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**Incidence and types of illness when traveling to the tropics:
A prospective controlled study of children and their parents**

THESE

préparée sous la direction du Docteur Blaise Genton, Privat-docent et
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RESUME

De plus en plus de familles se rendent vers des destinations tropicales, s'exposant à des agents infectieux et des maladies tropicales qu'ils ne rencontrent pas chez eux.

Nous avons étudié 157 enfants (0-16 ans) et leurs parents partant pour les tropiques, qui ont tous consulté une clinique pré-voyage et qui étaient généralement compliants aux conseils prodigués. Les taux d'incidence de maladies communes chez les enfants et les adultes étaient respectivement de 16.9 (14.3-19.7) et 15.1 (12.7-17.8) épisodes/100 personnes-semaines. La diarrhée, les douleurs abdominales et la fièvre représentaient les plaintes les plus fréquentes. Il n'y avait pas de différence significative d'incidence des épisodes morbides entre les enfants et les adultes sauf pour la fièvre (plus fréquente chez les enfants). La plupart des épisodes avaient lieu dans les dix premiers jours du voyage. L'incidence de morbidité similaire chez les enfants et les adultes ainsi que l'aspect bénin des épisodes remet en question l'opinion selon laquelle il n'est pas sage de voyager avec des jeunes enfants.

Incidence and Types of Illness When Traveling to the Tropics: A Prospective Controlled Study of Children and Their Parents

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Abstract. Increasingly, families travel to tropical destinations exposing them to infectious agents and tropical diseases not encountered at home. We studied 157 children (0–16 years) and their adult relatives traveling to the tropics, who attended a pretravel clinic and were generally adherent to prescribed advice. Incidence rates of common illness in children and adults were respectively 16.9 (14.3–19.7) and 15.1 (12.7–17.8) episodes/100 person-weeks. Diarrhea, abdominal pain, and fever were the most frequent complaints. There was no significant difference in the incidence of morbid episodes between children and adults, except for fever (more frequent in children). Most episodes occurred in the first 10 days of travel. The similar incidence of morbidity in children and adults and the episodes' mildness challenge the view that it is unwise to travel with small children.

INTRODUCTION

The number of families traveling with their children to tropical destinations has steadily increased over the last years leading to numerous potential exposures to tropical diseases. There is little published literature on the incidence and type of illness in traveling children, and the present study should serve to fill this gap. Previous studies on children traveling to tropical destinations are mostly retrospective, incomplete and concentrated on diseases such as fever, diarrhea and malaria, and also on children who were hospitalized on their return, taking no account of those who did not seek medical advice.^{1–6} It is assumed that children are more frequently sick while traveling, and some pediatricians argue that going to the tropics with small children is unwise, but there is no evidence to support this. As a matter of fact, precise estimates of incidence rates regarding illness in adults who travel abroad are not available either. Most studies are based on postal post-travel questionnaires that only provide estimates of the prevalence of travelers who presented a health problem while abroad or upon return.^{7–9}

The aim of this study was i) to precisely estimate the incidence rate of morbidity in family members traveling to tropical and subtropical countries, ii) to investigate the types of disease they experienced, iii) to identify potential risk factor(s), and iv) to compare the findings between children and corresponding adults. We therefore conducted a prospective controlled study among 157 children (cases) and their adult relatives (controls) who attended our travel clinic for pre-travel consultation.

MATERIALS AND METHODS

Study period and subjects. From October 2000 to May 2004, all parents of children of age 0–16 years attending the Travel Clinic for pretravel advice were asked to participate in a prospective study. If they agreed, the child (case) was included and 1 of the adult relatives who attended the consultation was randomly selected to serve as a control (matched for environmental and travel characteristics). If only 1 parent

attended, he/she was automatically selected as the control. A maximum of 2 children per family were recruited. When there were 3 children or more, 2 of them were selected randomly. Children whose journey exceeded 2 months were excluded because of the confounding effect of frequent health problems in children.

Study procedures. During the pretravel consultation, families received standardized pretravel information. We updated routine vaccinations. Specific vaccinations, such as hepatitis A and B, typhoid, meningitis, yellow fever, and rabies, were done if deemed necessary, following the recommendations of the Swiss expert group for travel medicine (<http://www.safetravel.ch>). Malaria chemoprophylaxis was prescribed when appropriate. A questionnaire was filled out for each child and adult with information on personal demographics, general health, vaccination status, and type of travel planned.

Self-administered questionnaires were then given to be completed weekly during travel and 4 weeks after return. This time period was chosen to cover the period of malaria prophylaxis after return (so that full adherence could be assessed), as well as the incubation period of most illnesses acquired during travel. These questionnaires included questions on preventive measures (use of repellent and mosquito net; avoidance of tap water, salad, and ice cubes) and health issues with both open-ended and directed questions. When an illness occurred, parents were requested to answer 21 questions about symptoms (general wellness, irritability, fatigue, fever, shivers, sweating, joint pain, muscular pain, rhinitis, otalgia, cough, headache, dizziness, abdominal pain, diarrhea, constipation, vomiting, rash, seizures, sleep disorder, motion sickness), to mention whether they had attended a medical practitioner, and whether they had taken any medication or not.

In addition, all parents were contacted by phone 2 months after return to check for new events and clarify the answers to the questionnaires if necessary.

Data analysis. Incidence rates of morbid episodes during the total observation period were calculated using a Poisson distribution. Days of illness were censored from the total observation period for all of the incidence calculations. A conditional maximum likelihood estimate of the rate ratio between both groups was calculated for each type of morbid episode using the polynomial multiplication method.¹⁰ This also provided mid-*P* estimates. For diseases whose incidence rate exceeded 2 episodes per 100 person-weeks, we compared

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incidence rates during travel and during the 4 weeks post-travel using the same method.

Life tables of the occurrence of morbid episodes were plotted for both groups. The occurrence of morbid episodes per week of observation both during travel and after return was plotted for both groups.

For diseases whose incidence exceeded 3 episodes per 100 person-weeks, we first investigated potential predictors in a univariate analysis using the conditional maximum likelihood estimate of rate ratios. We then entered variables whose *P* value was $< 0.20^{11}$ into a multivariate analysis using a Poisson regression model. The fit of the data to a Poisson distribution in the regression was tested by the deviance goodness-of-fit test. The adequacy of the fitted model was tested using the G^2 deviance (likelihood ratio) test statistic.¹² Data were analyzed using SPSS 12.0 (SPSS, Inc., Chicago, IL) and StatsDirect (StatsDirect Ltd, Cheshire, U.K.).

RESULTS

Response rate. There were 364 eligible child-adult pairs: 244 (67%) agreed to participate, 120 refused to participate, 84 were lost to follow-up, and 3 returned questionnaires with major lack of data. In total, 157 questionnaires were analyzed.

Study population. There were 157 child-adult pairs. Demographic and personal characteristics are summarized in Table 1. The following comorbidities were identified in children from their pretravel questionnaire: 23 (14.6%) had recurrent otitis media, 8 (5.1%) asthma, 17 (10.8%) eczema, and 17 (10.8%) hay fever. For adults, 85 (54.1%) presented at least 1 cardiovascular risk factor, and 17 (10.8%) were taking regular medication. Comorbidities were as follows: 10 (6.3%) asthma, 15 (9.6%) varicose veins, 4 (2.5%) hypertension, 10 (6.3%) eczema, 26 (16.6%) hay fever, 7 (4.5%) migraine, 7 (4.5%) depression, 2 (1.3%) cancer, and 1 (0.6%) was diabetic. Adults occupied the following professional categories¹³: 14% were stay-at-home parents, 37% were in classes 1 (legislators, senior officials, managers) or 2 (professionals), 30.6% in classes 3 (technicians and associate professionals) or 4 (clerks), and 14.6% in classes 5 (service, shop and market sales), or 7-9 (7, craft and related trades; 8, plant and machine operators and assemblers; 9, elementary occupations). Six participants did not indicate their profession.

TABLE 1
Baseline characteristics of study population

		Children	Adults
Age (years)	Mean \pm SD	7.6 \pm 4.2*	39.9 \pm 6.6
	Range	0.25-16	23-69
Sex	Male/female	86/71 (1.2:1)	39/118 (1:3)
Place of birth	Europe	153 (97.4%)	136 (86.6%)
	Africa	2 (1.3%)	6 (3.8%)
	South America	2 (1.3%)	13 (8.3%)
	Asia	0	2 (1.3%)
Nationality	Swiss	147 (93.6%)	133 (84.7%)
	Other European	8 (5.1%)	17 (10.8%)
	African	1 (0.6%)	3 (1.9%)
	South American	1 (0.6%)	4 (2.5%)
Previous travel to the tropics	65 (41.4%)	137 (87.3%)	
History of living in the tropics	7 (4.5%)	35 (22.3%)	
Regular medication	3 (1.9%)	33 (21%)	

* 12 children < 2 years; 44 children 3-5 years; 58 children 6-10 years; and 43 children 11-16 years.

Travel characteristics. Half of the families went to Africa (51.6%), 25.5% to Asia, and the remaining (22.9%) to South or Central America. Families remained abroad for 6-56 days (median 16). One hundred sixteen (73.9%) families were traveling for tourism, 50 (31.8%) to visit friends or relatives (immigrants returning to their home country, mixed marriage families, and Europeans visiting native or expatriate friends or relatives), and 5 (3.1%) for other reasons.

Preventive measures. One hundred eight (68.8%) children and 117 adults (74.5%) received all vaccinations recommended.¹⁴ Malaria chemoprophylaxis was prescribed to 74 (47.1%) families; 61 (82.4%) children and 65 (87.8%) adults were fully adherent (no missed dose). A further 52 (33.1%) children and 50 (31.8%) adults traveling to low-level endemic areas were prescribed standby treatment. None of them made use of it. One hundred forty-seven children and 147 adults (93.6%) used a mosquito net, a repellent lotion, or had an air-conditioned room. Fifty (31.8%) children and 26 (16.6%) adults were compliant to all 3 of the following measures of food-borne disease prevention: no tap water, no ice cubes, and no salads.

Morbid episodes. Ninety-six (61.1%) children and 88 (56.1%) adults presented at least 1 morbid episode during follow-up. In total, there were 157 episodes of illness in children and 140 in adults. The median time until the first episode of disease was 7.2 days in children and 8.0 days in adults, according to the survival analysis (Figure 1). Incidence rates for overall morbidity as well as specific illnesses are shown in Table 2. There were no significant differences in the incidence rates of morbid episodes between children and adults, except for fever, which occurred significantly more frequently in children (RR = 2.5, 95% CI 1.3-5.0; $P = 0.003$). Incidence rates were significantly higher during travel than after return for all types of disease (Table 3), except for rhinitis in adults.

As a consequence of these morbid episodes, 27 (17.2%) families abandoned at least once their planned activities, and 30 (19.1%) children and 24 (15.3%) adults sought medical attention. One hundred twenty-six (80.2%) of 157 children traveled to malaria-endemic areas. Six (19.4%) of the 31 children who traveled to nonmalaria-endemic areas developed fever, and 2 (6.5%) of them sought medical attention. Eighteen (14.3%) of the 126 children who traveled to malaria-endemic areas developed fever, and 6 (4.8%) of them sought medical attention. Thus in both groups only one-third of the

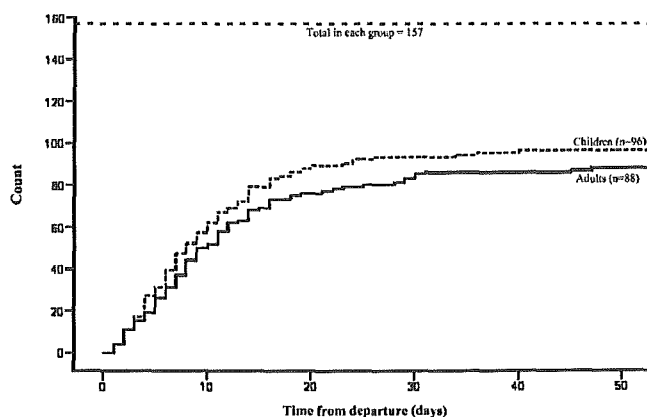


FIGURE 1. Occurrence of illness in adults and children after departure to tropical/subtropical destinations.

TABLE 2

Incidence rates of disease symptoms (episodes per 100 person-weeks) from departure to 4 weeks post-travel in adults and children and conditional maximum likelihood estimate of rate ratio between both groups

Morbid episode	Child incidence rate (95% CI)	Adult incidence rate (95% CI)	Rate ratio (95% CI)	P
Diarrhea	7.1 (5.6–9.1)	6.8 (5.2–8.7)	1.1 (0.7–1.5)	0.75
Abdominal pain	4.9 (3.6–6.6)	4.3 (3.1–5.9)	1.1 (0.7–1.8)	0.54
Fever	3.8 (2.6–5.2)	1.5 (0.8–2.5)	2.5 (1.3–5.0)	0.003
Rhinitis	2.9 (1.9–4.2)	1.9 (1.2–3.1)	1.5 (0.8–2.9)	0.19
Headache	2.4 (1.5–3.6)	3.0 (2.0–4.3)	0.8 (0.4–1.4)	0.39
Vomiting	1.9 (1.1–3.1)	1.8 (1.1–2.9)	1.1 (0.5–2.2)	0.88
Rash	1.5 (0.8–2.5)	1.2 (0.6–2.1)	1.3 (0.5–3.1)	0.57
Cough	1.5 (0.8–2.4)	1.1 (0.5–1.9)	1.3 (0.6–3.1)	0.47
Motion sickness	0.6 (0.2–1.4)	0.5 (0.2–1.3)	1.2 (0.3–4.9)	0.78
Constipation	0.4 (0.1–1.1)	0.8 (0.3–1.5)	0.6 (0.1–2.2)	0.38
Any illness*	16.9 (14.3–19.7)	15.1 (12.7–17.8)	1.1 (0.9–1.4)	0.35

*The incidence rate for any illness is lower than the sum of individual illness symptoms because each morbid episode could present with one or more symptoms.

children who developed fever sought medical attention. One hundred twenty-four (79%) of 157 adults were prescribed either malaria chemoprophylaxis or rescue treatments. One (3%) of the 33 adults who traveled to nonmalaria-endemic areas developed fever, and sought medical attention. Eleven (8.9%) of the 124 adults who traveled to malaria-endemic areas developed fever, and 4 (3.2%) of them sought medical attention.

Eighty-one (51.6%) children and 73 (46.5%) adults took medication. In total, 136 courses of medication were given to children and 135 to adults. The main classes of drugs used in children and adults were probiotics (respectively 38 and 25 courses), antipyretics/painkillers (respectively 26 and 25 courses), and anti-diarrheals (respectively 17 and 22 courses). Other drugs used included ENT and cough medication, antibiotics, antiemetics, and antihistamines. There was no significant difference in medication used between both populations. Antibiotics were prescribed to children for the following diagnoses: pharyngitis (4 cases), otitis media (3 cases), sinusitis (1 case), urinary tract infection (1 case), and gastroenteritis (1 case). They were prescribed to adults for otitis media (4 cases), gastroenteritis (4 cases), pharyngitis (3 cases), sinusitis (2 cases), giardiasis (1 case), and gynecologic infection (1 case). All courses of antibiotics were medically prescribed. Two (1.3%) adults and none of the children were hospitalized. One admission was for diverticulitis and the second for abortion, both after return.

Predictors of disease. Results of analyses for predictors of morbid episodes are shown in Table 4. Multivariate analyses indicated that incidence of overall morbidity increased with rising level (classes 1–2) of parental occupation ($P = 0.004$) and with use of ice cubes ($P = 0.034$) but was decreased by history of previous travel to the tropics ($P = 0.014$). Inci-

dence of fever was significantly higher in the 0- to 5-year age group ($P = 0.004$) and with use of ice cubes ($P = 0.018$). Abdominal pain was more frequent with parental occupation class 1–2 ($P = 0.039$). The incidence rate of headache was significantly lower in children of age 0–5 years ($P = 0.018$), in subjects who had previously traveled to the tropics ($P = 0.049$), and in those who used mosquito nets ($P = 0.023$) but was higher in persons who were poorly compliant with their malaria chemoprophylaxes ($P = 0.007$).

DISCUSSION

This prospective study differs from previous studies of illnesses in travelers to the tropics^{7,9,15,16} by providing precise estimates of the overall incidence and type of illnesses presented by children and adults, both during and on return from their travel. Parents completed questionnaires every week, thus decreasing the risk of recall bias, which is the one pitfall of airport post-travel surveys that cannot give accurate incidence data.

Around 60% of both children and adults presented at least 1 episode of illness during their follow-up. Previous studies based on post-travel interviews have shown variable figures: 15–38% in Swiss travelers,^{8,16} 36%¹⁵ in Scottish package tourists, and 64%⁹ in American subjects. It is likely that the high proportion in our study is primarily due to the absence of recall bias with families that knew they would have to fill in the questionnaire, probably inclining them to closely observe their own health status. It is also likely that other factors, such as destination,¹⁷ length of travel, and duration of follow-up, and also variable definitions of what constituted an episode of illness influenced the results of each study.

TABLE 3

Incidence rates of disease (IR, episodes per 100 person-weeks) during travel and during the 4-week follow-up period after return and conditional maximum likelihood estimate of rate ratio between both periods, in children and adults traveling to the tropics

		Any disease	Fever	Diarrhea	Abdominal pain	Headache	Rhinitis
Child IR (95% CI)	During travel	39.3 (32.6–46.9)	8.0 (5.2–11.8)	17.6 (13.3–22.9)	12.8 (9.1–17.4)	6.3 (3.9–9.9)	6.0 (3.7–9.5)
	After travel	5.6 (3.9–7.8)	1.7 (0.8–3.1)	2.0 (1.0–3.5)	0.9 (0.3–2.2)	0.7 (0.2–1.7)	1.3 (0.6–2.6)
	Rate ratio (95% CI)	7.0 (4.7–10.5)	4.8 (2.2–11.2)	8.8 (4.8–17.2)	12.8 (5.7–33.3)	9.6 (3.5–32.9)	4.6 (2.0–11.1)
Adult IR (95% CI)	During travel	33.9 (27.7–40.9)	3.2 (1.5–5.9)	17.2 (12.9–22.5)	10.5 (7.3–14.8)	5.1 (2.8–8.3)	2.5 (1.1–5.0)
	After travel	5.7 (4.0–8.0)	0.2 (< 0.1–0.9)	1.5 (0.7–2.9)	1.2 (0.5–2.4)	2.0 (1.0–3.5)	1.7 (0.8–3.1)
	Rate ratio (95% CI)	5.9 (4.0–9.0)	19.0 (3.2–415.8)	11.4 (5.8–24.5)	9.0 (3.9–24.0)	2.5* (1.2–5.5)	1.5** (0.6–3.9)

All rate ratios have a P value < 0.001, except * $P = 0.02$ and ** $P = 0.39$.

TABLE 4

Uni- and multivariate analyses of predictors of morbid episodes in children and adults traveling to the tropics (for the multivariate models, variables were included if *P* value < 0.20 on univariate analysis)*

	Any disease		Fever		Diarrhea		Abdominal pain		Headache	
	Univar OR (95% CI)	Multivar OR (95% CI)	Univar OR (95% CI)	Multivar OR (95% CI)	Univar OR (95% CI)	Multivar OR (95% CI)	Univar OR (95% CI)	Multivar OR (95% CI)	Univar OR (95% CI)	Multivar OR (95% CI)
Age (years)										
0–5 (<i>n</i> = 56)	1.37 (1.02–1.82)	1.10 (0.79–1.54)	4.48 (2.30–8.98)	3.09 (1.43–6.65)	1.22 (0.77–1.91)	Inadequate model	1.21 (0.67–2.12)	0.86 (0.46–1.63)	0.41 (0.12–1.08)	0.26 (0.08–0.79)
6–10 (<i>n</i> = 58)	0.87 (0.62–1.21)	0.85 (0.60–1.21)	1.33 (0.50–3.25)	1.07 (0.41–2.82)	0.88 (0.53–1.43)	<i>G</i> ² , <i>P</i> > 0.05	0.80 (0.40–1.49)	0.72 (0.36–1.43)	0.76 (0.32–1.62)	0.58 (0.25–1.33)
11–16 (<i>n</i> = 43)	1.12 (0.79–1.56)	0.98 (0.68–1.41)	1.52 (0.54–3.89)	1.36 (0.49–3.80)	1.07 (0.63–1.76)		1.51 (0.84–2.63)	1.33 (0.71–2.49)	1.52 (0.75–2.95)	1.35 (0.64–2.84)
> 16 (<i>n</i> = 157)	Reference variable									
Sex Female/male (<i>n</i> = 189/125)	1.02 (0.81–1.29)		0.48 (0.27–0.85)	0.64 (0.35–1.18)	1.03 (0.73–1.48)		1.27 (0.82–2.01)		1.03 (0.59–1.84)	
Parental occupation										
Classes 1–2 (<i>n</i> = 116)	1.87 (1.28–2.82)	1.81 (1.21–2.72)	1.24 (0.54–3.14)		1.60 (0.92–2.91)		2.54 (1.19–6.11)	2.35 (1.04–5.31)	1.45 (0.60–3.92)	
Classes 3–4 (<i>n</i> = 96)	1.23 (0.81–1.89)	1.20 (0.78–1.85)	0.83 (0.33–2.24)		0.97 (0.52–1.84)		1.45 (0.63–3.67)	1.38 (0.58–3.29)	1.37 (0.56–3.79)	
Stay-at-home parent (<i>n</i> = 44)	1.38 (0.86–2.23)	1.53 (0.94–2.49)	0.43 (0.09–1.64)		1.21 (0.61–2.44)		1.73 (0.63–5.18)	1.64 (0.63–4.26)	0.84 (0.20–3.30)	
Classes 5–9 (<i>n</i> = 46)	Reference variable									
Destination										
Asia (<i>n</i> = 80)	0.78 (0.57–1.04)	0.79 (0.57–1.07)	0.99 (0.47–1.99)		0.73 (0.46–1.13)		0.70 (0.39–1.21)		0.78 (0.38–1.51)	
America (<i>n</i> = 72)	1.11 (0.85–1.45)	0.97 (0.73–1.23)	1.22 (0.62–2.36)		0.96 (0.64–1.44)		1.02 (0.62–1.66)		0.77 (0.38–1.49)	
Africa (<i>n</i> = 162)	Reference variable									
Aim Tourism/other (<i>n</i> = 232/110)	0.90 (0.71–1.16)		0.57 (0.32–1.02)	0.58 (0.32–1.05)	0.77 (0.54–1.11)		0.70 (0.45–1.09)	0.67 (0.42–1.08)	1.18 (0.64–2.28)	
Tropical life Y/N (<i>n</i> = 42/272)	0.93 (0.65–1.28)		1.00 (0.41–2.13)		0.96 (0.57–1.55)		0.97 (0.51–1.74)		1.09 (0.48–2.23)	
Prev. tropical travel Y/N (<i>n</i> = 212/102)	0.75 (0.60–0.95)	0.71 (0.54–0.93)	0.50 (0.28–0.87)	0.71 (0.38–1.31)	0.78 (0.55–1.11)		0.69 (0.45–1.06)	0.66 (0.40–1.10)	0.65 (0.38–1.14)	0.53 (0.28–0.99)
Vaccination Y/N (<i>n</i> = 225/89)	1.01 (0.80–1.28)		0.63 (0.32–1.16)		0.92 (0.63–1.31)		1.25 (0.81–1.91)		0.70 (0.37–1.26)	
Chemoprophylaxis										
Good compliance (<i>n</i> = 126)	0.97 (0.75–1.23)		0.91 (0.49–1.65)		1.16 (0.80–1.67)		1.13 (0.72–1.75)		1.08 (0.58–1.96)	1.21 (0.64–2.25)
Bad compliance (<i>n</i> = 22)	1.28 (0.84–1.86)		0.78 (0.37–0.74)		1.47 (0.78–2.60)		0.81 (0.28–1.90)		2.33 (0.99–5.02)	3.21 (1.38–7.50)
Not indicated (<i>n</i> = 166)	Reference variable									
Mosquito spray Y/N (<i>n</i> = 273/41)	0.91 (0.66–1.28)		0.77 (0.37–1.76)		1.07 (0.65–1.86)		0.93 (0.52–1.78)		0.97 (0.46–2.32)	
Mosquito net Y/N (<i>n</i> = 134/180)	0.82 (0.65–1.04)	0.82 (0.64–1.06)	0.48 (0.24–0.89)	0.63 (0.32–1.21)	0.83 (0.58–1.17)		0.78 (0.50–1.21)		0.64 (0.35–1.14)	0.48 (0.26–0.91)
Air con† Y/N (<i>n</i> = 176/138)	0.97 (0.77–1.22)		0.98 (0.56–1.74)		1.02 (0.72–1.45)		1.34 (0.87–2.10)	1.59 (0.99–2.53)	1.09 (0.63–1.91)	
Tap water Y/N (<i>n</i> = 22/292)	0.98 (0.62–1.47)		1.62 (0.63–3.62)		1.29 (0.70–2.23)		0.87 (0.34–1.89)		1.24 (0.44–2.91)	
Ice cubes Y/N (<i>n</i> = 142/172)	1.24 (0.99–1.56)	1.31 (1.02–1.67)	1.82 (1.03–3.29)	2.09 (1.13–3.86)	1.19 (0.84–1.68)		1.10 (0.72–1.69)		1.15 (0.66–2.00)	
Salads Y/N (<i>n</i> = 196/118)	0.92 (0.73–1.17)		0.67 (0.38–1.18)	0.86 (0.47–1.55)	1.16 (0.81–1.68)		0.82 (0.54–1.27)		0.75 (0.43–1.30)	

* Bold, *P* < 0.05.

† Air conditioning.

AU5) Okay as edited?

AU6) Okay to add?

We showed that there is a steep rise in the number of episodes of illness during the first 15 days after departure; it then levels off to return to a baseline by ≈ 30 days of follow-up. Half of the children and adults who developed illnesses did so during the first 8 days after departure. We were not able to obtain baseline rates of illness before departure or incidence rates of illness in the general population (these data are not available in Switzerland); this would have enabled us to estimate the fraction of illness attributable to travel. However, given the length of our follow-up, we believe that the baseline attained at the end of follow-up approaches these rates.

Apart from fever, there were no differences between children and adults in the incidence of morbid episodes. This demonstrates that for this cohort of travelers, age was not a major determinant of morbidity during travel. The environment, which was exactly the same for children and their adult controls (with same levels of protective measures adherence), seems to be a much stronger determinant. The higher incidence of fever in children was principally due to an excess of febrile episodes in the youngest age group (0–5 years). Steffen and others⁷ previously described a tendency toward more fever in children traveling to the tropics; however, none of them was < 7 years old. Exposure to micro-organisms that are foreign to the home environment is inherent to travel to the tropics, and in young children who have not yet achieved mature immunity, this may manifest by an excess of febrile episodes. It is also possible that parents may be more likely to record children's temperature in this age group if they appear unwell.

Diarrhea and abdominal pain were the most frequent complaints encountered both in children and adults. This is in line with all of previous studies of morbidity in travelers to the tropics.^{7–9,15,16,18} Management of traveler's diarrhea, especially in children, relies essentially on the use of oral rehydration. This was systematically discussed in the pretravel consultations; 13% of the children took oral antidiarrheals (loperamide), despite concerns that this treatment can induce paralytic ileus, especially in children < 2 years of age.^{19,20} The youngest child to take loperamide in our group was 3 years old. The same type of behavior has been described by Pitzinger and others.²¹ Antidiarrheals are not recommended or prescribed for children in our travel clinic, nor are antibiotics for all travelers. Antidiarrheals were purchased through other channels, either in Switzerland or at travel destination, but antibiotics were always medically prescribed. Such behavior highlights the necessity to approach pretravel consultation, not only through prescription of adequate vaccines or drugs but also through specific advice on health-seeking behavior and drug use while sick abroad. Nineteen percent of all children and 15% of all adults sought medical attention, with a comparable figure of 12% reported by Hill,⁹ but $\approx 50\%$ of both adults and children used medication. This demonstrates that self-medication was very frequent. The nature of the drugs corresponded to the main symptoms that were reported, with a high consumption of antipyretics, antidiarrheals, and probiotics. An appropriate strategy would be to recommend a travel-medicine kit with a summary sheet that highlights the lower age limits for the different drugs included and their precise indication in terms of symptoms or signs.

Analysis of predictors of morbid episodes showed that a higher class of parental occupation was associated with both

an increase in overall illness, particularly frequent abdominal pain. This could be explained by an increased awareness and propensity to report unusual symptoms in these families, associated with a higher level of education. Use of ice cubes was associated with a higher incidence of fever episodes (not diarrhea), maybe as a marker of more risky behavior. As usual, standard advice to avoid ice cubes was poorly followed because 40% of children and nearly 50% of adults did not comply with this recommendation. How to improve this is a recurrent question with no satisfying answer.

The most important limitation of our study is the selection bias because our population was recruited among travel clinic attendants, who were therefore well prepared for their journey compared with a group of people who would have been taken randomly from a travel agency, for example, or at the airport. However, the design of our study, which included a formal informed consent, thorough initial pretravel assessment, and a detailed questionnaire to fill in every week during and after travel, required full understanding and some training that would have been impossible to perform in an airport or travel agency. We believe that precise estimates of incidence rates can only be realistically obtained through such thorough questioning and close follow-up of travelers. Such an approach often implies a relatively small sample size, as in this study, that may have limited our ability to identify weak potential risk factors for certain diseases as well as less-frequent disease episodes, such as travelers' malaria. Only 1 child had a presumptive diagnosis of malaria during travel and received artesunate treatment. Our incidence of $\approx 3/1000$ travelers is within the range of larger studies based mostly on post-travel questionnaires, i.e., 0.7–18 cases/1000.^{9,22–27} The latter observation suggests, as expected from the study subjects' selection, that the incidence rates estimated from our study sample are probably at the lower range of the ones that could be observed in the general population of travelers who often do not seek pretravel advice.^{28,29} Likewise, no cases of typhoid fever, meningitis, or hepatitis were reported. This may have been an effect of adequate immunization during the pretravel clinic, but again the attack rates for these diseases are low^{8,9} and our sample size may have limited our ability to detect such episodes.

In conclusion, the similar incidence of morbidity in children and adults, as well as the mildness of the morbid episodes, challenges the common view that it is unwise to travel with small children. In view of the high proportion of self-medication for mild symptoms, pretravel advice should also tackle appropriate response to disease.

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