnerella vaginalis* and *Atopobium vaginae*
31 acquisition rates were 12.9% and 13.9%, respectively. Being female, primarily travelling to
32 Vietnam, and living in basic accommodation conditions were independent risk factors for reporting
33 respiratory symptoms. Students reporting respiratory symptoms were three times more likely to
34 acquire *S. pneumoniae*. Travelling primarily to north India and Senegal were independent risk
35 factors for diarrhoea.

36 **Conclusion:** This study makes it possible to identify the main infectious diseases linked to travel in
37 a group of French medical students undertaking an internship abroad and the risk factors on which
38 to base targeting students for reinforced pre-travel advice.

39 **Keywords:** *respiratory symptoms, travellers' diarrhoea, medical students, Streptococcus*
40 *pneumoniae, E. coli, risk factor*

41

42 **Introduction**

43 International travellers are exposed to the acquisition of potential pathogens including viruses,
44 bacteria or parasites with the risk of community or hospital spread upon return, whether or not they
45 present health problems during their trip. Therefore, there is a risk of pathogens being imported into
46 France from endemic areas abroad, either from foreign travellers visiting France, from French
47 travellers visiting foreign countries, or via migrants and expatriates treated in France with a risk of
48 indigenous spread. This has been extensively described, by example, among French Hajj pilgrims
49 travelling to Mecca, Saudi Arabia [1].

50 An Australian organisation, Work the World, has enabled 15,000 medical students to take part in
51 internships abroad since 2005 [2]. Developing countries are becoming popular destinations of
52 internship. Medical internships abroad are generally hospital immersion experiences but, young
53 medical students also participate in humanitarian missions that are unrelated to clinical activities
54 such as school renovation for example [3, 4]. In one Australian survey, 64% of students experienced
55 some sort of health problems while taking part in electives abroad, and travellers' diarrhoea was the
56 most common problem (40%) [5]. In our preliminary report on a cohort of 134 French medical
57 students participating in international electives, we showed that 73.9%, 38.8% and 5% of them
58 reported gastrointestinal, respiratory, and vaginal symptoms, respectively [4]. We showed that the
59 acquisition rate of Enteropathogenic *Escherichia coli* (EPEC) and Enteroaggregative *E. coli* (EAEC)
60 was 41% and 53%, respectively. By contrast, the acquisition of respiratory viruses was low but was
61 associated with persistent respiratory symptoms at return. Respiratory bacterial acquisition ranged
62 from 3.3% for *Streptococcus pyogenes* to 15.0% for *Haemophilus influenzae*. *Atopobium vaginae*
63 and *Gardnerella vaginalis* percentage of acquisition were 14.3% and 7.7%, respectively. So far, to
64 our knowledge, the risk factors for acquisition of pathogens have not been clearly identified among
65 medical students abroad to date. The relationship between symptoms and the carriage of pathogens

66 also remain poorly understood, making it difficult to distinguish between infection and colonisation.
67 We aim to conduct this study to investigate the risk factors for symptoms of infections among
68 French medical students undertaking an internship abroad.

69

70 **Materials and methods**

71 *Study design*

72 A monocentric prospective cohort survey was conducted over two years (2018–2019) among
73 medical students from the Faculty of Medicine in Marseille, France who were planning to take part
74 in an internship abroad during the summer. Recruitment was performed on a voluntary basis, during
75 their vaccination and pre-travel consultation at the Institut Méditerranée Infection which is on the
76 Marseille University medical campus. Participants were asked to complete an inclusion
77 questionnaire including demographic data, history of chronic illness, intended travel dates and
78 destination. All participants received advice regarding the prevention of diarrhoea during travel
79 (hand hygiene, safe food, and water habits) but prophylaxis for traveller's diarrhoea was not
80 prescribed. Because dates of departure and return are different for each student, the samples were
81 not taken at once. The participants were given two sets of "pre-travel" and "post-travel" kits which
82 contained questionnaire and sampling equipment (commercial rigid cotton-tipped swab applicators
83 and viral transport media). They were also instructed how to self-collect samples, as following: 3 cm
84 in the nostril, 5 turns and post wall of the pharynx, 5 streaks for respiratory samples; rectal samples
85 were collected using two methods: rectal self-sampling when having a bowel movement, 3
86 centimetres through the anus, gently rubbing the inner walls of the rectum several times or stool
87 collection after emission; vaginal samples were collected by placing the swab about three
88 centimetres in the vagina and gently rubbing the inner walls several times, avoid touching the skin

89 and vulva with the swab. Samples were self-collected using commercial rigid cotton-tipped swab
90 applicators (Medical Wire & Equipment, Wiltshire, UK) and placed in viral transport media (Sigma
91 Virocul®) for further process at our laboratory. A document of instructions for self-sampling was
92 also provided in the kits. During the week before travel, each student was invited to deposit their
93 self-collect samples and a pre-travel questionnaire that collected information about their health
94 problems and antibiotic use if applicable. After their travel, they were invited to self-collect samples
95 during the week following their return to France. Students were also provided with a post-travel
96 questionnaire addressing the exact place of the internship, the type of activities during their stay,
97 including tourism and travel to other countries over the internship period. Accommodation
98 conditions, contact with animals or children, symptoms, onset of symptoms and treatment during
99 their stay were also documented. Influenza-like illness (ILI) was defined as sore throat, cough plus
100 subjective fever [6]. Diarrhoea was defined by at least three loose or liquid stools per 24 hours.

101 ***Microbiological methods***

102 The methods for identifying respiratory, gastro-intestinal, and vaginal pathogens by PCR assay are
103 detailed elsewhere [4]. The followed respiratory pathogens were screened: Influenza A and B
104 viruses, Human coronaviruses, Human parainfluenza viruses, Human rhinovirus, Human
105 metapneumovirus, Adenovirus, Respiratory syncytial virus, *Staphylococcus aureus*, *H. influenzae*,
106 *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, and *S. pyogenes*. The following gastro-intestinal
107 pathogens were screened for: Norovirus, Rotavirus, Adenovirus, Astrovirus, *Entamoeba histolytica*,
108 *Giardia lamblia*, *Cryptosporidium* spp, *Salmonella* spp, *Shigella* spp (EIEC), Enterohemorrhagic *E.*
109 *coli* (EHEC), Enteropathogenic *E. coli* (EPEC), Enteroaggregative *E. coli* (EAEC), *Campylobacter*
110 *jejuni* and *Tropheryma whipplei*. The following vaginal pathogens were screened for: *Chlamydia*
111 *trachomatis*, *Mycoplasma genitalium*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, *Mycoplasma*
112 *hominis*, *A. vaginae* and *G. vaginalis*.

113 PCR were considered positive for virus or bacteria detection when the cycle threshold (CT) value
114 was ≤ 35 . Bacterial vaginosis was defined by a *G. vaginalis* DNA load $\geq 10^9$ copies/mL (CT ≤ 18)
115 and/or an *A. vaginae* DNA load $\geq 10^8$ copies/mL (CT ≤ 21), as previously reported [7].

116 The acquisition of a pathogen was defined as negative before travel and positive when returning to
117 Marseille, France.

118 ***Statistical analysis***

119 STATA software version 14.2 was used to conduct statistical analysis. Differences in the
120 proportions were tested by using Fisher's exact or Pearson's chi-square tests, when appropriate.
121 McNemar's test was used to evaluate the potential acquisition of pathogens (prevalence after versus
122 before travel). Clinical symptoms during travel were reported only if onset of symptoms took place
123 during travel. Univariate analysis was used to evaluate unadjusted associations between the
124 prevalence of symptoms during travel and multiple factors. A p-value < 0.05 was considered to be
125 statistically significant. Only variables with a prevalence equal or more than 5.0% were considered
126 for statistical analysis. Variables with p-values < 0.2 in the univariate analysis were included in the
127 multivariate analysis. Log-binomial regression was used to estimate factors' adjusted risk ratios for
128 symptoms of infections.

129

130 **Ethics**

131 The protocol was approved by our Institutional Review Board (2019-006). It was performed in
132 accordance with the good clinical practices recommended by the Declaration of Helsinki and its
133 amendments. All participants gave their written informed consent.

134

135 **Results**

136 ***Characteristics of study participants***

137 A total of 293 students agreed to participate and answered the post-travel questionnaire. The M/F
138 gender ratio was 0.31 with a median age of 21 years (ranging from 18 to 25 years). Most
139 participants (80.9%) were students in their second year of medical studies and were taking part in a
140 non-medical humanitarian mission. The remaining participants were in their 4th year of study and
141 were assigned to different departments of medicine or surgery for clinical training (Supplementary
142 Table S1).

143 The primary travel destinations for internships were in Africa (29.0%), South East Asia (27.7%),
144 South America (21.8%) and South Asia (18.8%). The top five primary destination countries were
145 Vietnam (24.2%), India (18.8%), Peru (16.4%), Tanzania (10.2%) and Madagascar (9.2%). The
146 mean travel duration was 41 days \pm 11.1 days (ranging from 16 to 78 days). Accommodation
147 conditions were judged as being “very clean” by 14.7% (43/293) of students, “clean” by 44%
148 (129/293) and “very basic” by 41.3% (121/293). 42.7% and 79.9% of the participants reported
149 contact with animals and local children, respectively (Supplementary Table S2). During their stays,
150 94.2% also travelled as tourists in the country of primary destination and 50 (17.1%) visited other
151 countries. The top five additional destination countries were Laos (4.8%), Cambodia (4.4%), Bolivia
152 (3.4%), Thailand (1.7%) and Argentina (1.7%).

153 A total of 55/293 (18.8%) were vaccinated against influenza and only 2/293 (0.7%) against invasive
154 pneumococcal infections at inclusion. In addition, 260/293 (88.7%) and 273/ 293 (93.2%) student
155 were vaccinated against hepatitis A and hepatitis B before travel, respectively.

156 Overall, 5.1% took antibiotics in the week before departure and 17.8% took doxycycline as a
157 chemoprophylaxis against malaria during their stay.

158 ***Respiratory infections***

159 A total of 35.8% (105/293) students reported respiratory symptoms during travel. The median time
160 between arrival at the travel destination and the onset of symptoms was 17 days [ranging from 1 to
161 58 days]. The most frequent respiratory symptoms were rhinitis (27.1%), sore throat (21.8%) and
162 cough (20.1%), followed by fever (9.6%) and dyspnoea (6.5%) (Figure 1a). 7.9% of students
163 declared persistence of symptoms on their return to France and 5.5% took antibiotics (ATB) for
164 respiratory symptoms during travel.

165 A total of 275 (93.9%) students provided paired nasopharyngeal swabs. 52.4% of students acquired
166 at least one respiratory pathogen. 17.8% of (49/275) students acquired at least one respiratory virus
167 with human rhinovirus (14.6%) being the most frequent. Twenty-three students were still
168 symptomatic after returning to France. Of whom, 16 (69.6%) were positive for at least one
169 pathogens. Bacterial acquisition rates were higher (40.7%), with *S. aureus* (18.9%) being the most
170 frequent, followed by *H. influenza* (17.1%) (Table 1). A total of 6.2% students acquired a virus-
171 bacteria combination and 11.6% a bacteria combination. When comparing the post- versus pre-
172 travel prevalence of pathogens, a significant increase was observed for rhinovirus and *S.*
173 *pneumoniae*.

174 ***Gastro-intestinal infections***

175 A proportion of 63.5% of students reported at least one gastro-intestinal symptom, all during travel
176 and only one following return. The median time between arrival at the travel destination and the
177 onset of symptoms was 13 days [ranging from 1 to 65 days]. The most frequent symptoms were
178 diarrhoea (48.1%) and abdominal pain (46.4%), followed by nausea (26.3%) and constipation
179 (19.8%) (Figure 1b). 8.9% reported persistent symptoms on return to France and 3.4% took an
180 antibiotic for diarrhoea during their stay.

181 A total of 274 (93.5%) students provided paired rectal swabs. Three students reported
182 gastrointestinal symptoms at day 1 after departure. But all rectal samples pre-travel were negative
183 for gastrointestinal pathogens. 51.5% students acquired at least one gastrointestinal pathogen. Nine
184 students (3.3%) acquired at least one virus (adenovirus, astrovirus and norovirus). Bacterial
185 acquisition rates were higher (49.3%), notably for EAEC (40.9%) and EPEC (18.6%). Additionally,
186 2.6% of individuals acquired *Shigella* spp/EIEC, 1.5% *Salmonella* spp and 1.1% *G. lamblia* (Table
187 2). When comparing the post- versus pre-travel prevalence of pathogens, a significant increase was
188 observed for viruses overall, EAEC, EPEC, *Salmonella* spp and *Shigella* spp/EIEC.

189 ***Vaginal infections***

190 Of the 224 female students, eight (3.6%) reported vaginal symptoms such as leucorrhoea, during
191 their stay, and two took antibiotics for this purpose. The median time between arrival at the travel
192 destination and the onset of symptoms was 26 days [ranging from 6 to 59 days]. Three students
193 (1.3%) were still symptomatic on returning to France.

194 209 (93.3%) of the participants provided paired vaginal samples. 15.8% of the participants acquired
195 at least one vaginal microorganism with the highest acquisition rate for *A. vaginae* (13.9%) and *G.*
196 *vaginalis* (12.9%) (Table 3). Nine students (4.0%) had molecular criteria for bacterial vaginosis on
197 return. When comparing the post- versus pre-travel prevalence of microorganisms, a significant
198 increase was observed for *G. vaginalis* (CT<18), indicative of vaginosis.

199 ***Risk factors for symptoms of infections***

200 Being female, primarily travelling to Vietnam, and living in basic accommodation conditions were
201 independent risk factors for reporting respiratory symptoms. Students suffering respiratory
202 symptoms were 3 times more likely to acquire *S. pneumoniae* during travel. Travelling primarily to
203 north India and Senegal were independent risk factors for reporting diarrhoea (Table 4).

204

205 **Discussion**

206 Most students in our study travelled to low-income tropical countries for about two months and
207 participated in humanitarian missions in relatively basic conditions of housing and in close contact
208 with local children and animals. Two-thirds of students reported gastrointestinal symptoms (notably
209 diarrhoea, abdominal pain and nausea-vomiting which are suggestive of gastroenteritis) and one-
210 third of students reported respiratory symptoms (notably rhinitis, a sore throat and a cough which
211 are suggestive of an upper respiratory tract infection). These symptoms appeared within 2 weeks of
212 their arrival at destination of their internship. Moreover, we observed a low proportion of travel-
213 associated vaginal symptoms. Overall, symptoms were relatively mild with fewer than 5% students
214 requiring antibiotics and most symptoms resolved before students came back to France. This result
215 is consistent with other studies realized on medical students abroad, confirming the fact that despite
216 reinforced pre-travel counselling, travel-associated respiratory infections and travellers' diarrhoea
217 were very frequent among medical students who were fully aware of the ways to prevent these
218 illnesses [5, 8-10].

219 We found a significant acquisition of human rhinovirus and *S. pneumoniae* as reported previously
220 among international travel as well as among Hajj pilgrims [1, 11, 12]. We also observed a high
221 acquisition rate of EAEC (40.9%) and EPEC (18.6%) among health students, as documented in
222 other studies realized in different populations of domestic and international travellers [13-18].

223 Our results showed that respiratory symptoms were significantly more frequent in female. We have
224 no explanation for this observation. Interestingly, the travel destination was distinctly associated
225 with symptoms. Travel to India and Senegal was a risk factor for diarrhoea while travel to Vietnam
226 was a risk factor for respiratory symptoms. Our results are discordant with those of a previous study

227 on 649 international travellers showing that respiratory infections (sore throat or cough) were
228 significantly increased in travellers returning from the non-tropical regions (7.6%) than those from
229 tropical regions, including Vietnam (2.0%) [19]. Differences by travel destination are also known to
230 be relative to the incidence of travellers' diarrhoea. This result was in line with most other studies
231 that have also found that travelling to the Indian subcontinent was a highest relative risk for
232 diarrhoea, followed by African regions [16, 20-23].

233 In addition, the observed correlation between respiratory symptoms and very basic accommodation
234 conditions suggests that precarious housing conditions may encourage respiratory infections. A
235 significant association between the acquisition of *S. pneumoniae* and respiratory symptoms was also
236 observed in cohorts of Hajj pilgrims [24].

237 We observed no significant association between *E. coli* acquisition and diarrhoea in our study, in
238 contrast to other studies where EAEC or EPEC have been reported to be more frequent in travellers
239 with diarrhoea returning from several geographical areas [14, 16, 25]. This may be explained by the
240 onset of gastro-intestinal symptoms occurring early during the trip, while sampling was performed
241 on return, several weeks later. Furthermore, asymptomatic carriage of potential pathogens was also
242 observed in participants. In a study by Adachi *et al.*, EAEC was detected in the stools of 26% of
243 patients with traveller's diarrhoea returning from Mexico, Jamaica, or India [26]. On the other hand,
244 a recent case-controlled study conducted on German and Dutch travellers showed that EAEC
245 detection was not significantly different in diarrheal persons and asymptomatic controls. However,
246 the prevalence of this bacterium among participants suffering from diarrhoea during international
247 travel was high (40.0%) [14]. Such results are in line with ours.

248 Our study has a few limitations. First, this study was monocentric and conducted on a very specific
249 population of travellers which impairs generalisation of our findings. Also, qPCR does not

250 differentiate between dead and viable microorganisms. Finally, sampling was realized during the
251 week preceding departure and during the week following return, samples at onset of symptoms were
252 not available. Among students who reported clinical symptoms early after their arrival abroad, we
253 are not sure whether these students were infected before or after departure, since incubation times of
254 diseases are very different and may vary (Supplementary table S3). Likewise, post-travel samples
255 were collected at a significant time after the onset of symptoms during travel and responsible
256 pathogens may have been partly cleared.

257 This study makes it possible to identify the main infectious diseases linked to travel in a group of
258 French medical students undertaking an internship abroad and risk factors upon which to base
259 targeting students for reinforced pre-travel advice. Sampling at the time of the onset of symptoms
260 should be carried out in future studies to better understand the relationship between the carriage of
261 pathogens and symptoms.

262

263 **Transparency declaration**

264 The authors declare that there are no conflicts of interest.

265

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270

271 **Reference**

- 272 [1] Hoang VT, Gautret P. Infectious Diseases and Mass Gatherings. *Curr Infect Dis Rep.* 2018;
273 20:44.
- 274 [2] Work the World. Healthcare placements in Africa, Asia and Latin America. Available at:
275 <https://www.worktheworld.com.au/> (Accessed December 11th, 2019)
- 276 [3] Watson DA, et al. Healthy, safe and effective international medical student electives: a
277 systematic review and recommendations for program coordinators. *Trop Dis Travel Med*
278 *Vaccines.* 2019; 5: 4.
- 279 [4] Dao TL, et al. Infectious disease symptoms and microbial carriage among French medical
280 students travelling abroad: A prospective study. *Travel Med Infect Dis.*
281 <https://doi.org/10.1016/j.tmaid.2019.101548>.
- 282 [5] Goldsmid JM, et al. A preliminary study on travel health issues of medical students undertaking
283 electives. *J Travel Med.* 2003;10:160-3.
- 284 [6] Rashid H, et al. Influenza and the Hajj: defining influenza-like illness clinically. *Int J Infect Dis.*
285 2008;12:102–3.
- 286 [7] Menard JP, et al . Molecular quantification of *Gardnerella vaginalis* and *Atopobium vaginae*
287 loads to predict bacterial vaginosis. *Clin Infect Dis.* 2008;47:33-43.
- 288 [8]. Meltzer E, et al. Acute Diarrhea in North American Students after Relocation to Israel: A Pilot
289 Study. *Isr Med Assoc J.* 2019;21(8):538-41.
- 290 [9] Sharafeldin E, et al. Health risks encountered by Dutch medical students during an elective in the
291 tropics and the quality and comprehensiveness of pre-and post-travel care. *BMC Med Educ.*
292 2010;10:89.

- 293 [10] Angelin M, et al. Risk factors for colonization with extended-spectrum beta-lactamase
294 producing *Enterobacteriaceae* in healthcare students on clinical assignment abroad: A
295 prospective study. *Travel Med Infect Dis.* 2015;13:223-9.
- 296 [11] Jennings LC, et al. Respiratory viruses in airline travellers with influenza symptoms: Results of
297 an airport screening study. *J Clin Virol.* 2015; 67:8-13.
- 298 [12] Gautret P, et al. The spectrum of respiratory pathogens among returning Hajj pilgrims: myths
299 and reality. *Int J Infect Dis.* 2016; 47:83-5.
- 300 [13] Brehm TT, et al. Risk Factors for Different Intestinal Pathogens among Patients with Traveler's
301 Diarrhea: A Retrospective Analysis at a German Travel Clinic (2009-2017). *Travel Med Infect*
302 *Dis.* 2020. <https://doi.org/10.1016/j.tmaid.2020.101706>.
- 303 [14] Schaumburg F, et al. Aetiology of traveller's diarrhea: A nested case-control study. *Travel Med*
304 *Infect Dis.* 2010. <https://doi.org/10.1016/j.tmaid.2020.101696>.
- 305 [15] van Hattem JM, et al. Risk of acquisition of human diarrhoeagenic *Escherichia coli* virulence
306 genes in intercontinental travellers: A prospective, multi-centre study. *Travel Med Infect Dis.*
307 2019. <https://doi.org/10.1016/j.tmaid.2018.12.005>.
- 308 [16] Paschke C, et al. Controlled study on enteropathogens in travellers returning from the tropics
309 with and without diarrhoea. *Clin Microbiol Infect.* 2011; 17:1194–200.
- 310 [17] Paredes-Paredes M, et al. Seasonality of diarrheagenic *Escherichia coli* pathotypes in the US
311 students acquiring diarrhea in Mexico. *J Travel Med.* 2011; 18:121-5.
- 312 [18] Sow D, et al. Acquisition of enteric pathogens by pilgrims during the 2016 Hajj pilgrimage: A
313 prospective cohort study. *Travel Med Infect Dis.* 2018;25:26-30.
- 314 [19] Pai HH, Lai JL. Health problems among international travellers: from a subtropical region to
315 tropical and non-tropical regions. *Travel Med Infect Dis.* 2008; 6(4):201-4.

- 316 [20] Zamarrón Fuertes P, et al. Clinical and epidemiological characteristics of imported infectious
317 diseases in Spanish travelers. *J Travel Med.* 2010; 17(5):303-9.
- 318 [21] Belderok SM, et al. Incidence, risk factors and treatment of diarrhoea among Dutch travellers:
319 reasons not to routinely prescribe antibiotics. *BMC Infect Dis.* 2011; 11:295.
- 320 [22] Hill DR, Beeching NJ. Travelers' diarrhea. *Curr Opin Infect Dis.* 2010; 23(5):481-7.
- 321 [23] Rack J, et al. Risk and Spectrum of Diseases in Travelers to Popular Tourist Destinations.*J*
322 *Travel Med* , 2005;12(5):248-53.
- 323 [24] Hoang VT, et al. Respiratory tract infections among French Hajj pilgrims from 2014 to 2017.
324 *Sci Rep.* 2019; 9(1):17771.
- 325 [25] Lääveri T, et al. Prospective study of pathogens in asymptomatic travellers and those with
326 diarrhoea: aetiological agents revisited. *Clin Microbiol Infect.* 2016; 22(6):535-41
- 327 [26] Adachi JA, et al. Enteroaggregative *Escherichia coli* as a major etiologic agent in traveler's
328 diarrhea in 3 regions of the world. *Clin Infect Dis* 2001; 32:1706–9.

Table 1: Prevalence of respiratory pathogens

Variables	Pre-travel		Post-travel		Acquisition		p*
	n = 275 ¹	%	n = 279 ²	%	n =275 ³	%	
Viruses							
Adenovirus	1	0.4	0	0	0	0	NA
Coronaviruses	1	0.4	6	2.2	6	2.2	0.06
Coronavirus HKU1	0	0	3	1.1	3	1.1	0.08
Coronavirus 229E	0	0	2	0.7	2	0.7	0.16
Coronavirus NL63	1	0.4	1	0.4	1	0.4	1.0
Coronavirus OC43	0	0	0	0	0	0	NA
Influenza A	0	0	1	0.4	1	0.4	0.32
Influenza B	0	0	2	0.7	2	0.7	0.16
Metapneumovirus	0	0	0	0	0	0	NA
Parainfluenza virus	0	0	0	0	0	0	NA
Respiratory syncytial virus	1	0.4	2	0.7	2	0.7	0.56
Rhinovirus	25	9.1	44	15.8	40	14.6	0.015
At least one virus	26	9.5	54	19.6	49	17.8	0.001
Bacteria							
<i>Haemophilus influenzae</i>	122	44.4	119	42.7	47	17.1	0.76
<i>Klebsiella pneumoniae</i>	23	8.4	28	10.0	19	6.9	0.38
<i>Staphylococcus aureus</i>	63	22.9	83	29.8	52	18.9	0.052
<i>Streptococcus pneumoniae</i>	5	1.8	15	5.4	15	5.5	0.025
<i>Streptococcus pyogenes</i>	3	1.1	8	2.9	7	2.6	0.096
At least one bacteria	161	58.6	180	64.5	112	40.7	0.11
Virus and bacteria combination							
H. <i>influenzae</i> -rhinovirus	9	3.3	13	4.7	4	1.5	0.37
K. <i>pneumoniae</i> -rhinovirus	1	0.4	1	0.4	0	0	NA

<i>S. pneumoniae</i> -rhinovirus	0	0	1	0.4	1	0.4	0.32
<i>S. aureus</i> -rhinovirus	6	2.2	12	4.3	8	2.9	0.16
Bacteria combination of two bacteria	61	22.2	87	31.2	32	11.6	<0.000
<i>H. influenzae</i> - <i>K. pneumoniae</i>	12	4.4	15	5.4	3	1.1	0.49
<i>H. influenzae</i> - <i>S. pneumoniae</i>	4	1.5	11	3.9	5	1.8	0.07
<i>H. influenzae</i> - <i>S. aureus</i>	36	13.1	40	14.3	12	4.4	0.55
<i>H. influenzae</i> - <i>S. pyogenes</i>	3	1.1	5	1.8	1	0.4	0.41
<i>K. pneumoniae</i> - <i>S. pneumoniae</i>	0	0	3	1.1	3	1.1	0.08
<i>K. pneumoniae</i> - <i>S. aureus</i>	4	1.5	7	2.5	2	0.7	0.26
<i>K. pneumoniae</i> - <i>S. pyogenes</i>	0	0	0	0	0	0	NA
<i>S. pneumoniae</i> - <i>S. aureus</i>	1	0.4	6	2.1	6	2.2	0.06
<i>S. pneumoniae</i> - <i>S. pyogenes</i>	0	0	0	0	0	0	NA
<i>S. aureus</i> - <i>S. pyogenes</i>	1	0.4	0	0	0	0	NA
At least one pathogen	174	63.3	205	73.5	144	52.4	0.008

* p-value: pre- versus post-travel, McNemar's test

1, 2: 275 and 279 students provided pre- and post-travel nasopharyngeal swabs, respectively

3: Acquisition of respiratory pathogens was calculated in 275 students who provided both pre- and post-travel nasopharyngeal samples

Table 2: Prevalence of gastrointestinal pathogens

Pathogens	Pre-travel		Post-Travel		Acquisition		p*
	N = 282 ¹	%	N = 283 ²	%	N = 274 ³	%	
Viruses							
Adenovirus	0	0	3	1.1	3	1.1	0.08
Astrovirus	0	0	3	1.1	3	1.1	0.08
Norovirus	0	0	3	1.1	3	1.1	0.08
Rotavirus	0	0	0	0	0	0	NA
At least one virus	0	0	9	3.2	9	3.3	0.003
Bacteria							
<i>Campylobacter jejuni</i>	2	0.7	5	1.8	5	1.8	0.26
Enteroaggregative <i>Escherichia coli</i>	10	3.6	119	42.1	112	40.9	< 0.000
Enterohemorrhagic <i>E. coli</i>	3	1.1	4	1.4	2	0.7	0.65
Enteropathogenic <i>E. coli</i>	25	8.9	66	23.3	51	18.6	< 0.000
<i>Salmonella spp</i>	0	0	4	1.4	4	1.5	0.05
<i>Shigella spp</i> /EIEC	0	0	7	2.5	7	2.6	0.008
<i>Tropheryma whipplei</i>	1	0.4	1	0.4	0	0	NA
At least one bacteria	38	13.5	147	51.9	135	49.3	< 0.000
Parasites							
<i>Cryptosporidium parvum/hominis</i>	0	0	0	0	0	0	NA
<i>Entamoeba histolytica</i>	0	0	0	0	0	0	NA
<i>Giardia lamblia</i>	1	0.4	3	1.1	3	1.1	0.32
At least one gastrointestinal pathogen	39	13.8	153	54.1	143	52.2	< 0.000

* p-value: pre- versus post- travel, McNemar's test

1, 2: 282 and 283 students provided pre- and post-travel rectal swabs, respectively

3: Acquisition of gastrointestinal pathogens was calculated in 274 students who provided both pre- and post-travel rectal samples

Table 3: Prevalence of vaginal microorganisms

Microorganisms	Pre-travel N = 212 ¹ (%)	Post-travel N = 221 ² (%)	Acquisition N = 209 ³ (%)	p *
Bacteria				
<i>Atopobium vaginae</i>	42 (19.8)	42 (19.0)	29 (13.9)	0.896
<i>Atopobium vaginae</i> (CT<21)	1 (0.5)	1 (0.5)	1 (0.5)	1.0
<i>Chlamydia trachomatis</i>	1 (0.5)	1 (0.5)	1 (0.5)	1.0
<i>Gardnerella vaginalis</i>	59 (27.8)	55 (24.9)	27 (12.9)	0.439
<i>Gardnerella vaginalis</i> (CT<18)	2 (0.9)	9 (4.1)	9 (4.3)	0.035
<i>Mycoplasma genitalium</i>	0	2 (0.9)	2 (0.96)	0.16
<i>Mycoplasma hominis</i>	4 (1.9)	3 (1.4)	2 (0.96)	0.65
<i>Neisseria gonorrhoeae</i>	0	0	0	NA
Parasites				
<i>Trichomonas vaginalis</i>	0	0	0	NA
At least one vaginal pathogen	82 (38.7)	78 (35.3)	33 (15.8)	0.42

* p-value: pre- versus post-travel, McNemar's test

1, 2: 212 and 221 students provided pre- and post-travel vaginal swabs, respectively

3: Acquisition of vaginal pathogens was calculated in 209 students who provided both pre- and post-travel vaginal samples

Table 4: Risk factors for respiratory symptoms and diarrhoea during travel

	Risk factors for respiratory symptoms during the travel					Risk factor for diarrhoea during the travel				
	Univariate analyse			p	Multivariate analyse	Univariate analyse			p	Multivariate analyse
	No	Yes	RR			No	Yes	RR		
n (%)	n (%)	[95%CI]	aRR	n (%)	n (%)	[95%CI]	aRR			
Gender										
Female	136 (72.3)	88 (83.8)	1.50 [1.06-2.11]	0.02	1.55 [1.08-2.22], p= 0.02	121 (54.0)	103 (46.0)	0.77 [0.51-1.15]	0.19	-
Male	52 (27.7)	17 (16.2)				31 (44.9)	38 (55.1)			
Age (mean ± SD)	20.7±1.1	20.7±1.1	t= 0.38 0.70	0.70		20.7 ± 1.1	20.6± 1.1	t=0.70	0.48	
Medical history										
Vaccination against influenza	83 (34.9)	22 (40.0)	1.15 [0.78-1.70] 0.48	0.48		NA	NA	NA	NA	
Primary travel destination										
South East Asia	71 (33.5)	34 (42.0)	1.26 [0.89-1.77]	0.18	-	104 (49.1)	37 (45.7)	0.93 [0.71-1.22]	0.61	

Vietnam	73 (32.9)	32 (45.1)	1.40 [0.97-2.00]	0.07	1.57 [1.07-2.31], p= 0.02	111 (50.0)	30 (42.3)	0.85 [0.62-1.14]	0.26	
South Asia	86 (36.1)	19 (34.6)	0.96 [0.65-1.40]	0.82		107 (45.0)	34 (61.8)	1.38 [1.07-1.77]	0.02	-
South India	98 (37.4)	7 (22.6)	0.66 [0.41-1.05]	0.08	-	125 (47.7)	16 (51.6)	1.08 [0.75-1.56]	0.68	
North India	93 (34.6)	12 (50.0)	1.53 [0.84-2.79]	0.16	-	123 (45.7)	18 (75.0)	1.64 [1.26-2.14]	<0.01	2.57 [1.13-5.85] p= 0.025
Africa	77 (37.0)	28 (32.9)	0.89 [0.65-1.24]	0.51		105 (50.5)	36 (42.4)	0.84 [0.63-1.11]	0.21	
Tanzania	99 (37.6)	6 (20.0)	0.61 [0.38-0.97]	0.04	-	137 (52.1)	4 (13.3)	0.26 [0.10-0.64]	<0.000	0.37 [0.22-0.60] p <0.000
Madagascar	91 (34.2)	14 (51.9)	1.63 [0.92-2.90]	0.09	-	129 (48.5)	12 (44.4)	0.92 [0.59-1.42]	0.69	
Senegal	98 (35.3)	7 (46.7)	1.37 [0.82-2.83]	0.40		129 (46.4)	12 (80.0)	1.72 [1.30-2.29]]	0.01	3.31 [1.05-10.45] p= 0.04
South America	84	21	0.90	0.569		108	33	1.09	0.53	

	(36.7)	(32.8)	[0.63-1.29]			(47.2)	(51.6)	[0.83-1.44]	
Peru	87	18	1.06	0.79		114	27	1.21	0.22
	(35.5)	(37.5)	[0.70-1.58]			(46.5)	(56.3)	[0.91-1.60]	
Condition during travel									
Contact with children	18	87	1.20	0.33		27	114	1.06	0.69
	(30.5)	(37.2)	[0.83-1.73]			(45.8)	(48.7)	[0.78-1.45]	
Contact with animals	52	53	1.37	0.046	-	77	64	1.12	0.36
	(31.0)	(42.4)	[1.01-1.86]			(45.8)	(51.2)	[0.88-1.42]	
Type of accommodation									
Very clean	34	9	rfr	rfr	rfr	22	21	rfr	Rfr
	(79.1)	(20.9)				(51.2)	(48.8)		
Clean	84	45	1.49	0.07	-	73	56	0.86	0.54
	(65.1)	(34.9)	[0.96-2.29]			(56.6)	(43.4)	[0.53-1.40]	
Basic	70	51	1.81	<0.01	1.43 [1.02-1.99], p= 0.04	57	64	1.13	0.65
	(57.9)	(42.2)	[1.16-2.82]			(47.1)	(52.9)	[0.68-1.86]	
Mission during travel									
Humanitarian mission in an orphanage	94	11	0.60	<0.01	-	115	26	1.02	0.88
	(39.2)	(20.8)	[0.41-0.87]			(47.9)	(49.1)	[0.76-1.39]	

School renovation	49 (31.4)	56 (40.9)	1.29 [0.96-1.75]	0.09	-	79 (50.6)	62 (45.3)	0.89 [0.70-1.14]	0.36
Supply of medical equipment and health advice	86 (35.0)	19 (40.4)	1.16 [0.77-1.76]	0.48		117 (47.6)	24 (51.1)	1.07 [0.79-1.46]	0.66
Internships in hospital	86 (36.3)	19 (33.9)	0.94 [0.64-1.37]	0.74		112 (47.3)	29 (51.8)	1.10 [0.82-1.46]	0.54
Internships in surgery department	97 (35.3)	8 (44.4)	1.29 [0.82-1.12]	0.45		130 (47.3)	11 (61.1)	1.29 [0.88-1.91]	0.26
Duration of travel (mean \pm SD)	40.5 ± 10.7	41.8 ± 11.9	t=-0.95	0.34		39.6 \pm 10.7	42.6 \pm 11.4	t=-2.35	0.02
Acquisition of respiratory pathogens²⁷⁵									
Rhinovirus	86 (36.6)	11 (27.5)	0.78 [0.51-1.19]	0.25		NA	NA	NA	NA
At least one respiratory virus	84 (37.2)	13 (26.5)	0.75 [0.50-1.10]	0.14	-	NA	NA	NA	NA
<i>Haemophilus influenzae</i>	79 (34.7)	18 (38.3)	1.10 [0.73-1.67]	0.64		NA	NA	NA	NA
<i>Klebsiella pneumoniae</i>	89 (34.8)	8 (42.1)	1.22 [0.65-2.29]	0.53		NA	NA	NA	NA

<i>Staphylococcus aureus</i>	78 (35.0)	19 (36.5)	1.04 [0.70-1.55]	0.83		NA	NA	NA	NA
<i>Streptococcus pneumoniae</i>	87 (33.5)	10 (66.7)	2.70 [1.10-6.62]	0.03	2.79 [1.13-6.88], p= 0.03	NA	NA	NA	NA
At least one respiratory bacteria	56 (34.4)	41 (36.6)	1.06 [0.78-1.45]	0.70		NA	NA	NA	NA
Acquisition of digestive pathogens²⁷⁴									
Enteropathogenic <i>E. coli</i>	NA	NA	NA	NA		78 (48.2)	58 (51.8)	1.08 [0.85-1.37]	0.55
Enteropathogenic <i>E. coli</i>	NA	NA	NA	NA		110 (49.3)	26 (51.0)	1.03 [0.77-1.40]	0.83
At least one gastrointestinal bacteria	NA	NA	NA	NA		68 (48.9)	68 (50.4)	1.04 [0.74-1.47]	0.81
At least one gastrointestinal pathogen	NA	NA	NA	NA		64 (48.9)	72 (50.4)	1.04 [0.74-1.47]	0.81

NA: not applicable

RR: relative risk, aRR: adjusted relative risk, CI: confidence interval, p: p value, rfr: reference

‡ Number of individuals for whom data were available

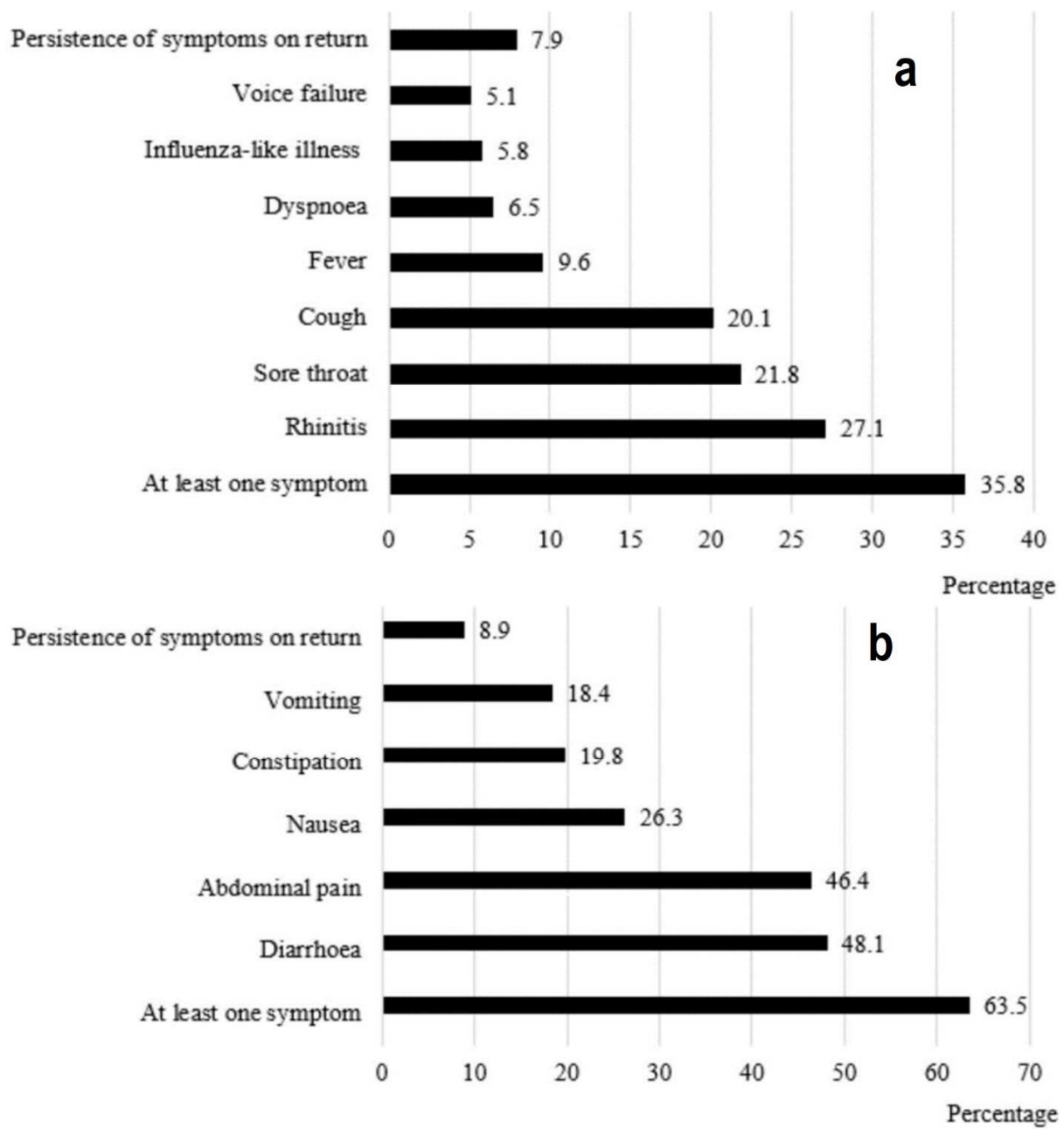


Figure 1: Prevalence of respiratory (a) and gastrointestinal (b) symptoms during travel