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Missed opportunities for MMR vaccination among departing U.S. adult travelers receiving pretravel health consultations

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Abstract

Background—Measles outbreaks continue to occur in the United States and are mostly due to infections in returning travelers.

Objective—We described how providers assessed the measles immunity status of departing U.S. adult travelers seeking pretravel consultation and assessed reasons given for nonvaccination among those considered eligible to receive the measles-mumps-rubella (MMR) vaccine.

Design—Observational study in U.S. pretravel clinics.

Setting—24 sites associated with Global TravEpiNet (GTEN), a Centers for Disease Control and Prevention-funded consortium.

Patients—Adults (born in or after 1957) attending pre-travel consultations at GTEN sites (2009-2014).

IRB Approval: An institutional review board at all 24 participating sites either approved the study or considered it exempt from review.

Measurements—Structured questionnaire completed by traveler and provider during pretravel consultation.

Results—We included 40,810 adult travelers; providers considered 6,612 (16%) to be eligible for MMR vaccine at the time of pretravel consultation. Of the MMR-eligible, 3,477 (53%) were not vaccinated at the visit; of these, 1,689 (48%) were not vaccinated due to traveler refusal, 966 (28%) due to provider decision, and 822 (24%) due to health systems barriers. Most MMR-eligible travelers who were not vaccinated were evaluated in the South (2,262 travelers, 65%) or at nonacademic centers (1,777 travelers, 51%). Nonvaccination due to traveler refusal was most frequent in the South (1,432 travelers, 63%) or at nonacademic centers (1,178 travelers, 66%).

Limitations—Our estimates could underrepresent the opportunities for MMR vaccination, as providers accepted verbal histories of disease and vaccination as evidence of immunity.

Conclusions—Sixteen percent of U.S. adult travelers who presented for pretravel consultation at GTEN sites met criteria for MMR vaccination according to the provider's assessment, but fewer than half of these travelers were vaccinated. An increase in MMR vaccination of eligible U.S. adult travelers could reduce the likelihood of measles importations and transmissions.

Introduction

In 2000, endemic measles was eliminated in the United States (1). Nevertheless, measles outbreaks persist due to imported cases (2). More than half of such measles importations occur in returning unvaccinated U.S. travelers who acquire infection with measles while abroad; these individuals may infect others following their return to the United States (3).

Since 1989, the Advisory Committee on Immunization Practices (ACIP)has recommended two documented doses of measles-mumps-rubella (MMR) vaccine for all adult international travelers without evidence of prior measles immunity (4, 5). The risk of acquiring measles is greatly increased outside the U.S. (6, 7), and air travel has been associated with measles transmission (8). When evaluating patients before international travel, some healthcare providers may not be aware that measles is a travel-associated illness, despite ACIP recommendations (7).

A single imported measles case can lead to many secondary and tertiary cases, so imported measles cases often have a wide-reaching impact in the United States (2). Measles spreads via aerosolized droplets and is highly infectious; ninety percent of exposed, unvaccinated people will become ill with measles after entering a room that housed an infected person for up to two hours beforehand (9). The risks of measles transmission are magnified in communities with a higher prevalence of unvaccinated adults and children (10), such as occurred with the so-called "Disneyland" outbreak of measles in 2015, when an infected visitor to Disneyland led to 147 reported cases in 7 states (11). Similarly, just two imported measles cases from travelers returning from the Philippines in 2014 led to an outbreak of 383 cases in Ohio in a primarily unvaccinated Amish community (12, 13).

In this multisite observational study, our goal was to describe how clinicians who are experienced in providing pretravel medical advice assess for measles immunity at pretravel

medical encounters and to examine reasons for nonvaccination among those who are MMR vaccine-eligible.

Methods

Study setting

Global TravEpiNet (GTEN) is a consortium of clinical sites throughout the United States that provide pretravel health advice and vaccination (14). Fourteen sites are academic centers which have affiliations with university hospitals or medical schools; the 10 other sites are primary care practices, pharmacies, and public health clinics. Each GTEN site prospectively and systematically collects data regarding every pretravel health consultation. The 24 sites that contributed data to this analysis are in four census regions of the United States: Northeast (8 sites), Midwest (2 sites), South (8 sites), and West (6 sites) (15).

Study population and eligibility criteria

Travelers were included if they were aged 18 years or older when they visited a GTEN clinical site for pretravel health consultation between January 1, 2009 and December 31, 2014. Travelers born before 1957 were excluded because life-long natural measles immunity is assumed in this age group and thus ACIP does not recommend MMR vaccination (5).

Data collection, assessment of measles immunity and vaccine eligibility, and clinical management of the vaccine-eligible

During the pretravel consultation, travelers and providers used an online structured questionnaire, as previously described (14),(16). Travelers entered information into the structured questionnaire regarding their age, medical conditions, and travel itinerary (e.g., destination(s), reason for travel, and duration of travel). Providers confirmed the information entered by the traveler, and then entered additional data about immunization history, health advice provided, vaccines administered (including MMR), and medications prescribed during the pretravel consultation.

Providers assessed travelers' measles immunity status during the pretravel health encounter in accordance with their routine clinical practice. As such, self-reported immunization or measles illness history may have been accepted. The structured questionnaire required providers to characterize their assessment of measles immunity in one of four ways: (1) a history of two MMR vaccinations, (2) a positive measles serology, (3) a prior measles illness, or (4) "immune per provider judgment" (i.e. the provider considered the traveler immune but did not indicate a specific reason).

Regardless of the time until departure, the structured questionnaire required providers to consider MMR vaccination for all travelers not considered immune for one of the reasons listed above and who had no medical contraindication to MMR vaccination (i.e. pregnancy or immunosuppression), as per ACIP guidelines (4, 5). In this analysis, we term these travelers "MMR-eligible". If providers did not vaccinate a MMR-eligible traveler, they were required to select one of the following five explanations: (1) traveler refusal, (2) vaccination not indicated for this patient/itinerary, (3) insufficient time for vaccination before departure,

(4) vaccine unavailable at the clinic, or (5) referral to another provider for vaccination. Before 2012, providers did not record a specific reason for traveler refusal of a recommended MMR vaccine. Beginning in 2012, providers were required to select only one of the following three reasons for why travelers refused vaccination: (1) traveler is concerned about vaccine safety, (2) traveler is concerned about vaccine cost, or (3) traveler is not concerned about the vaccine-preventable illness.

Statistical analyses

We characterized adult travelers into two cohorts depending on their birth year (1957-89 and 1990) because the recommendation to vaccinate all children aged 1 year routinely with two doses of MMR vaccine began in 1989 (4, 5).

We grouped destination countries into six geographic regions, as defined by the World Health Organization (WHO) in 2012: Americas, Africa, Eastern Mediterranean, Europe, South-East Asia, and Western Pacific (17). Reasons for travel included business, humanitarian service work, leisure, research/education, visiting friends and relatives (VFR), and other (18). We defined VFR travelers according to the CDC definition: travelers to a low- or low-middle-income country of their or their parents' birth who stated the reason for travel was "traveling to region of origin of self or family to visit friends or relatives" or who noted that they would stay with relatives during the itinerary (19). We dichotomized travel duration into <14 days and 14 days (14 days being the median duration). We categorized the location of GTEN clinic sites into the four U.S. census regions (i.e., Northeast, Midwest, South, West). We dichotomized the type of clinic into academic centers (i.e., 14 sites that were affiliated with university hospitals or medical schools) and nonacademic centers (i.e., 10 sites that were primary care practices, pharmacies, and public health clinics). We grouped reasons that were provided for not vaccinating the MMR-eligible into three categories: traveler refusal (i.e., traveler declined because of lack of concern about measles or concerns about vaccine safety or cost); provider decision (i.e., provider considered that the vaccine was not indicated or provider reported that there was insufficient time to vaccinate before travel); and health systems barriers (i.e., referral of the traveler to another provider for vaccination or the vaccine was unavailable at the travel clinic).

Analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC). We obtained summary statistics (proportions, means, medians and standard deviations) for the demographic and travel-related characteristics, overall and within subgroups of travelers with measles immunity, medical contraindication to vaccination, vaccine eligibility, and nonvaccination among the MMR-eligible, in the four U.S. census regions.

Results

Providers assessed 54,100 adult travelers at 24 GTEN sites (Figure 1). We excluded 13,290 travelers because they were born before 1957 and therefore were presumed to be immune to measles infection. The distribution of sites and travelers from different U.S. census regions is described in Supplementary Appendix Table A1.

Of the 40,810 study participants, 22,987 (56%) were female (Table 1). The median age of travelers was 33 years (interquartile range [IQR] 26-44); 35,035 (86%) were born between 1957 and 1989. Africa was the most common destination region with 14,471 (36%) travelers, followed by 11,562 (28%) travelers to the Americas. Of all travelers, 20,507 (50%) were planning travel for leisure; 3,208 (8%) were VFR travelers. The median duration of travel was 14 days (IQR 10-24).

Providers deemed 34,092 travelers (84%) to be immune to measles based on their clinical assessment. Of these, providers considered 24,884 (73%) to be immune because of a history of receiving 2 MMR vaccinations, a positive measles serology (3,479; 10%), or a history of measles illness (1,024, 3%); the remainder were considered immune per provider judgment (5,985, 18%) (Figure 1). Among the 6,718 nonimmune travelers, 106 had a medical contraindication to MMR vaccination. A total of 6,612 (16%) adult travelers were therefore eligible for MMR vaccination at the pretravel consultation.

Providers were required to consider MMR vaccination for all international travelers. Of the 6,612 MMR-eligible travelers, 3,477 (53%) were not vaccinated at the pretravel encounter (Figure 1). We observed variability in the proportion of MMR-eligible travelers who were not vaccinated across GTEN sites. At three sites, providers considered no travelers to be MMR-eligible. Of the MMR-eligible travelers evaluated at the remaining 21 sites, providers vaccinated none of the MMR-eligible travelers (84 travelers, 1% of MMR-eligible) at two sites, <10% of all MMR-eligible travelers (1,477 travelers, 22% of MMR-eligible) at three, additional sites, and 10-50% of all MMR-eligible travelers (3,563 travelers, 54% of MMR-eligible) at only six sites.

We evaluated the demographic and travel-related characteristics of MMR-eligible travelers who were vaccinated or not (Table 2). More than half (1,887 travelers, 54%) of the 3,477 MMR-eligible travelers who were not vaccinated were female; 401 (12%) were VFR travelers. The majority of MMR-eligible travelers who were not vaccinated were seen at GTEN sites in the South (2,265 travelers, 65%), and more were seen at non-academic centers (1,777 travelers, 51%) than at academic centers (1,700 travelers, 49%).

Providers were required to provide a rationale when MMR vaccine was not administered to those who were MMR-eligible (Figure 1). Of the 3,477 MMR-eligible travelers who were not vaccinated, 1,689 (48%) were not vaccinated because of traveler refusal, 966 (28%) due to provider decision, and 822 (24%) due to health systems barriers.

Beginning in 2012, providers assessed the reasons why travelers refused MMR vaccine (Figure 1). Of the 958 travelers who refused MMR vaccine in 2012 or after, the most frequent reason cited for refusal was that the traveler was "not concerned about illness" (711 travelers, 74%). We also assessed the reasons why providers did not offer MMR vaccine to MMR-eligible travelers. Of the 966 travelers who were not vaccinated because of the provider's decision, most were not vaccinated (911 travelers, 94%) because the provider thought the MMR vaccine was not indicated; only 55 (6%) travelers were not vaccinated because the provider thought there was insufficient time before travel. Of the 822 travelers

who were not vaccinated due to health systems barriers, the predominant barrier was referral to another provider for vaccination (812 travelers, 99%).

The majority of MMR-eligible travelers (51%) who were not vaccinated were evaluated at nonacademic sites (Table 2), despite the fact that only 27% of all travelers were seen at nonacademic sites (Table 1). Of the 1,777 MMR-eligible travelers evaluated at nonacademic centers who were not vaccinated, 1,178 (66%) were not vaccinated due to traveler refusal.

We further examined the differences observed in MMR eligibility and vaccination among GTEN sites in different U.S. census regions (Table 3; demographic data in Supplementary Appendix Table 2). Providers at the eight clinical sites in the South evaluated 9,692 travelers and considered 2,952 (30%) of these travelers to be MMR-eligible. Of the MMR-eligible travelers in the South, 2,262 (77%) were not vaccinated with MMR, and the most common reason stated for nonvaccination was traveler refusal (1,432 travelers, 63%). In contrast, 2,695 (17%) of the 15,477 travelers seen at the eight clinical sites in the Northeast were considered eligible for MMR vaccination, and only 751 (28%) were not vaccinated. Provider decision was the most common reason for failure to vaccinate an MMR-eligible traveler in the Northeast (391 travelers, 52%).

Discussion

Routine assessment of measles immunity and vaccination with MMR before international travel is an essential means to reduce measles importations into the United States (20, 21). We evaluated the clinical practice of MMR vaccination in GTEN, the largest consortium of clinical sites providing pretravel health care in the U.S. Providers concluded that 16% of adults traveling internationally needed MMR vaccination at the time of their pretravel health consultation, yet more than half (53%) of those individuals were not vaccinated at the pretravel encounter. Our findings underscore that strategies are needed to improve provider and traveler knowledge of measles as a travel-related illness and to increase pretravel uptake of the MMR vaccine. Improving vaccination rates is particularly important for communities with a higher percentage of nonimmune individuals, since there is a greater risk of transmission events following an index case in these settings (10, 22, 23).

Nonvaccination was most commonly due to traveler refusal of MMR, with lack of concern about measles cited as the most common reason. This is consistent with prior GTEN analyses of vaccine uptake at pretravel encounters (24). Although clinics in the GTEN consortium are not selected on the basis of vaccination coverage in specific communities, traveler refusal was particularly predominant in clinical sites in the South, suggesting geographic variability in the understanding of measles and the benefits of MMR vaccination (18). Travelers were also more likely to refuse MMR vaccination after evaluation at nonacademic centers than at academic centers; patients evaluated in the South were not more likely to be seen at a nonacademic center. These findings support that providers may benefit from additional training on how to discuss beliefs regarding measles vaccine and the realities of clinical illness with measles, which vaccine-hesitant patients often minimize (25, 26). Few travelers in this study expressed concerns about MMR vaccine safety or cost; providers

should ask travelers explicitly about any safety or cost concerns, as travelers may not state them directly (27).

Our findings also indicate that providers might benefit from education regarding pretravel MMR vaccination. More than a quarter of all missed opportunities for vaccination were because the provider did not recommend the MMR vaccine to eligible travelers. Providers at nonacademic centers, in particular, were less likely to recommend MMR vaccination to eligible travelers. This observation is consistent with previous work indicating that providers deviate from ACIP and CDC recommendations for other travel-related vaccines (28, 29).

Health systems barriers played a role in 24% of missed opportunities for vaccination. In the majority of instances, providers referred travelers to another provider, likely a primary care provider, for MMR vaccination. Although some travelers may have obtained MMR vaccination from a primary care provider before departure, attrition after referral may have occurred in some travelers because an additional clinic visit is required. Referral to another provider could be an attempt to ensure that records of vaccinations stay with primary care providers, given that the Immunization Information Systems (IIS) are not in widespread use (30). Alternatively, providers could refer patients in an attempt to reduce costs for travelers because "travel-related" vaccinations are not uniformly covered by health insurance even if they are covered as part of routine care. Given the serious public health implications of undervaccination, strong consideration should be given to requiring insurers to cover MMR vaccination regardless of the site of delivery.

With more than 30 million U.S. residents traveling internationally by air every year (31), almost 5 million travelers could be at risk for measles infection when traveling abroad, if our study's findings apply to the overall population of U.S. travelers. MMR vaccination for nonimmune travelers could be a cost-effective strategy to reduce measles cases in the United States given the low cost of vaccination (32), the vaccine's two-dose effectiveness of 97% (6), and the low likelihood of vaccine-related adverse events (33), especially in the context of the morbidity and costs associated with measles infection (34-36), secondary cases caused by transmission (37, 38), and the expensive outbreak investigations required with any new case of measles in the United States (37, 38). Further evaluation of the cost-effectiveness of pretravel measles vaccination is warranted given the low probability of exposure during travel but high impact of any imported measles cases.

Our study has limitations. While GTEN is the largest consortium of clinics providing pretravel health care in the United States, clinical practice at GTEN sites may not be representative of all pretravel health consultations and GTEN patients may not be representative of all U.S. travelers. In particular, health-seeking behavior may be more common among travelers who pursue a pretravel consultation; our study population may therefore be more likely to be up-to-date on routine vaccines and to agree to recommended vaccines than the general population of international travelers. GTEN providers assessed measles immunity as it is commonly carried out in clinical practice, but their estimates may be imprecise. For instance, GTEN providers at times relied on immunization histories obtained by traveler recall and also allowed a history of measles illness and self-reported vaccination to be considered adequate evidence of measles immunity. This is more lenient

than current ACIP guidelines (4, 5), and overestimation of measles immunity may therefore have occurred. However, an overestimation of measles immunity would result in even more opportunities for MMR pretravel vaccination than our analysis suggests. Because our study provides data only regarding actions taken at GTEN sites, we were not able to report the percentage of travelers who were successfully vaccinated with MMR by another provider prior to travel.

In conclusion, our results indicate that measles immunity could be increased among U.S. international travelers. Increasing measles immunity in travelers should substantially reduce the risk of measles importation and, by extension, decrease the number of new measles cases seen due to transmission within the U.S. Strategies to improve traveler knowledge are essential to these efforts and should include materials specifically designed for travelers who express lack of concern about measles illness. Measles education strategies should also be targeted to providers and focus on geographic regions with low uptake of MMR vaccination for international travelers. Because MMR vaccination is recommended for all immunocompetent and non-pregnant U.S. international travelers, primary care providers could routinely ask patients about upcoming travel plans and vaccinate those eligible for MMR. Further study of the role of primary care providers in improving measles population immunity is warranted. In light of recent measles outbreaks associated with travel, pretravel measles immunity screening for U.S. adults traveling internationally and MMR vaccination for those eligible should be prioritized.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Assessment of adult travelers' measles immunity and action regarding MMR vaccination by providers at 24 GTEN sites (2009-2014).

Abbreviations: MMR, measles-mumps-rubella; GTEN, Global TravEpiNet; h/o, history of. *At least one specific reason supporting measles immunity was documented for 28,107 (82%) of these travelers (i.e., a history of two MMR vaccinations, a known positive serology, or a self-reported history of illness). Providers were able to select more than one supporting reason:1,017 (4%) travelers had 2 MMR vaccinations and a positive serology; 220 (0.8%) travelers had 2 MMR vaccinations and a self-reported history of illness; and 53 (0.2%) travelers had a positive serology and a self-reported history of illness.

[†]Of the 24,884 travelers for which providers noted two prior doses of MMR vaccine, providers noted specific supporting evidence (i.e. a date) for prior vaccinations in 11,326 (46%).

[‡]Between 2009 and 2012, providers did not have to specify reason for traveler refusal. [§]Between 2012 and 2014, providers had to select one of three reasons for traveler refusal.

Table 1

Demographics and travel-related characteristics of adult travelers evaluated at GTEN clinics (2009-2014).

Characteristics	All travelers (N=40,810)	MMR-eligible travelers (N=6,612)	
Sex			
Female	22,987 (56)	3,355 (51)	
Male	17,823 (44)	3,257 (49)	
Birth cohort			
1957-1989	35,053 (86)	6,404 (97)	
>=1990	5,757 (14)	208 (3)	
Region of travel †			
Africa	14,471 (35)	2,735 (41)	
Americas	11,562 (28)	1,444 (22)	
Eastern Mediterranean	2,156 (5)	432 (7)	
Europe	2,025 (5)	399 (6)	
South East Asia	10,090 (25)	1,655 (25)	
Western Pacific	7,052 (17)	1,054 (16)	
Reason for travel †			
Business	8,775 (22)	1,910 (29)	
Humanitarian service work	3,180 (8)	253 (4)	
Leisure	20,507 (50)	3,241 (49)	
Other	4,935 (12)	722 (11)	
Research/education	5,272 (13)	467 (7)	
VFR	3,208 (8)	596 (9)	
Duration of travel (days)			
<14	17,014 (42)‡	2,983 (45)‡	
14	23,766 (58) [‡]	3,622 (55) [‡]	
GTEN clinic site *			
Northeast	15,477 (38)	2,695 (41)	
Midwest	5,632 (14)	435 (7)	
South	9,692 (24)	2,952 (45)	
West	10,009 (25)	530 (8)	
Type of clinic			
Academic center	29,937 (73)	4,464 (68)	
Nonacademic center	10,873 (27)	2,148 (32)	

*Percentages within a group might not sum to 100 given rounding.

 \ddagger Sample sizes do not equal the total due to missing values; 30 travelers had an unknown duration of travel, of whom 7 were MMR-eligible, 3 were MMR-eligible travelers NOT vaccinated (all 3 of whom were travelers who declined MMR vaccination).

Abbreviations: GTEN, Global TravEpi Net; MMR, measles-mumps-rubella; VFR, visiting friend and relatives.

Chanastanistiss MMD alisible travelars received (N. 2.125)		MMD aligible travelors NOT vegeingted (N-3.477)		
Char acter isues	minintengible travelers, vaccillateu (11=3,135)	mark-engine travelets, nO1 vaccinateu (n=3,4//)		
Sex	1 460 (47)	1.007.(54)		
Female	1,408 (47)	1,887 (54)		
Male	1,667 (53)	1,590 (46)		
Birth cohort				
1957-1989	3,079 (98)	3,325 (96)		
>=1990	56 (2)	152 (4)		
Region of travel \ddagger				
Africa	1,112 (35)	1,623 (47)		
Americas	668 (21)	776 (22)		
Eastern Mediterranean	205 (7)	227 (7)		
Europe	268 (9)	131 (4)		
South East Asia	977 (31)	678 (19)		
Western Pacific	587 (19)	467 (13)		
Reason for travel ^{\ddagger}				
Business	1,067 (34)	843 (24)		
Humanitarian service work	142 (5)	111 (3)		
Leisure	1,627 (52)	1,614 (46)		
Other	266 (8)	456 (13)		
Research/education	192 (6)	275 (8)		
VFR	195 (6)	401 (12)		
Duration of travel (days)				
<14	$1,492 (48)^{\$}$	1,491 (43) [§]		
14	$1,639\ (52)^{\$}$	1,983 (57) [§]		
GTEN clinic site *				
Northeast	1,944 (62)	751 (22)		
Midwest	234 (7)	201 (6)		
South	690 (22)	2,262 (65)		
West	267 (9)	263 (8)		
Type of clinic				
Academic center	2,764 (88)	1,700 (49)		
Nonacademic center	371 (12)	1,777 (51)		

Table 2 Demographics and travel-related characteristics of adult MMR-eligible travelers who were vaccinated and not vaccinated with MMR

*Percentages within a group might not sum to 100 given rounding.

 ‡ Not mutually exclusive groups.

\$Sample sizes do not equal the total due to missing values; 7 MMR-eligible travelers had an unknown duration of travel, of whom 3 were MMR-eligible travelers NOT vaccinated.

Abbreviations: MMR, measles-mumps-rubella; VFR, visiting friend and relatives; GTEN, Global TravEpi Net.

Table 3

Action regarding MMR vaccinations among eligible adult travelers stratified by geographic region of GTEN clinic.

	U.S. Census Regions N (%)				
	Northeast	Midwest	South	West	
Adult travelers (n=40,810)	(N=15,477)	(N=5,632)	(N=9,692)	(N=10,009)	
Preexisting measles immunity	12,743 (82)	5,187 (92)	6,690 (69)	9,472 (95)	
Medical contraindication	39 (0.3)	10 (0.2)	50 (0.5)	7 (0.1)	
MMR-eligible	2,695 (17)	435 (8)	2,952 (30)	530 (5)	
	(N=2,695)	(N=435)	(N=2,952)	(N=530)	
Vaccinated	1,944 (72)	234 (54)	690 (23)	267 (50)	
Not vaccinated	751 (28)	201 (46)	2,262 (77)	263 (50)	
MMR-eligible travelers, NOT vaccinated (n=3,477)	(N=751)	(N=201)	(N=2,262)	(N=263)	
Traveler refusal	125 (17)	70 (35)	1,432 (63)	62 (24)	
Provider decision	391 (52)	64 (32)	331 (15)	180 (68)	
Health systems barriers	235 (31)	67 (33)	499 (22)	21 (8)	

Abbreviations: MMR, measles-mumps-rubella; GTEN, Global TravEpi Net.

* From 2009-11, providers did not have to specify a reason for traveler refusal.

 † From 2012-14, providers had to select one of three reasons for traveler refusal Figure Legends