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Background. International travel poses a risk of destination-specific illness and may contribute to the global spread of infectious diseases. Despite this, little is known about the health characteristics and pretravel healthcare of US international travelers, particularly those at higher risk of travel-associated illness.

Methods. We formed a national consortium (Global TravEpiNet) of 18 US clinics registered to administer yellow fever vaccination. We collected data regarding demographic and health characteristics, destinations, purpose of travel, and pretravel healthcare from 13,235 international travelers who sought pretravel consultation at these sites from January 2009 through January 2011.

Results. The destinations and itineraries of Global TravEpiNet travelers differed from those of the overall population of US international travelers. The majority of Global TravEpiNet travelers were visiting low- or lower-middle-income countries, and Africa was the most frequently visited region. Seventy-five percent of travelers were visiting malaria-endemic countries, and 38% were visiting countries endemic for yellow fever. Fifty-nine percent of travelers reported ≥1 medical condition. Atovaquone/proguanil was the most commonly prescribed antimalarial drug, and most travelers received an antibiotic for self-treatment of travelers’ diarrhea. Hepatitis A and typhoid were the most frequently administered vaccines.

Conclusions. Data from Global TravEpiNet provide insight into the characteristics and pretravel healthcare of US international travelers who are at increased risk of travel-associated illness due to itinerary, purpose of travel, or existing medical conditions. Improved understanding of this epidemiologically significant population may help target risk-reduction strategies and interventions to limit the spread of infections related to global travel.

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The number of travelers crossing international borders is increasing—worldwide, international tourist arrivals increased from 25 million in 1950 to 935 million in 2010 [1]. Countries with emerging economies, particularly in Africa and Asia, are receiving unprecedented numbers of international travelers [2]. This increase is epidemiologically significant because international travelers may be susceptible to a unique spectrum of diseases related to their destination country [3], their purpose of travel [4, 5], their duration of travel [6], and their existing medical conditions [7]. Travelers may also import infectious diseases to their country of origin, as is suggested by the outbreak of dengue fever in Florida in 2010 [8], the reemergence of measles in the United States in 2011 [9], and the rapid spread of severe acute respiratory syndrome in 2002–2003 [10] and influenza A virus subtype H1N1 in 2009 [11].

The Office of Travel and Tourism Industries (OTTI) of the Department of Commerce is the sole source of data on international travel to and from the United States. The OTTI periodically surveys a sample population of travelers departing from major US airports, but health-related data are not collected. To fill this gap, the Global TravEpiNet surveillance network was initiated by the US Centers for Disease Control and Prevention (CDC) in 2009 to collect data on demographic characteristics, travel patterns, and pretravel healthcare of US international travelers seen at authorized yellow fever vaccine clinics. Clinics authorized by their state or territorial health department to provide yellow fever vaccine are important sources of pretravel health advice, particularly for travelers at higher risk of illness on the basis of destination, purpose or type of travel, or existing health conditions. A better understanding of the health characteristics of these high-risk international travelers will help target preventive strategies aimed at minimizing the risk of acquiring and spreading infectious diseases related to travel. Here, we describe the characteristics of 13,235 US international travelers seen at Global TravEpiNet sites from 2009 through 2011.

METHODS

Global TravEpiNet Clinics

Global TravEpiNet clinics are distributed across the United States and include academic practices, healthcare consortia, health maintenance organizations, and pharmacy-based and public health clinics (Supplemental Figure 2). Data collection began in January 2009. An institutional review board at each participating clinic reviewed and approved the study.

Study Population

Data were collected on all individuals seen for pretravel consultation at participating clinics from January 2009 through January 2011, using a secure Internet-based tool. For each unique clinic visit, travelers provided details about their medical history, itinerary, and travel purpose. Clinicians verified the information provided by travelers and entered additional data on immunization history, health advice provided, vaccines administered, and medications prescribed during the pretravel encounter. If a traveler had an indication for a specific vaccine according to current guidelines of the CDC but did not receive the vaccine, the clinician was required to provide a reason for not administering the vaccine; available options included preexisting immunity, vaccine not indicated, referred to primary care provider for vaccination, patient declined, medical contraindication, insufficient time, or vaccine not available.

Data Analysis

Geographic destinations were classified into regions according to the grouping of member states of the World Health Organization (WHO; available at: http://www.who.int/about/regions/en/index.html) and into income categories (low-income, low-middle-income, upper-middle-income, or high income) according to the 2009 World Bank World Development Report (available at: http://econ.worldbank.org) [12]. For purposes of analysis, we considered travel to low-income or low-middle-income (LLMI) countries to be highest risk, and travelers to these 2 destination categories were considered together.

Travelers selected ≥1 of the following purposes for their trip: leisure, business, returning to region of origin of self or family to visit friends and relatives, adoption, providing medical care, receiving medical care, research/education, nonmedical service work, missionary work, military service, adventuring, attending large gathering or event, or other activities. For purposes of analysis, we combined nonmedical service work, providing medical care, and missionary work into a category termed “service work.” Travelers who are returning to their region of origin to visit friends and relatives (VFR) in low-income countries are at higher risk of acquiring illness during travel [13]. Travelers participating in the Global TravEpiNet who [1] selected “returning to region of origin of self or family to visit friends or relatives” and [2] were visiting LLMI countries were termed VFR travelers, in accordance with the CDC definition of the term [13]. Some travelers reported 2 purposes of travel. For purposes of analysis, travelers who reported leisure along with a second purpose of travel were categorized as pursuing the second purpose of travel. (For example, if the traveler reported leisure and business as purposes of travel, we categorized the purpose of travel as business.)

Data analyses were performed using SAS 9.2 (SAS Institute). We examined univariate and bivariate relationships in the data. To test for significant differences between groups, we used 2-sided $\chi^2$ tests for categorical variables or nonparametric tests (Wilcoxon signed-rank tests) for continuous variables.
RESULTS

This analysis includes data on 13,235 travelers seen at 18 US clinics that participated in the Global TravEpiNet consortium from January 2009 to January 2011. The median number of travelers entered per site was 201 (interquartile range [IQR], 136–580).

Traveler Characteristics

Travelers enrolled in Global TravEpiNet represented a broad range of ages (range, 1 month–94 years); the median age of travelers was 35 years (IQR, 25–52 years). Overall, there was a slight preponderance of female travelers (Table 1). The median duration of travel was 14 days, although 22% of travelers pursued trips of >28 days, and 3% of travelers pursued trips of >6 months. Global TravEpiNet travelers sought medical care a median of 3.5 weeks before departure.

A total of 10,831 travelers (82%) seen at Global TravEpiNet sites were visiting LLMI countries (Table 1). Compared with travelers to upper-middle or high-income countries, travelers to LLMI countries pursued more trips with a duration of >28 days (23% vs 15%; P < .001; Table 1) and stayed more frequently in homes (29% vs 19%; P < .001).

Leisure (49%) was the most commonly reported purpose of travel (Table 1). Business (15%) and service work (15%) were other frequently reported purposes of travel. Eleven percent of travelers were VFR travelers. Destinations and personal characteristics differed with the purpose of travel. Business travelers were older than nonbusiness travelers, were more likely to be male, and pursued trips of shorter duration. Business travelers sought pretravel health advice a median of 17 days prior to departure (Table 1). VFR travelers were younger than other travelers and pursued trips of longer duration (median trip duration, 30 days for VFR travelers vs 14 days for those with other purposes of travel; P < .0001). VFR travelers sought pretravel health advice a median of 16 days prior to departure (Table 1).

Destinations

The WHO African Region was the most commonly visited region among Global TravEpiNet travelers (Supplemental Figure 1). The Region of the Americas and the South-East Asia Region were also frequent destination regions. A total of 3,870 travelers (29%) were visiting >1 country.

Travel most commonly took place in June, July, and August (32% of all trips). The month of peak travel differed between regions of the world; travel to the African Region peaked in June and travel to the Region of the Americas peaked in March (data not shown).

India, South Africa, and China were the most common destination countries overall (Table 1). In particular, India was the most common destination country among a variety of subtypes of travelers, including business travelers (20% of all business travelers), VFR travelers (11% of all VFR travelers), and leisure travelers (7% of all leisure travelers; Table 1). Other common destination countries among VFR travelers were Ghana (7%), Ethiopia (7%), and Nigeria (7%). China was the most common destination country among individuals traveling for research/education, and Haiti was the most common destination country among travelers performing service work (Table 1).

A total of 9,912 travelers (75%) were visiting countries that include areas endemic for malaria. Five thousand twenty-three (38%) were visiting countries with yellow fever.

Preexisting Health Conditions

One or more medical conditions were reported in 7,755 (59%) of travelers (Table 2). The most common medical condition was seasonal allergies (30%), followed by cardiovascular conditions, such as hyperlipidemia and hypertension (17%). There were 1,099 travelers (9%) who reported a neuropsychiatric condition and 810 travelers (6%) who reported an intestinal system disturbance. Immunocompromising conditions, such as human immunodeficiency virus infection and AIDS, organ transplant, or receipt of immunocompromising medications, were present in 3% of travelers. The majority of travelers with immunocompromising conditions (98%) were traveling to LLMI countries.

A total of 7,703 travelers (58%) reported taking a daily medication. The median number of daily medications was 1 (range, 0–15). Cardiovascular medications and cholesterol-lowering medications were the most common prescription medications (20% of travelers). Eight percent of travelers were taking a prescription medication for mood or anxiety issues, and 6% had been prescribed an asthma inhaler.

Pretravel Healthcare

Of the 9,912 travelers visiting countries that include areas endemic for malaria, 7,137 (72%) were prescribed a medication for malaria chemoprophylaxis. Atovaquone/proguanil was the most commonly prescribed antimalarial drug overall (70% of all antimalarial prescriptions), and it was also the most commonly prescribed antimalarial when destination regions were considered separately (Figure 1). The median duration of travel for those prescribed atovaquone/proguanil was 15 days (IQR, 10–21 days). Overall, 11% of antimalarial prescriptions were for mefloquine, and 6% were for doxycycline. Among travelers prescribed mefloquine or doxycycline, the majority (59% and 61%, respectively) were pursuing trips of >28 days. Thirteen percent of antimalarial prescriptions were for chloroquine; the majority of travelers receiving chloroquine were visiting the Region of the Americas. Primaquine as primary prophylaxis was never prescribed for this cohort. When considering destination countries where malaria is holoendemic, most travelers to Haiti (92%), Ghana (91%), and Nigeria (90%) were prescribed malaria chemoprophylaxis. Among travelers to India, where malaria
Table 1. Characteristics and Destinations of US International Travelers in Global TravEpiNet, by Purpose of Travel

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Travelers, No. (%)</th>
<th>Travelers to LLMI Countries, No. (%)</th>
<th>Purpose of Travel,(^a) travelers, No. (%)</th>
<th>Research/Education, No. (%)</th>
<th>Service Work(^b), No. (%)</th>
<th>(P^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 13 235)</td>
<td>(n = 10 831)</td>
<td>Leisure (n = 6 548)</td>
<td>Business (n = 1 959)</td>
<td>VFR (n = 1 399)</td>
<td></td>
</tr>
<tr>
<td>Age, ≤1 year</td>
<td>69 (0.5)</td>
<td>58 (0.5)</td>
<td>20 (0.3)</td>
<td>0</td>
<td>43 (3)</td>
<td>0</td>
</tr>
<tr>
<td>1–5 years</td>
<td>400 (3)</td>
<td>349 (3)</td>
<td>90 (1)</td>
<td>12 (0.6)</td>
<td>269 (19)</td>
<td>6 (0.5)</td>
</tr>
<tr>
<td>6–17 years</td>
<td>779 (6)</td>
<td>642 (6)</td>
<td>311 (5)</td>
<td>6 (0.3)</td>
<td>245 (18)</td>
<td>7 (0.7)</td>
</tr>
<tr>
<td>18–49 years</td>
<td>8176 (62)</td>
<td>6681 (62)</td>
<td>3646 (56)</td>
<td>1419 (72)</td>
<td>634 (45)</td>
<td>897 (70)</td>
</tr>
<tr>
<td>50–64 years</td>
<td>2677 (20)</td>
<td>2174 (20)</td>
<td>1602 (24)</td>
<td>449 (23)</td>
<td>165 (12)</td>
<td>100 (9)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>1134 (9)</td>
<td>927 (9)</td>
<td>879 (13)</td>
<td>73 (4)</td>
<td>43 (3)</td>
<td>44 (4)</td>
</tr>
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<td></td>
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<tr>
<td>Sex, male</td>
<td>6061 (46)</td>
<td>4934 (46)</td>
<td>2962 (45)</td>
<td>1181 (60)</td>
<td>651 (47)</td>
<td>436 (39)</td>
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</tr>
<tr>
<td></td>
<td>female</td>
<td>7174 (54)</td>
<td>5897 (54)</td>
<td>3586 (55)</td>
<td>778 (40)</td>
<td>748 (53)</td>
</tr>
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<tr>
<td>Duration of travel</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–7 days</td>
<td>1710 (13)</td>
<td>1286 (12)</td>
<td>575 (9)</td>
<td>557 (28)</td>
<td>40 (3)</td>
<td>107 (10)</td>
</tr>
<tr>
<td>8–14 days</td>
<td>5004 (38)</td>
<td>3914 (36)</td>
<td>3013 (46)</td>
<td>750 (38)</td>
<td>217 (16)</td>
<td>275 (25)</td>
</tr>
<tr>
<td>15–28 days</td>
<td>3672 (28)</td>
<td>3152 (29)</td>
<td>2278 (35)</td>
<td>282 (14)</td>
<td>395 (29)</td>
<td>244 (22)</td>
</tr>
<tr>
<td>29–180 days</td>
<td>2418 (18)</td>
<td>2128 (20)</td>
<td>645 (10)</td>
<td>240 (12)</td>
<td>687 (49)</td>
<td>412 (37)</td>
</tr>
<tr>
<td>≥6 months</td>
<td>413 (3)</td>
<td>338 (3)</td>
<td>34 (0.5)</td>
<td>127 (6)</td>
<td>55 (4)</td>
<td>82 (7)</td>
</tr>
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<td></td>
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<td></td>
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<tr>
<td>Destination type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban only</td>
<td>3992 (30)</td>
<td>3300 (30)</td>
<td>1442 (22)</td>
<td>1146 (59)</td>
<td>625 (45)</td>
<td>326 (29)</td>
</tr>
<tr>
<td>Rural only</td>
<td>1286 (10)</td>
<td>1015 (9)</td>
<td>605 (9)</td>
<td>62 (3)</td>
<td>51 (4)</td>
<td>116 (10)</td>
</tr>
<tr>
<td>Both</td>
<td>7923 (60)</td>
<td>6488 (60)</td>
<td>4485 (68)</td>
<td>750 (38)</td>
<td>712 (51)</td>
<td>680 (61)</td>
</tr>
<tr>
<td>Days to departure, median (range)</td>
<td>24 (0–468)</td>
<td>24 (0–462)</td>
<td>28 (0–450)</td>
<td>17 (0–460)</td>
<td>16 (0–462)</td>
<td>25 (0–468)</td>
</tr>
<tr>
<td>Top 3 destination countries</td>
<td>India, 2046 (9); South Africa, 1123 (5); China, 1065 (5)</td>
<td>India, 2046 (10); South Africa, 765 (6); China, 802 (7);</td>
<td>India, 756 (20); China, 260 (7); South Africa, 146 (4)</td>
<td>India, 201 (11); Ghana, 121 (7); Ethiopia, 119 (7); China, 175 (8); India, 152 (7); South Africa, 76 (4); Vietnam, 76 (4); Haiti, 307 (11); Kenya, 169 (6); Honduras, 154 (5)</td>
<td></td>
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</tr>
</tbody>
</table>

Abbreviations: LLMI, low-income or low-middle income; VFR, visit friends and relatives.
\(^a\) Travelers whose purpose of travel could be categorized into a single category. The purpose of travel for 282 travelers could not be categorized.
\(^b\) Including nonmedical service work, providing medical care, and missionary work.
\(^c\) Calculated to determine the association between the characteristic and the purpose of travel; values are based on a 2-sided \(\chi^2\) test, unless otherwise indicated.
\(^d\) \(P < .0001\) compared with travelers to upper-middle-income or high-income countries, based on a 2-sided \(\chi^2\) test.
\(^e\) Based on a nonparametric test (ie, the Wilcoxon signed-ranks test).
is endemic in low-altitude regions, 90% received malaria chemoprophylaxis.

There were 11,495 travelers (87%) who were prescribed an antibiotic for presumptive self-treatment of travelers’ diarrhea. Azithromycin and the fluoroquinolone class of antibiotics made up 99% of prescriptions. Azithromycin was more likely to be prescribed to travelers to the South-East Asia Region than to travelers to other regions (66% vs 41%; \( P < .001 \)) (Figure 2). Prophylactic antibiotics were prescribed to 1192 (9%) travelers.

We classified travelers’ vaccination status for travel-related vaccinations and routine vaccinations on the basis of the information provided by travelers and clinicians. Hepatitis A and typhoid were the most commonly administered vaccines (Figure 2). The majority of travelers had preexisting immunity to measles, mumps, and rubella (84% of travelers), tetanus/diptheria (63%), and hepatitis B (52%). Nearly one-third of travelers (32%) received routine tetanus-diptheria or tetanus-diptheria–acellular pertussis immunization during their pretravel consultation. Rabies vaccine is recommended for long-term travelers to areas with a significant risk of exposure [13]; rabies vaccine was recommended for but declined by 23% of individuals traveling for >28 days in Global TravEpiNet. Nineteen percent of all travelers declined influenza immunization. Lack of available vaccine was cited as the reason for not vaccinating individuals for whom immunization would otherwise be indicated for influenza (8% of travelers), Japanese encephalitis (4% of travelers), and rabies (2% of travelers).

**DISCUSSION**

According to OTTI, US travelers made 61.5 million international trips in 2009, and most of these trips (31%) were to Europe [14]. Travelers seen at Global TravEpiNet sites are distinct from this general population of US international travelers. Most notably, the majority of Global TravEpiNet travelers were visiting LLMI countries, as defined by the World Bank [12]. The WHO African Region was the most common destination region among Global TravEpiNet travelers, whereas only 1% of all US overseas trips were to Africa [14]. Three-quarters of Global TravEpiNet travelers were visiting regions endemic for malaria, and more than one-third were visiting regions with yellow fever. Compared with results from a 2005 OTTI airport survey, Global TravEpiNet travelers were more commonly visiting multiple countries (29% vs 19%) and were traveling for longer periods (median trip duration, 14 days vs 10 days) [15]. Because of their destinations and itineraries, Global TravEpiNet travelers are a population at increased risk of travel-associated illness [3, 6]. A better understanding of the health and demographic features of these travelers will inform preventive strategies aimed at minimizing the risk of illness during travel and decreasing the global spread of infectious diseases.

Certain destination countries were particularly popular among Global TravEpiNet travelers. India was the most common destination country for leisure, business, and VFR travelers during the study period. Surveillance data have identified unique infectious disease risks associated with travel to India. An analysis from the GeoSentinel international network of travel medicine reporting sites found that the majority of enteric (typhoid and paratyphoid) fever is acquired in south-central Asia, including India [3]. In our Global TravEpiNet cohort, 96% of travelers to India had up-to-date immunizations for typhoid at the time of their visit or received a typhoid vaccine. Aside from India, destination countries in Africa, including Ghana, Ethiopia, and Nigeria, were also common among VFR travelers in Global TravEpiNet. Surveillance data from 2008 demonstrate that almost half of imported malaria cases in the United States are acquired in Africa, with Nigeria and Ghana being the 2 most common source countries in the continent [16]. Our findings indicate that >90% of travelers to malaria holoendemic countries in Western Africa were prescribed malaria chemoprophylaxis. Maximizing the use of malaria prophylaxis among travelers to Western Africa may be a particularly effective strategy for decreasing imported cases of malaria in the United States.

Service workers traveled to destination countries that were distinct from those of other types of travelers. Haiti was the most common destination country for service workers during the study period, likely because of the 2010 earthquake and cholera relief efforts. Service workers may face unique physical and psychological risks related to extreme environments and prolonged duration of deployment [5]. Pretravel counseling for
such individuals needs to be thorough and tailored to the purpose of the trip and the destination country.

Posttravel surveillance has identified international travel, particularly long-term travel, as a risk for diarrheal syndromes and neuropsychiatric conditions [3, 6]. Our data demonstrate that 9% of travelers had neuropsychiatric conditions and that 6% had gastrointestinal conditions prior to departure. Information about preexisting conditions needs to be incorporated into risk assessment and posttravel surveillance. Complicated medical conditions, such as immunocompromising illnesses and diabetes mellitus, were also present in Global TravEpiNet travelers. These conditions may affect vaccine efficacy and be associated with drug interactions [7].

In this cohort, atovaquone/proguanil was the most commonly prescribed malaria chemoprophylaxis, even outside regions with mefloquine-resistant *Plasmodium falciparum*. The decision to use malaria chemoprophylaxis in US travelers is based on the risk of malaria in the destination country, the efficacy of the chemoprophylactic drug, and the adverse events of the drug. The frequent use of atovaquone/proguanil, the most costly antimalarial agent, and the distribution of destinations among Global TravEpiNet travelers suggest that a cost-effectiveness analysis regarding the choice of malaria chemoprophylaxis for US travelers is warranted.

Vaccine-preventable diseases contribute significantly to morbidity and potential mortality in travelers. In an analysis of returned travelers in the GeoSentinel Surveillance Network, enteric fever (typhoid and paratyphoid fever) was the most commonly diagnosed vaccine-preventable disease; 38% of these individuals had had a pretravel medical encounter, although whether they received the typhoid vaccine was not known [17]. Furthermore, >20% of travelers returning with hepatitis A, influenza, and varicella had also had a pretravel medical encounter. In our population of individuals seen at experienced travel clinics, we found that immunization with travel-related vaccines was frequently pursued. Travel clinics also commonly administered routine vaccines. Nevertheless, even at specialty travel clinics, opportunities for vaccination were missed because
of patient refusal, time constraints, or lack of availability of vaccine. Strategies to improve vaccine availability and uptake during the pretravel encounter should be public health priorities.

The travel medicine practice guidelines of the Infectious Diseases Society of America recommend that health advice be sought 4–6 weeks prior to travel in order to fully prepare the traveler and to accommodate the completion of vaccination series [18]. Business travelers and VFR travelers in Global TravEpiNet were less likely than other travelers to seek pretravel health advice within this time frame. Numerous reports have linked VFR travel to a disproportionate likelihood of travel-related infections such as malaria, hepatitis A, and enteric fever; such travelers are also particularly likely to delay or defer pretravel health advice [4]. Notably, we observed that business travelers were similar to VFR travelers with regard to the timing of their pretravel health consultation. Consistent with previous reports, we observed that fewer men than women sought pretravel health advice [19]. These findings underscore the need to focus education efforts on these populations.

Our study has a number of limitations. Most importantly, the surveillance data were obtained from individuals who sought pretravel healthcare at clinics registered to administer yellow fever vaccination. Studies of travelers departing from major US airports have shown that between one-half and two-thirds of travelers to low-income countries do not seek any medical advice prior to traveling [20, 21]; de facto, the Global TravEpiNet surveillance system does not capture these travelers. Furthermore, primary care providers and other practitioners who are not registered to administer yellow fever vaccine are a common source of health information for US travelers, particularly VFR travelers [20]. More studies are needed to characterize the pretravel healthcare and advice that is provided in nonspecialist settings.

Despite these limitations, Global TravEpiNet represents the largest national network of providers systematically collecting pretravel health data regarding high-risk US international travelers. Our results provide insight into the health conditions, travel destinations, travel duration, and pretravel medical care of an epidemiologically significant population and should facilitate the targeting of risk-reduction strategies for this group. Such knowledge could assist in limiting the spread of infections related to international travel.

**Supplementary Data**

Supplementary materials are available at *Clinical Infectious Diseases* online (available at: http://www.oxfordjournals.org/our_journals/cid/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

**Notes**

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References