

Bayesian hierarchical model (BHM) smoothed standardized incidence ratios (SIRs) for travel-acquired infections (TAIs) and estimated risk levels (a and c) with insets for the Greater Toronto Area (b and d). High-risk areas are defined as those with smoothed SIR 95% CIs greater than 2, and low-risk areas with smoothed SIR 95% CIs less than 0.25.

Conclusion. Urban neighbourhoods in the GTA had elevated risks of becoming ill with TAIs. However, geographic proximity to a travel clinic was not associated with an area-level risk reduction in TAI, suggesting other barriers to seeking and adhering to pre-travel advice.

Disclosures. Isaac Bogoch, MD, MSc, BlueDot (Consultant)/National Hockey League Players' Association (Consultant) Andrea Boggild, MSc MD DTMH FRCPC, Nothing to disclose Shaun Morris, MD, MPH, DTM&H, FRCPC, FAAP, GSK (Speaker's Bureau)/Pfizer (Advisor or Review Panel member)/Pfizer (Grant/Research Support)

738. Comparison of Characteristics of US International Travelers Seeking Pretravel Health Consultations at US Global TravEpiNet Sites Before and During the COVID-19 Pandemic

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Session: P-35. Global Health

Background. In January–March 2020, the Centers for Disease Control and Prevention (CDC) issued multiple warnings regarding COVID-19 travel-associated risks. We sought to describe US travelers seeking pretravel consultation regarding international travel at US Global TravEpiNet (GTEN) sites before and after the initial COVID-19 travel warnings.

Methods. We prospectively collected data at 22 GTEN sites pre-COVID-19 (January–December 2019) and 18 GTEN sites during the COVID-19 pandemic (April 2020–March 2021). We excluded travelers evaluated during January–March 2020, when CDC travel guidance was evolving rapidly. Travelers used standardized questionnaires to self-report data regarding demographics and travel-related characteristics. Providers confirmed these data and documented their recommendations during pretravel consultation, which could be performed virtually. We conducted descriptive analyses of differences in demographics, travel-related characteristics, vaccinations, and medications (SAS v9.4; Cary, NC).

Results. Compared with 16,903 pre-COVID-19 consultations, only 1,564 consultations occurred during the COVID-19 pandemic, a 90% reduction (Table). During COVID-19, a greater proportion of travelers were children aged 1–5 years, visiting friends and relatives (VFR), with itineraries ≥ 30 days, and going to Africa; a smaller proportion of travelers were aged > 55 years, or traveling to Southeast Asia or the Western Pacific. During COVID-19, fewer vaccine-eligible travelers received vaccines at the pretravel consultation except for yellow fever, and a greater proportion were referred to another provider for vaccination (Figure).

Table. Demographics and travel-related characteristics of international travelers seeking pretravel consultation at Global TravEpiNet sites before and during the COVID-19 pandemic

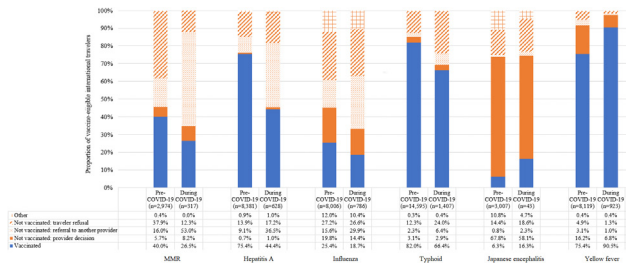
Characteristics	Pre-COVID-19 January 1, 2019 to December 31, 2019 (N = 16,903)	During COVID-19 April 1, 2020 to March 15, 2021 (N = 1,564)	p-value
Sex, No. (Col. %)			<0.001
Male	9,823 (58)	737 (47)	
Female	7,080 (42)	827 (53)	
Age, No. (Col. %)			<0.001
6 months–1 year	46 (<1)	10 (<1)	
1–5 years	454 (3)	158 (10)	
6–17 years	1,776 (11)	169 (11)	
18–55 years	12,565 (74)	1,152 (74)	
≥ 55 years	2,062 (12)	75 (5)	
Duration of travel, No. (Col. %)			<0.001
≤ 13 days	7,674 (45)	295 (19)	
14–29 days	6,740 (40)	445 (28)	
≥ 30 days	2,428 (15)	820 (53)	
Region of travel, No. (Col. %)*			<0.001
Africa	8,049 (48)	1,084 (69)	
Americas	4,370 (26)	295 (19)	
Southeast Asia	3,082 (18)	65 (4)	
Western Pacific	2,381 (14)	78 (5)	
Europe	805 (5)	69 (4)	
Eastern Mediterranean	988 (6)	141 (9)	
Reason for travel, No. (Col. %)*			<0.001
Visiting friends and relatives	1,525 (9)	501 (32)	
Business	1,948 (11)	239 (15)	
Humanitarian service work	2,347 (14)	284 (18)	
Research/education	1,146 (7)	35 (2)	
Leisure	9,322 (55)	395 (25)	
Other	615 (4)	110 (7)	

Table continued. Demographics and travel-related characteristics of international travelers seeking pretravel consultation at Global TravEpiNet sites before and during the COVID-19 pandemic

Characteristics	Pre-COVID-19 January 1, 2019 to December 31, 2019 (N = 16,903)	During COVID-19 April 1, 2020 to March 15, 2021 (N = 1,564)	p-value
Disease-endemic travel destination, No. (%)			
Destinations endemic for yellow fever	9,967 (59)	1,245 (80)	<0.001
Destinations endemic for Japanese encephalitis	3,069 (18)	57 (4)	<0.001
Destinations endemic for malaria	15,931 (94)	1,431 (92)	<0.001
Medications, No. (%)			
Prescribed any anti-malarial drugs	10,067 (63)	1,022 (71)	<0.001
Prescribed any medicines for travelers' diarrhea	11,666 (69)	653 (42)	<0.001
Prescribed any medicines for altitude sickness	1,040 (6)	38 (2)	<0.001
US census region of clinic site, No. (Col. %)			<0.001
Northeast	9,078 (54)	720 (46)	
Midwest	421 (2)	0 (0)	
South	4,488 (27)	519 (33)	
West	2,916 (17)	325 (21)	
Type of clinic, No. (Col. %)*			<0.001
Academic center	10,450 (62)	1,350 (86)	
Nonacademic center	6,453 (38)	214 (14)	

Abbreviations: Col., column
 * Travelers can contribute to ≥ 1 region if their itinerary includes multiple countries.
 † Travelers who noted more than one reason for travel are put into one category within this order (top to bottom).
 ‡ Academic centers are affiliated with university hospitals or medical schools; Non-academic centers include 7 public health clinics, 2 primary care clinics, 1 health network, and 1 pharmacy.

Figure. Vaccinations and reasons for nonvaccination among vaccine-eligible international travelers at pretravel consultations at Global TravEpiNet (GTEN) sites before and during the COVID-19 pandemic.



Among vaccine-eligible travelers, we summarized those who were vaccinated at the visit (blue) and not vaccinated (orange). We then categorized reasons for nonvaccination into: provider decision (solid), referral to another provider (dots), traveler refusal (striped), or other (hatched). COVID-19 vaccination was not available at GTEN sites during the analysis period; although COVID-19 vaccinations outside of GTEN sites might have affected vaccination recommendations, they were unlikely to have had a large effect given their limited availability in January–March 2021.

Conclusion. Compared with pre-COVID-19, US travelers seeking pretravel consultations at GTEN sites during the pandemic might be at higher risk for travel-related infections given VFR status, traveling for ≥ 30 days, and going to Africa. Fewer vaccine-eligible travelers were vaccinated at pretravel consultations, which could reflect more virtual pretravel consultations. Counseling and vaccination for international travelers continue to be priorities during the COVID-19 pandemic.

Disclosures. All Authors: No reported disclosures

739. Self-Reported Prevalence of Insect Bites During International Travel

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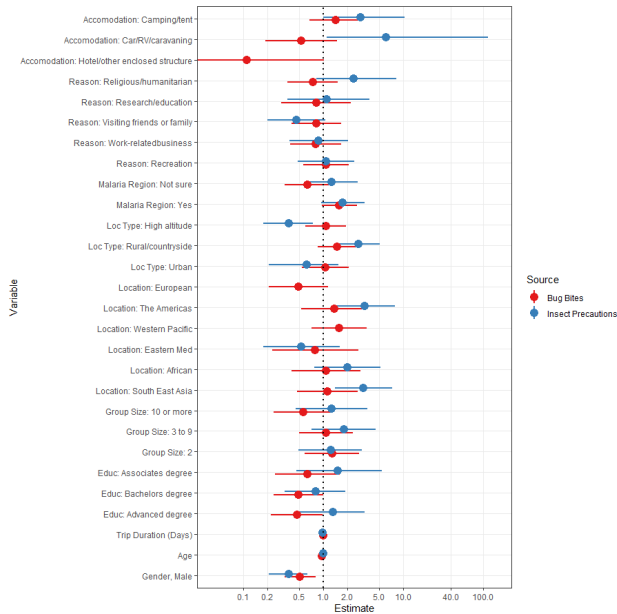
Session: P-35. Global Health

Background. Vector borne diseases are responsible for almost one fifth of global infectious disease burden. International travelers are at risk for potentially life-threatening conditions when visiting areas with endemic vector borne disease, but this risk can be mitigated when proper insect precautions are taken. This study sought to evaluate the prevalence of insect precaution use and subsequent insect bites among Utah travelers who have attended pre-travel consultations.

Methods. A cross-sectional study at the University of Utah and Salt Lake County travel clinics was analyzed. Descriptive statistics and multivariable logistic regression were used to explore factors associated with insect repellent use, and reporting bug bites despite insect repellent use.

Results. A total of 463 individuals completed the survey and were included in our analytic sample. The majority of respondents (80%) reported using insect repellent, and close to half (45%) reported bug bites. Insect repellent use was positively associated with visiting rural/countryside (OR 2.78, 95% CI 1.50 – 5.15), and traveling to South East Asia (OR 3.16, 95% CI 1.40 – 7.26), or Americas regions (OR 3.34, 95% CI 1.45 – 7.92). Being of male gender (OR 0.37, 95% CI 0.21 – 0.64) or traveling to high altitude locations (OR 0.37, 95% CI 0.18 – 0.74) was negatively associated with using insect repellent. Longer trip duration (OR 1.01, 95% CI 1.00 – 1.02) was positively associated with reporting insect bites, while male gender (OR 0.51, 95% CI 0.33 – 0.80), older age (OR 0.96, 95% CI 0.95 – 0.98), and having an advanced degree (OR 0.47, 95% CI 0.22 – 0.99) were negatively associated.

Estimated Risk Factors of Insect Bites and Insect Repellent Use



Characteristics of international travelers were self-reported in a cross-sectional study. Use of insect repellent and reporting bug bites despite repellent use was examined through multivariate logistic regression and used to calculate odds ratios and 95% confidence intervals. Due to multicollinearity and data skewness, the following variables were omitted from the insect repellent model: Accommodation: Hotel/other enclosed structure, Location: European, Location: and Western Pacific. Reference categories are Gender: Female, Education: High school diploma/GED or less, Group size: 1 (Traveled alone), Location type: Urban, and Malaria region: No. All other categories are not mutually exclusive and evaluated as separate binary variables.

Conclusion. We show that gender, age, trip duration, and education level were associated with self-reported bug bites during travel abroad. Given the number of vector-borne diseases affecting health of travelers, our findings will contribute towards strategies to advise travelers for disease prevention.

Disclosures. All Authors: No reported disclosures

740. Elucidation of the Mode of *Clostridioides difficile* Transmission Based on One Health Approach

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Session: P-35. Global Health

Background. Community-onset *Clostridioides difficile* (*C. difficile*) infection (CACDI) has been increasing in recent years. To explore the transmission route of CACDI, we performed the whole-genome sequencing of *C. difficile* isolated from CACDI patients and compared it to the isolates from livestock, companion animals, and soil.

Methods. From October 2020 until April 2021, fecal specimens of cattle, poultry, swine, felines, canines, CACDI patients, their families, and soil from the CACDI patients' living environment were applied for isolation of *C. difficile*. Whole-genome sequencing of *C. difficile* was performed on the MiSeq system (Illumina). Using the draft genome obtained from these analyses, the house-keeping gene (*tpi*), MLST, toxin genes (*tcdA*, *tcdB*, *cdtA*, *cdtB*), and resistance genes (*gyrA*, *gyrB*, *rpoA*, *rpoB*, *rpoC*) were comprehensively analyzed.

Results. As of March 31, 2021, 275 specimens were collected. Forty-five fecal specimens of companion animal origin (23 feline and 22 canines) were collected and the positive rate of *C. difficile* was 28.9% (2 felines, 11 canines). In MLST analysis, ST 15 (4 strains), ST 26 (2 strains), ST 42, ST 3, ST 28, ST 100, and ST 185 were detected in canines, and ST 203 and ST 297 strains were detected in felines. Samples of livestock origin were collected from 135 cattle, 41 poultries, and 20 swine. The detection rate in cattle was 11%, toxin-gene positivity was 60%. MLST analysis of 9 strains revealed ST 11 (5 strains), ST 2, ST 15, ST 58, and ST 101. No isolates were found from poultry

or swine. Patient-derived strains of CACDI were collected from 14 patients at 2 sites. MLST analysis revealed ST42, ST37, ST100, and ST203 (two isolates, respectively), ST 224, ST 81, ST 28, and ST 47. 2 isolates were unclassifiable. One case was a healthy 1-year-old girl, whose family revealed no isolation of *C. difficile*. Impressively, the soil in the parks (A and B) related to the child detected *C. difficile* from 4/4 samples (toxin-gene positivity; 75% in Park A and 1/4 samples (toxin-gene positive) in Park B. MLST analysis demonstrated ST 42, the same as that in the affected child and core-genome single-nucleotide polymorphisms (SNPs) analysis suggested closely related strain.

Conclusion. Our results suggest one health approach is fundamental to prevent the transmission of *C. difficile*.

Disclosures. All Authors: No reported disclosures

741. *Ehrlichia chaffeensis* Induced Hemophagocytic lymphohistiocytosis: A Descriptive Case Series

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Session: P-35. Global Health

Background. Hemophagocytic lymphohistiocytosis (HLH) secondary to tick borne illnesses is rarely reported. Clinical signs and symptoms of tick borne illnesses and HLH might overlap with fever, cytopenias and increased liver enzymes being common. We describe findings from case series of ehrlichiosis induced HLH.

Fever	16/16 (100%)
Splenomegaly (%)	5/16 (31%)
Cytopenias of 2 or more lineages	13/14 (92.8%)
Hypertriglyceridemia > 265mg/dL	13/16 (80%)
Fibrinogen (<1.5 g/dL)	4/13 (31%)
Soluble CD25 >2400 U/mL	7/7 (100%)
NK activity (low or absent)	N/A
Hemophagocytosis on Bone marrow	10/14 (71%)

Methods. We reviewed patients with ICD-10 codes corresponding to a diagnosis of HLH or macrophage activation syndrome (MAS) at University of Kentucky Medical Center between January 2008 and April 2020. Inpatients who were >18 years of age without known immune compromise were included. 4 cases with confirmed underlying ehrlichiosis were identified at our institution. We searched PubMed for English-language articles containing the terms "Hemophagocytic lymphohistiocytosis" and "infection" or "tick borne" or "Ehrlichia". Data on patient demographics, clinical signs and symptoms, laboratory data such as ferritin, platelet count, IL-2, NK cell activity, and outcomes were collected.

Results. We identified 16 cases of ehrlichiosis (1 had a coinfection with Rocky Mountain Spotted fever). Eleven out of 16 (68%) were male, median age was 58. All patients were febrile and thrombocytopenic on presentation and 8/14 (57%) were neutropenic. All had elevated ferritin (mean 36187 ng/mL, range 860 – more than 100000). CNS involvement was reported in 4 patients with a positive CSF *Ehrlichia chaffeensis* PCR. All patients met at least 5 2004-HLH defining criteria and 10/14 (71%) patients had evidence of hemophagocytosis on bone marrow biopsy (table 1). Fourteen out of 15 (93%) patients received doxycycline and 9/15 (60%) received steroids +/- etoposide. Mortality for Ehrlichia induced HLH was 12.5%, significantly lower than that reported for all secondary HLH mortality (45%).

Conclusion. This review highlights the importance of considering Ehrlichiosis as a cause of HLH in endemic areas particularly as clinical signs and symptoms of the 2 entities overlap. While overall mortality rate due to HLH is elevated, Ehrlichia induced HLH seems to have a much favorable prognosis with prompt institution antimicrobial treatment. Additional prognostic factors that correlate with a more severe course dictate need for immunosuppressive treatment need to be further elucidated.

Disclosures. Gerhard Hildebrandt, MD, Bayer, Scotts-Miracle, Charlottes Webb CWBHF, Alimmune Therapeutics Inc AIMT, Medical PPTYS TR Inc. MPW, Caretrust Reit Inc CTRE, ANGI Homeservices Inc (Shareholder) Bristol-Myers Squibb/Medarex, Crispr therapeutics, IDEXX Laboratories, Johnson & Johnson, Pfizer, Procter & Gamble, Vertex (Shareholder) Falk Foundation, Incyte, Takeda (Other Financial or Material Support, Travel, Accommodations, Expenses) Jazz Pharmaceuticals, Incyte, Morphosys, Alexion Pharmaceuticals, Karyopharm Therapeutics, Seattle Genetics (Consultant) Jazz Pharmaceuticals, Pharmacyclics, Incyte, AstraZeneca (Grant/Research Support) Novartis, Insys Therapeutics, Abbvie,