A Comparison of Pretravel Health Care, Travel-Related Exposures, and Illnesses among Pediatric and Adult U.S. Military Beneficiaries

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Abstract. We evaluated differences in pretravel care, exposures, and illnesses among pediatric and adult travelers, using a prospective, observational cohort. Eighty-one pediatric travelers were matched 1:1 with adult military dependents by travel region, destination's malaria risk, and travel duration. Pediatric travelers were more likely to have coverage for hepatitis A and B (90% versus 67% of adults; 85% versus 44%), visit friends and relatives (36% versus 16%), report mosquito bites (69% versus 44%), and have close contact with wild or domesticated animals (40% versus 20%) than adults ($P < 0.05$). Subjects < 10 years of age were less likely to be prescribed antibiotics (28% versus 95%; RR = 0.63; 95% CI: 0.46–0.85) and antidiarrheals (9% versus 100%; RR = 0.10; 95% CI: 0.03–0.29) for travelers' diarrhea (TD) self-treatment than adults. Travel medicine providers should emphasize strategies for vector avoidance, prevention of animal bites and scratches, and TD self-treatment in pediatric pretravel consultations.

Children account for a significant proportion of U.S. travelers visiting overseas destinations,¹ but there are limited data regarding compliance with preventive measures, exposures, and self-limited diseases such as traveler's diarrhea (TD) which rarely result in a medical evaluation.^{2,3} The TravMil study (Deployment and Travel Related Infectious Disease Risk Assessment, Outcomes, and Prevention Strategies Among Department of Defense [DoD] Beneficiaries) prospectively evaluates infectious disease risks in DoD beneficiaries traveling outside the continental United States for ≤ 6.5 months.⁴ We used the TravMil cohort to evaluate differences in pretravel care, compliance with preventive measures, exposures, and illnesses among pediatric and adult military dependents.

Consenting adult and pediatric travelers were enrolled pretravel at four U.S. military travel clinics. Adults were enrolled between 2010 and 2016 at the Naval Medical Center Portsmouth (NMCP), Portsmouth, VA; San Antonio Military Medical Center, San Antonio, TX; Naval Medical Center San Diego (NMCS), San Diego, CA; and Walter Reed National Military Medical Center, Bethesda, MD. Pediatric subjects were enrolled between 2010 and 2014 at NMCP and NMCS. Itineraries limited to western or northern Europe, Canada, or New Zealand were excluded. Travel medicine physicians counseled travelers and provided prescriptions for immunizations, TD self-treatment, and malaria chemoprophylaxis. Counseling was not standardized for this study. Participant demographics, itineraries, vaccinations, and prescriptions were abstracted. Immunizations and prescriptions refused by participants (and reasons for refusal) were not captured. A post-travel survey, completed up to 8 weeks after return, was carried out to collect information on compliance with malaria chemoprophylaxis and personal protective measures, exposures, and occurrence of diarrhea, influenza-like illness or

febrile illness. The study was approved by the Uniformed Services University Infectious Disease Institutional Review Board.

Pediatric subjects (aged < 18 years at the time of travel) were matched 1:1 with adult military dependents (i.e., family members of either active duty or retired U.S. military personnel) using the following criteria: 1) geographic region of travel (i.e., Africa, South America/Central America/Caribbean, and Southeast Asia/North Asia/Oceania⁵); 2) malaria-risk region categorized by the provider as follows: a) none or minimal malaria risk—no chemoprophylaxis indicated, b) chloroquine-sensitive region, c) chloroquine-resistant region, and d) mefloquine-resistant region; and 3) travel duration < 1 or ≥ 1 month.⁶ We excluded active duty or retired U.S. military personnel because of targeted pretravel care (deployment readiness or military business, respectively) and travelers who visited ≥ 1 geographic region during a single trip. Each subject was included once in the analysis, and pediatric subjects were not matched to adults traveling with them.

Coverage rates and prescription practices for routine and/or travel-related vaccinations were evaluated using the criteria outlined in Table 1.² Partial or noncompliance with malaria chemoprophylaxis was defined as missing ≥ 2 doses of weekly antimalarials (mefloquine or chloroquine) in a row or ≥ 3 doses of daily antimalarials (doxycycline, atovaquone/proguanil, or primaquine primary prophylaxis) in a row. Definitions for exposures and illnesses are included in Table 2.

Statistical analysis was conducted using SAS version 9.4 (SAS Institute, Cary, NC). McNemar's test was used to assess differences between matched pediatric and adult subjects ($\alpha = 0.05$). A multivariate Poisson regression with robust error variance was used to evaluate differences in antibiotics and/or antidiarrheal prescriptions for TD self-treatment.

A total of 2,736 DoD active duty service members, retirees, and dependents were enrolled in the study. Of these, 86 children and 786 adult dependents were used to create 81 matched pairs (Table 2). The median age of pediatric subjects was 11 years (IQR: 8–16). Thirty subjects (36%) were < 10

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TABLE 1
Definitions for vaccine indications and up-to-date status

Category	Vaccination	Indication	Up-to-date status defined as follows
Travel vaccinations	Rabies	Travel to regions with risk of rabies transmission (Southeast Asia, South Asia, North Africa, Central America/Caribbean ¹⁷)	Prior vaccination or provided at pretravel visit
	Meningococcus	≥ 2 months of age and traveling to African meningitis belt	Prior vaccination ≤ 5 years ago or provided at pretravel visit
	Yellow fever	≥ 9 months of age and traveling to a yellow fever endemic country (Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Republic of the Congo, Côte d'Ivoire, Equatorial Guinea, French Guiana, Gabon, The Gambia, Ghana, Guinea, Guinea-Bissau, Guyana, Liberia, Nigeria, Rwanda, Sierra Leone, Senegal, Suriname, Togo, Uganda ¹⁸)	Any prior vaccination or provided at pretravel visit
	Japanese encephalitis	≥ 2 months of age and traveling to a Japanese encephalitis endemic country (Cambodia, Indonesia, Thailand, Vietnam, China, Japan, South Korea, Nepal, India, Bangladesh, Brunei, Myanmar, Laos, Malaysia, Papua New Guinea, Philippines, Sri Lanka, Taiwan)	Prior vaccination ≤ 1 year ago or provided at pretravel visit
	Typhoid	> 2 years of age and traveling to regions with risk of typhoid transmission (Africa, South America/Central America/Caribbean, and Southeast Asia/North Asia/Oceania)	Intramuscular vaccination ≤ 2 years ago or oral vaccination ≤ 5 years ago or prescribed at pretravel visit ¹⁹
Routine vaccinations*	Hepatitis A	Pediatric subjects: all subjects ≥ 1 year of age Adult subjects: subjects traveling to countries with intermediate to high hepatitis A endemicity	Prior vaccination series completion or vaccination prescribed at pretravel visit
	Hepatitis B	Pediatric subjects: all subjects of any age Adult subjects: subjects traveling to countries with intermediate to high hepatitis B endemicity	Completion of vaccination series before pretravel visit or vaccination prescribed at pretravel visit

* Advisory Committee on Immunization Practices (ACIP) recommendations for routine hepatitis A and B vaccination of children were issued after subjects in the adult cohort had become adults. ACIP recommends hepatitis A and B vaccination for adults with risk factors for infection, including those traveling to endemic areas. The U.S. Department of Defense requires all active duty military personnel to be vaccinated for hepatitis A and B.

years of age and seven subjects (9%) were ≤ 2 years of age. Most adult dependents were female (93% versus 52% of pediatric subjects). Thirty-one (38%) paired subjects traveled to Southeast Asia/North Asia/Oceania, 30 (37%) traveled to South America/Central America/Caribbean, and 20 (25%) traveled to Africa. Children were more likely to be visiting friends and relatives (VFRs) (36% versus 16% of adult subjects). With respect to malaria-risk region, 26 paired subjects (32%) traveled to a low or non-malaria risk area that did not require chemoprophylaxis, seven (9%) traveled to a chloroquine-sensitive malaria-risk area, 47 (58%) traveled to a chloroquine-resistant malaria-risk region, and one (1%) traveled to a mefloquine-resistant region.

There were significant differences in hepatitis A and B coverage rates between pediatric and adult subjects (Figure 1). Less than 50% of adults and children with potential indications for Japanese encephalitis or rabies vaccination were up-to-date on the series (see Table 1 for definitions). Atovaquone-proguanil was the most commonly prescribed antimalarial (79% [44/56] pediatric subjects and 71% [40/56] adults). Adult subjects received antibiotics (95% versus 77%) and antidiarrheals (e.g., loperamide) (100% versus 41%) for TD self-treatment more frequently than pediatric subjects ($P < 0.05$ for both comparisons). Further stratified by age, pediatric

subjects < 10 years of age were less likely to have received a prescription for antibiotics (60% versus 95%; $RR = 0.63$; 95% $CI: 0.47-0.85$) and antidiarrheals (10% versus 100%; $RR = 0.10$; 95% $CI: 0.03-0.30$) than adult subjects. A limited number of antidiarrheal prescriptions was also observed in subjects aged ≥ 10 years (59% versus 100%; $RR = 0.56$; 95% $CI: 0.46-0.74$) compared with adults.

Forty-eight pediatric travelers and 69 adult travelers completed a post-travel survey (Table 2). The median duration between trip return and completion of the post-travel survey was 23 days (IQR: 10–46 days). Pediatric subjects were more compliant with daily skin insect repellent use, reported mosquito bites more frequently, and were more likely to have been in contact with animals than adult subjects. There were no significant differences in rates of self-reported illnesses.

To demonstrate that our results were not skewed by gender (adult dependents consisted largely of women), we looked at a matched set of active duty personnel and found they were similar with respect to compliance with protective measures and illnesses (Supplemental Table 1).

Pediatric subjects traveled to regions with intermediate or high risk of TD,⁷ and two-thirds traveled to regions endemic for malaria. Although the study was limited by a relatively small sample size, our results are consistent with prior studies.^{8,9}

TABLE 2

Demographic and trip characteristics of 81 pediatric travelers matched by geographic region of travel, malaria risk at destination, and duration of travel adult military dependents

Demographic and trip characteristic	Pediatric travelers (n = 81)	Dependent adult travelers (n = 81)	P-value
Male, N (%)	40 (48)	6 (7)	< 0.01
Nonwhite race, N (%)	46 (57)	26 (32)	0.02
Born outside the United States, N (%)	9 (11)	26 (32)	< 0.01
Interval between pretravel visit and departure date ≤ 14 days, N (%)	24 (29)	19 (23)	0.45
Median trip duration—days (IQR)	16 (11–25)	15 (9–23)	0.65
Reason for travel: visiting friends and relatives, N (%)	29 (36)	13 (16)	0.01
Exposures, compliance with preventive measures, and illnesses*	Pediatric travelers (n = 48)	Dependent adult travelers (n = 69)	
Skin exposure†	27 (56)	28 (41)	0.1
Animal contact‡	19 (40)	14 (20)	0.02
Feeding	4 (8)	3 (4)	0.44
Hunting/fishing	1 (2)	0 (0)	0.41
Riding/touching/petting	16 (33)	11 (16)	0.03
Other	1 (2)	4 (6)	0.65
Dietary risk behaviors			
Food prepared by street vendors	37 (82)	49 (75)	0.51
Consuming raw foods	30 (67)	36 (55)	0.29
Drinking untreated water	7 (16)	18 (28)	0.1
Ice in beverages	23 (51)	37 (57)	0.43
Mosquito bites reported	33 (69)	30 (44)	< 0.01
> 10 mosquito bites	15 (31)	6 (9)	< 0.01
Used a skin insect repellent greater than or equal to once/day	33 (69)	30 (45)	0.01
Used an insecticide on outer clothing	7 (17)	18 (32)	0.10
Used a bed net‡	11/24 (46)	16/32 (50)	0.97
Partial or noncompliance with malaria chemoprophylaxis§	3/32 (9)	8/46 (17)	0.64
TD	7 (15)	15 (22)	0.33
Influenza-like illness	4 (8)	12 (17)	0.16
Febrile illness	5 (10)	2 (3)	0.12

TD = traveler's diarrhea. Statistically significant differences ($P < 0.05$) are represented in bold.

* Exposures, compliance with preventive measures, and illnesses only evaluated in subjects who completed a post-travel survey.

† Definitions for exposures reported by subjects (or their guardians): Skin exposure: walking barefoot on a rural terrain or beach, or wading in fresh water. Animal contact: close contact with wild or domesticated animals. Insect vectors: mosquito, tick, or other insect bites.

‡ Bed net use reported among those who were recommended a bed net at the pretravel consultation.

§ Partial or noncompliance with malaria chemoprophylaxis reported in those who were prescribed an antimalarial and was defined as missing ≤ 2 doses of weekly antimalarials (mefloquine or chloroquine) in a row or ≥ 3 doses of daily antimalarials (doxycycline, atovaquone/proguanil, or primaquine primary prophylaxis) in a row.

|| Definitions for travel-related illness: TD: as ≥ 3 unformed stools or two unformed stools with ≥ 1 accompanying symptom (nausea, vomiting, abdominal pain, fever, and blood in stool) within 24 hours. Influenza-like illness: subjective fever associated with either a sore throat or cough. Febrile illness: subjective fever not associated with diarrhea or influenza-like illness.

Children were more likely to be VFRs than matched adults—an important finding because children with foreign-born parents are more likely to travel before 5 years of age, have longer trip durations, and visit high-risk destinations for yellow fever, malaria, and typhoid, potentially increasing the risk of travel-associated infections.^{2,8} In addition, a higher proportion of children ≤ 5 years of age presenting for a travel-related illness in the GeoSentinel cohort were VFRs.² Providing effective pretravel counseling to VFR pediatric travelers with foreign-born parents may be challenging because of language barriers and perceptions regarding the risk of travel-related infections.¹⁰

Differences observed in hepatitis A and B coverage rates represent a missed opportunity for catch-up vaccination of adults (Table 1). Approximately 25% of travelers planned to depart within 14 days of the pretravel visit, decreasing the protective efficacy especially in cases with no prior vaccination. We observed low coverage rates in pediatric (12%) and adult (28%) subjects with a potential indication for rabies vaccination. Pediatric subjects reported animal contact at higher rates (40% versus 20% in adults) despite having a relatively short duration of travel (median duration was approximately 2 weeks). Given the risk of animal scratches or bites in young children, and the possibility for caregivers to be

unaware of such exposures, pretravel counseling should include the potential benefits of rabies vaccination in short-term pediatric travelers going to endemic countries. We also observed a higher incidence of mosquito bites and higher compliance with repellent use among children, similar to findings in prior studies showing a positive correlation between skin repellent use and mosquito bite frequency.^{11,12} Pretravel consultations should emphasize the importance of compliance with protective measures as an effective means of preventing both nuisance bites and vector-borne diseases.

Pediatric subjects, especially those younger than 10 years, were less likely to be prescribed antibiotics or antidiarrheal agents for the TD self-treatment than adult subjects despite similar rates of TD risk behaviors and incidence. These results are in line with published data¹³ and emphasize the need for evidence-based treatment guidelines for pediatric travelers. In adults with moderate or severe TD, antimicrobial agents have been demonstrated to effectively reduce clinical symptoms and shorten the duration of illness to about 1.5 days, and to less than one half day when combined with loperamide.¹⁴ Providers must also consider regional differences in pathogen distribution when selecting an antibiotic, as well as the potential for harm due to side effects or acquisition of multidrug-resistant organisms.^{15,16}

A **B**

Pediatric subjects	33	14	13	30	81	81	81
Adults	36	8	8	30	81	81	81

FIGURE 1. Pretravel preventive care provided to pediatric and adult travelers. (A) Coverage rates for routine and travel-related vaccinations among matched adult and pediatric travelers in whom vaccination was indicated ($P < 0.05$ indicated by asterisk on bar graph). (B) No. of subjects for whom vaccination was indication based (see Table 1 for indications).

This study has several limitations. Our assessment of travel risk and preventive care may not be generalizable to travelers who do not seek pretravel care or are seen by nonspecialized providers. By excluding active duty personnel and retirees, our adult comparator group consisted largely of women. Pediatric subjects had a lower post-travel survey response rate (41%) than adults (85%), likely because adults were required to complete an in-person post-travel study visit for a blood draw with a \$50 compensation, which was not performed in children. Other limitations include the potential for recall bias on surveys and the inability to capture additional factors relevant to vaccine administration (e.g., season of travel and exposure risk for Japanese encephalitis vaccine, or vaccine administration outside the military health system).

Our findings demonstrate important differences between adult and pediatric travelers that should be considered during pretravel consultation when prescribing relevant preventive and treatment measures.

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