

Original Article

Refusal of recommended travel-related vaccines among U.S. international travellers in Global TravEpiNet

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Abstract

Background: International travellers are at risk of travel-related, vaccine-preventable diseases. More data are needed on the proportion of travellers who refuse vaccines during a pre-travel health consultation and their reasons for refusing vaccines.

Methods: We analyzed data on travellers seen for a pre-travel health consultation from July 2012 through June 2014 in the Global TravEpiNet (GTEN) consortium. Providers were required to indicate one of three reasons for a traveller refusing a recommended vaccine: (1) cost concerns, (2) safety concerns or (3) not concerned with the illness. We calculated refusal rates among travellers eligible for each vaccine based on CDC recommendations current at the time of travel. We used multivariable logistic regression models to examine the effect of individual variables on the likelihood of accepting all recommended vaccines.

Results: Of 24 478 travellers, 23 768 (97%) were eligible for at least one vaccine. Travellers were most frequently eligible for typhoid ($N=20\,092$), hepatitis A ($N=12\,990$) and influenza vaccines ($N=10\,539$). Of 23 768 eligible travellers, 6573 (25%) refused one or more recommended vaccine(s). Of those eligible, more than one-third refused the following vaccines: meningococcal: 2232 (44%) of 5029; rabies: 1155 (44%) of 2650; Japanese encephalitis: 761 (41%) of 1846; and influenza: 3527 (33%) of 10 539. The most common reason for declining vaccines was that the traveller was not concerned about the illness. In multivariable analysis, travellers visiting friends and relatives (VFR) in low or medium human development countries were less likely to accept all recommended vaccines, compared with non-VFR travellers (OR = 0.74 (0.59–0.95)).

Conclusions: Travellers who sought pre-travel health care refused recommended vaccines at varying rates. A lack of concern about the associated illness was the most commonly cited reason for all refused vaccines. Our data suggest more effective education about disease risk is needed for international travellers, even those who seek pre-travel advice.

Key words: International travel, vaccine refusal

Introduction

International travel by U.S. residents is increasing. In 2014, U.S. residents took more than 68 million trips to foreign countries, an increase of more than 10% from the previous year.¹ Many vaccine-preventable diseases in the United States, including

typhoid fever, hepatitis A, measles and influenza, are associated with international travel.² For instance, approximately 90% of all U.S. cases of typhoid fever between 2007 and 2011 occurred in travellers returning from overseas,³ and international travel is the most common risk factor for hepatitis A.⁴ In addition to

posing a risk to the individual traveller, vaccine-preventable diseases acquired during international travel can also spread among susceptible populations in the United States.^{5,6}

The pre-travel health consultation is the best opportunity for clinicians to optimize the health of international travellers, including the administration of recommended vaccines.⁷ This is especially important for travellers who may be at higher risk for travel-associated illnesses, such as those travellers who are visiting friends and relatives (VFRs) in lower-income countries.⁸ However, more data are needed describing the frequency with which travellers accept or refuse recommended vaccines at the pre-travel consultation.

We evaluated a large cohort of international travellers who obtained a pre-travel health consultation at clinical practices in Global TravEpiNet, a consortium of U.S. practices that provide health advice for international travellers. Our goal was to evaluate the proportion of travellers who refused recommended vaccines and to identify characteristics of the travellers that were associated with vaccine acceptance.

Methods

Global TravEpiNet

Global TravEpiNet (GTEN), supported by the Centers for Disease Control and Prevention (CDC), is a consortium of U.S. clinical practices that provide pre-travel health care to international travellers.⁹ GTEN sites are geographically distributed across the United States and include academic practices, health care consortia, health maintenance organizations, pharmacy-based clinics, private practices, and public health clinics. An institutional review board at each participating site either approved or exempted the study.

Study Population

We evaluated international travellers seen at 23 GTEN sites from July 1, 2012 through June 30, 2014. For each clinic visit associated with a unique itinerary, travellers used a secure internet tool to provide details about their medical history, destination countries, purpose(s) of travel, geographic type of travel (urban, rural, or both), planned activities and accommodations, and duration and dates of travel. Travellers were able to indicate multiple responses for purpose of travel and destination country. Clinicians verified the information provided by travellers and entered additional data about immunization history, health advice provided, vaccines administered or refused, and medications prescribed during the pre-travel encounter.

Countries were categorized based on the 2011 United Nations Human Development Index (UNHDI) (very high human development, high human development, medium human development, and low human development), as well as the 2009 World Health Organization geographical regions.^{10,11} In accordance with the CDC term, we defined a VFR traveller as an individual who was born in a low or medium human development country or whose parents were born in a low or medium human development country, who (1) selected 'travelling to region of origin of self or family to visit friends or relatives' as their purpose of travel or (2) stated that they would be pursuing a home stay with relatives on their trip.^{8,12} We categorized each GTEN site into one of four geographic regions, as defined by the U.S.

census: northeast (seven clinics), midwest (two clinics), south (eight clinics) and west (six clinics).¹³

Vaccine Eligibility

We evaluated refusal of nine vaccines; refusal of the measles-mumps-rubella (MMR) vaccine is being evaluated separately. Vaccine recommendations were continuously updated in accordance with guidance issued by the CDC Travellers' Health Branch (www.cdc.gov/travel). Clinicians were prompted to consider administration of each of these vaccines in the following circumstances:

- hepatitis A, influenza, meningococcal, tetanus-diphtheria/tetanus-diphtheria-acellular pertussis, and typhoid fever vaccines for all travellers;
- rabies vaccine for all travellers to a high-risk country with duration of travel greater than 28 days;^{8,14}
- polio vaccine for travellers to countries where polio vaccine was indicated, as defined by CDC recommendations current at the time of the visit;⁸
- Japanese encephalitis vaccine for individuals travelling to countries endemic for Japanese encephalitis; or¹⁵
- yellow fever vaccine for travellers to countries entirely endemic or partially endemic for yellow fever, as defined by CDC recommendations current at the time of the visit.⁸

We excluded travellers from our analysis of refusal of a given vaccine if (1) they had pre-existing immunity (as defined by a positive serology, a history of vaccination or if the provider deemed them immune based on their clinical review), (2) they had a medical contraindication to the vaccine or (3) the clinician deemed the vaccine as not indicated for the traveller's itinerary. We defined a vaccine 'refuser' as an individual who refused one or more of the recommended vaccines and a vaccine 'accepter' as an individual who accepted all the recommended vaccines. If a traveller refused a recommended vaccine, the clinician was required to indicate the traveller's rationale by selecting from one of the three choices: (1) traveller is not concerned about the illness, (2) traveller has cost concerns or (3) traveller has safety concerns.

Data Analysis

We first obtained frequency distributions of whether the traveller was provided vaccine at the visit, was eligible but refused, or was eligible and did not get vaccine for other reasons among the nine vaccines of interest. We also obtained the median (interquartile range [IQR]) number of vaccines that travellers were eligible to receive. We then obtained the distribution of the socio-demographic and travel characteristics among the vaccine accepters and refusers. We conducted multivariable models using random intercept logistic regression, with clinic site as the random effect, to examine the effect of individual variables on the likelihood of a traveller accepting all recommended vaccines. We obtained odds ratios (OR) and 95% confidence intervals (CI) from the multivariable model that included the following variables: the traveller's gender (female, male), purpose of travel (VFR, business, leisure, research/education, humanitarian service work), WHO destination region (East Asia and the Pacific, Europe and Central Asia, Latin America and the

Caribbean, Middle East, South Asia, Sub-Saharan Africa, North Africa, Western Europe), UNHDI region (very high human development, high human development, medium human development, low human development), presence of any medical problems (yes, no), geographic type of destination (rural or urban), U.S. region of clinic (northeast, midwest, south, west), age in years (0–5, 6–17, 18–64, 65+), time to departure in days (0–27, 28+) and length of trip in days (0–27, 28+). A two-sided *P* value < 0.05 was considered significant. Data analyses were performed using SAS 9.3 (Cary, N.C).

Results

Eligible Travellers

From 1 July 2012 to 30 June 2014, 24 478 international travellers were seen for pre-travel health consultation at 23 GTEN sites; 23 786 (97%) were eligible for at least one of the nine vaccines included in this analysis (Figure 1). Based on their travel plans and medical conditions, travellers were eligible for a median of three vaccines (range: 2–4). Clinicians recommended typhoid fever (*N* = 20 092), hepatitis A (*N* = 12 990) and influenza (*N* = 10 539) vaccines to the greatest number of travellers (Table 1). Rabies (*N* = 2650) and Japanese encephalitis (*N* = 1846) vaccines were recommended to the least number of travellers. High proportions of individuals eligible for rabies (43%), Japanese encephalitis (37%) and influenza (30%) vaccines did not receive the vaccine due to other reasons, such as referral to another provider, lack of time or lack of vaccine availability.

Refused Vaccines

Of the 23 786 travellers eligible for vaccination, 6573 (28%) refused one or more recommended vaccines (Figure 1). Among the 6573 who refused vaccines, 3418 (52%) refused one vaccine, 1117 (17%) refused two vaccines and 2038 (31%) refused three or more vaccines (data not shown). Meningococcal (2232 (44%) of 5029), rabies (1155 (44%) of 2650) and Japanese encephalitis (761 (41%) of 1846) were the three vaccines with the

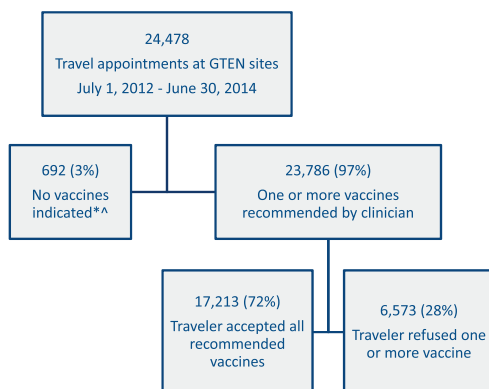


Figure 1. Acceptance or refusal of vaccines in the GTEN study population.

*Vaccines considered in this analysis included hepatitis A, influenza, Japanese encephalitis, meningococcal, polio, tetanus/diphtheria or tetanus/diphtheria/acellular pertussis, typhoid, rabies and yellow fever.

^Vaccines were deemed 'not indicated' if the traveller had pre-existing immunity, a medical contraindication, or if the provider stated that the vaccine was not indicated for the traveller.

Table 1. Traveller refusal of vaccines in the GTEN study population

Vaccine (N eligible)	Typhoid (N = 20 092) (%)		Hepatitis A (N = 12 990) (%)		Influenza (N = 10 539) (%)		Td/Tdap (N = 7923) (%)		Yellow fever (N = 7103) (%)		Polio (N = 5382) (%)		Meningococcal (N = 5029) (%)		Rabies (N = 2650) (%)		Japanese encephalitis (N = 1846) (%)	
	Vaccinated at visit	Traveller refused	Vaccinated at visit	Traveller refused	Vaccinated at visit	Traveller refused	Vaccinated at visit	Traveller refused	Vaccinated at visit	Traveller refused	Vaccinated at visit	Traveller refused	Vaccinated at visit	Traveller refused	Vaccinated at visit	Traveller refused	Vaccinated at visit	Traveller refused
	17 928 (89)	1690 (8)	10 608 (82)	1598 (12)	3813 (36)	3527 (33)	5648 (71)	1498 (19)	6038 (85)	917 (13)	3793 (70)	1367 (25)	2300 (46)	2232 (44)	351 (13)	1155 (44)	401 (22)	761 (41)
Not vaccinated for other reasons ^a	474 (2)	784 (6)	3199 (30)	777 (10)	148 (2)	222 (4)	777 (10)	148 (2)	222 (4)	497 (10)	1144 (43)	497 (10)	684 (37)					

^aOther reasons include referred to another provider for administration, insufficient time to complete prior to departure, vaccine not available.

highest proportions of vaccine refusers; of the 10 539 individuals offered the influenza vaccine, 3527 (33%) refused (Table 1).

Demographic Characteristics of Vaccine Refusers and Accepters

Table 2 shows the demographic characteristics of vaccine refusers and accepters. The most common purpose of travel was leisure, and 24% of leisure travellers refused one or more vaccines. Thirty-eight percent of VFR travellers refused one or more vaccines. The most common destinations of all travellers were Sub-Saharan Africa (39%), Latin American and the Caribbean (27%) and East Asia and the Pacific (22%). Among travellers to Sub-Saharan Africa, 33% of travellers refused one or more vaccines. Travellers to Europe and Central Asia and Western Europe had the lowest rates of vaccine refusal (20% each). Forty-four percent of travellers seen at GTEN sites in the south refused one or more vaccines; less than 15% of travellers seen at sites in the northeast refused one or more vaccines.

Reasons for Refusing Recommended Travel-Related Vaccines

We examined the reasons that travellers cited for declining each vaccine. For all vaccines, the most commonly cited reason for declining was that the traveller was not concerned about the illness (Table 3). Between 60% and 81% of all vaccine refusers, depending on the specific vaccine, cited a lack of concern about illness as their reason for refusing a given vaccine. Other reasons were prominent for some vaccines; more than one-third (35%) of those who refused Japanese encephalitis were concerned about cost and one-quarter of travellers who refused the yellow fever vaccine were concerned about the safety of the vaccine. We further evaluated the reason cited for declining vaccines among the subgroup of VFR travellers; the most commonly cited reason for all refused vaccines was not being concerned about the illness (data not shown).

Multivariable Predictors of Vaccine Acceptance

We performed a multivariable analysis to evaluate predictors of accepting all vaccines recommended at the pre-travel encounter (Table 4). VFR travellers were less likely to accept all of the recommended vaccines, compared with non-VFR travellers (OR [95% CI] = 0.74 [0.59–0.95]). Travellers with medical conditions were more likely to accept all vaccines (OR [95% CI] = 1.41 [1.11–1.80]). Age was inversely associated with vaccine acceptance, with the youngest patients (0–5 years) most likely to accept recommended vaccines (Table 4). Travellers with trip durations of less than 4 weeks were more likely to accept all vaccines than travellers with trip durations of greater than 4 weeks (OR [95% CI] = 1.41 [1.03–1.92]).

Discussion

Vaccine refusal has been receiving attention in the United States in recent years, and outbreaks of vaccine-preventable disease have occurred in clusters of under-immunized populations in the U.S.^{16,17} Ill returning international travellers have frequently played a role in precipitating these outbreaks, underscoring the importance of appropriate vaccination of international

Table 2. Demographics of vaccine refusers and accepters in the GTEN study population

	Vaccine eligible (<i>n</i> = 23 786)	
	Vaccine refusers ^a (<i>n</i> =6573) N (%) ^b	Vaccine accepters (<i>n</i> =17 213) N (%)
Gender		
Female	3760 (57)	9618 (56)
Male	2813 (43)	7595 (44)
Age (years)		
0–5	270 (4)	660 (4)
6–17	672 (10)	1538 (9)
18–64	5064 (77)	13337 (77)
65 +	567 (9)	1678 (10)
Purpose ^c (row %)		
VFR traveller (<i>n</i> = 2 284)	859 (38)	1425 (62)
Business traveller (<i>n</i> = 3894)	886 (23)	3008 (77)
Leisure traveller (<i>n</i> = 12 732)	3033 (24)	9699 (76)
Research/education (<i>n</i> = 2587)	598 (23)	1989 (77)
Humanitarian service work ^d (<i>n</i> = 4507)	1347 (30)	3160 (70)
Regions visited (WHO categories) ^e (row %)		
East Asia and the Pacific (<i>n</i> = 5207)	1355 (26)	3852 (74)
Europe and Central Asia (<i>n</i> = 480)	94 (20)	386 (80)
Latin America and the Caribbean (<i>n</i> = 6451)	1459 (23)	4992 (77)
Middle East (<i>n</i> = 1007)	267 (27)	740 (73)
South Asia (<i>n</i> = 3245)	758 (23)	2487 (77)
Sub-Saharan Africa (<i>n</i> = 9240)	3040 (33)	6200(67)
North Africa (<i>n</i> = 356)	75 (21)	281 (79)
Western Europe (<i>n</i> = 830)	165 (20)	665 (80)
UN Human Development Index ^{g,h}		
Very high human development	145 (2)	534 (3)
High human development	1016 (15)	3261 (19)
Medium human development	2797 (43)	7995 (46)
Low human development	2615 (40)	5423 (32)
Any medical condition		
Yes	3539 (54)	11 182 (65)
No	3034 (46)	6031 (35)
Geographic type of destination		
Urban only		
Rural only	568 (9)	1873 (11)
Both	4176 (63)	9977 (58)
Time to departure at clinic visit (days)		
0–27	3648 (55)	9415 (55)
≥ 28	2925 (45)	7798 (45)
Length of trip (days)		
0–27	4527 (69)	13678 (80)
≥ 28	2046 (31)	3535 (20)
Region of the United States ^e (row %)		
Northeast (<i>N</i> = 9125)	1351 (15)	7774 (85)
Midwest (<i>N</i> = 1168)	257 (22)	911 (78)
South (<i>N</i> = 7021)	3074 (44)	3947 (56)
West (<i>N</i> = 6472)	1891 (29)	4581 (71)

^aRefused one or more recommended vaccines.

^bPercentages are column percents unless otherwise indicated.

^cTravellers with multiple purposes of travel/destinations visited were included more than once; therefore, totals sum to >100%.

^dHumanitarian service work includes medical service work, non-medical service work, and missionary work &Based on the region visited with the lowest 2011 UN Human Development Index score.

^eLocation of GTEN sites in the four US census regions: Northeast includes Massachusetts, New Jersey, New York and Pennsylvania; Midwest includes Illinois and Minnesota; South includes District of Columbia, Florida, Georgia, Louisiana, Maryland, Texas, Virginia and West Virginia; West includes California, Hawaii and Utah.

Table 3. Reason for refusing vaccines among travellers in the GTEN study population

Vaccine (N refused)	Reason traveller refused vaccine		
	Not concerned with illness N (%)	Concerned with vaccine safety	Concerned with vaccine cost
Influenza (N = 3527)	2851 (81)	526 (15)	150 (4)
Meningococcal (N = 2232)	1744 (78)	311 (14)	177 (8)
Typhoid (N = 1690)	1230 (73)	171 (10)	289 (17)
Hepatitis A (N = 1598)	1169 (73)	245 (15)	184 (12)
Tetanus (N = 1498)	1140 (76)	257 (17)	101 (7)
Polio (N = 1367)	1098 (80)	181 (13)	88 (6)
Rabies (N = 1155)	3340 (78)	421 (10)	517 (12)
Yellow fever (N = 917)	612 (67)	225 (25)	80 (9)
Japanese encephalitis (N = 761)	460 (60)	35 (5)	266 (35)

travellers.^{6,18} In our study, we observed that more than one-quarter of travellers who sought pre-travel health advice refused at least one vaccine during the pre-travel health encounter.

A lack of concern about the illness was the single most common reason that travellers cited for refusing recommended vaccines during the pre-travel health encounter. This was true for all nine of the vaccines we evaluated and included both travel-related vaccines (e.g. typhoid, yellow fever, rabies and Japanese encephalitis) and vaccines with routine indications (e.g. influenza and Td/Tdap). U.S. travellers may be unfamiliar with diseases that have low incidence and prevalence outside this country; hence, it is expected that their level of concern for such diseases is low. For instance, Japanese encephalitis, a disease not present in the United States, was among the vaccines with the highest proportion of refusers (41% of eligible travellers). Notably, more than one-third of travellers refused influenza vaccine, which is recommended for all U.S. individuals who are 6 months of age or older without contraindications.¹⁹ Previous studies have shown that U.S. adults refuse influenza vaccine at similar or even higher rates than our study participants, often due to lack of concern about the illness.^{20,21}

Prior to our study, some had hypothesized that cost might be an important barrier to uptake of vaccines among international travellers, since out-of-pocket expenses can be higher for travel-related vaccines than for routine vaccines.^{22,23} In fact, we found that cost was rarely cited as a motivating factor for vaccine refusal, with the notable exception of the Japanese encephalitis vaccine. Not surprisingly, nearly one-quarter of travellers who refused the yellow fever vaccine cited safety concerns, which likely reflects the known risk of viscerotropic and neurotropic adverse events after the vaccine.²⁴ Of note, we observed that other barriers, aside from refusal by the traveller (i.e. lack of time prior to departure or lack of available vaccine), contributed to the failure to vaccinate many travellers for rabies and Japanese encephalitis.

Certain types of travellers were more likely to refuse vaccines, including VFR travellers and long-term travellers (≥ 28 days). This observation is of particular note because these travellers have previously been identified as being at higher risk of travel-related illness. For instance, a large study of returned travellers

Table 4. Multivariable logistic regression model of acceptance of all recommended vaccines

Variable	Odds ratio (95% confidence intervals) ^a
Gender	
Female	0.96 (0.85, 1.08)
Male	REF
Purpose of Travel	
Leisure traveller ^b	1.14 (0.87, 1.49)
Business traveller ^b	1.28 (0.99, 1.65)
Humanitarian Service Work ^b	1.07 (0.80, 1.44)
Research/Education ^b	1.30 (0.99, 1.69)
VFR traveller ^b	0.74 (0.59, 0.95) ^d
Region Visited (based on lowest income country visited, WHO)	
East Asia and the Pacific ^b	0.80 (0.56, 1.14)
Europe and Central Asia ^b	1.25 (0.74, 2.09)
Latin America and the Caribbean ^b	1.19 (0.81, 1.75)
Middle East ^b	1.05 (0.64, 1.72)
North Africa ^b	1.08 (0.54, 2.17)
Western Europe ^b	1.21 (0.83, 1.75)
South Asia ^b	0.97 (0.73, 1.27)
Sub-Saharan Africa ^b	0.87 (0.60, 1.26)
Human Development	
Low Human Development	0.76 (0.45, 1.30)
Medium Human Development	0.80 (0.51, 1.26)
High Human Development	0.72 (0.45, 1.16)
Very High Human Development	REF
Medical condition	
Yes	1.41 (1.11, 1.80) ^d
No	REF
Geographic destination	
Rural Only	1.17 (0.90, 1.53)
Both Rural and Urban	1.08 (0.85, 1.38)
Urban Only	REF
United States region ^c	
Midwest	1.09 (0.03, 46.18)
South	0.99 (0.06, 16.90)
West	1.16 (0.06, 23.31)
Northeast	REF
Age (years)	
6–17 years	0.62 (0.34, 1.12)
18–64 years	0.46 (0.31, 0.69) ^d
65+ years	0.51 (0.32, 0.80) ^d
0–5 years	REF
Time to departure (days)	
0–27 days	1.06 (0.82, 1.39)
28 + days	REF
Length of travel (days)	
0–27 days	1.41 (1.03, 1.92) ^d
28 + days	REF

^aObtained from random intercept logistic regression models with clinic site as the random effect. Adjustment for small number of clinics was made for all analyses.

^bVariables were coded as Yes/No with the group 'No' used as the reference (Example: VFR-Traveller (Yes vs No)).

^cGTEN sites distributed in the four U.S. census regions: Northeast includes Massachusetts, New Jersey, New York and Pennsylvania; Midwest includes Illinois and Minnesota; South includes District of Columbia, Florida, Georgia, Louisiana, Maryland, Texas, Virginia and West Virginia; West includes California, Hawaii and Utah.

^dStatistically significant.

from the GeoSentinel network found that being a VFR traveller was an independent predictor of acquiring a vaccine-preventable disease during travel.² Similarly, long-term travellers have been identified to be at higher risk of a number of infectious diseases, including hepatitis, typhoid and rabies, as the risk of illness increases with increased duration of travel.^{8,25,26} Additionally, nearly half (44%) of travellers seen at clinics in the south refused vaccines, suggesting regional variability in vaccine refusal.

Our findings are similar to studies of vaccine refusal among parents of school-aged children, which have identified that a low perceived susceptibility to, and severity of, vaccine-preventable diseases were important factors associated with failure to vaccinate.²⁷ This similarity suggests that the development of strategies to address vaccine refusal during the pre-travel health encounter could be informed by lessons learned in the paediatric population. In particular, studies have shown that health care providers are the most frequent and most trusted source of vaccine-related information, even for those who refuse vaccines—indicating that health care providers can have a positive influence on those who are hesitant to receive vaccines.^{27,28} Travel medicine providers may, therefore, focus more on sharing destination-specific information about disease risk and educating travellers on the health consequences of travel-related vaccine-preventable diseases. Materials that are culturally appropriate and considered to be from trustworthy sources would be useful in these efforts.

Our study has limitations. Travellers seen at GTEN sites may not be representative of all U.S. international travellers, and clinical practice at GTEN sites may differ from other settings where pre-travel health care is provided. We did not collect information regarding the nature of pre-travel health counselling about vaccine-preventable diseases and, hence, cannot comment on the quality or content of this effort in our study population. We also are unable to evaluate the consistency of the reasons that providers used to characterize vaccine refusal.

Our study suggests that educating travellers about travel-related illness, including a focus on those who are already seeking pre-travel health care, might be a valuable tool for increasing vaccine uptake. We found that lack of concern about the illness was the most commonly cited reason for refusing vaccines; hence, educational efforts should appropriately focus on the natural history and potential severity of these illnesses. Increasing the uptake of travel-related vaccines is important, not only for the individual traveller's health, but also for the health of their home communities.

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