Journal of Travel Medicine

International Society of Travel Medicine
Established 1991
Promoting healthy travel worldwide

Journal of Travel Medicine, 2019, 1–6
doi: 10.1093/jtm/taz031
Original article

Original article

Characteristics and preparation of the last-minute traveler: analysis of vaccine usage in the Global TravEpiNet Consortium

Johnnie A. Yates, MD[1,*], Sowmya R. Rao, PhD[2,3], Allison Taylor Walker, PhD[4], Douglas H. Esposito, MD, MPH[4], Mark Sotir, PhD[4], Regina C. LaRocque, MD, MPH[5,6], Edward T. Ryan, MD[5,6,7] and The Global TravEpiNet Consortium

[1]Hawaii Permanente Medical Group, Honolulu, HI 96825, USA, [2]Biostatistics Center, Massachusetts General Hospital, Boston, MA 02114, USA, [3]Department of Global Health, Boston University School of Public Health, Boston, MA 02114, USA, [4]Division of Global Migration and Quarantine, Travelers' Health Branch, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA, [5]Travelers' Advice and Immunization Center, Massachusetts General Hospital, Boston, MA 02114, USA [6]Harvard Medical School, Boston, MA 02114, USA and [7]Harvard T.H. Chan School of Public Health, Boston, MA 02114, USA

*To whom correspondence should be addressed. Email: johnnie.a.yates@kp.org

Submitted 20 February 2019; Revised 15 April 2019; Editorial Decision 25 April 2019; Accepted 25 April 2019

Abstract

Background: Last-minute travellers (LMTs) present challenges for health care providers because they may have insufficient time for recommended vaccinations or pre-travel preparation. Our objective was to obtain a better understanding of LMTs in order to help travel medicine providers develop improved strategies to decrease the number of LMTs and potentially reduce travel-related morbidity.

Methods: We defined LMTs as travellers with a departure date of 7 days or fewer from the medical encounter. We analysed the characteristics and health preparation of 12 494 LMTs who presented to a network of US clinical practices for pre-travel health advice between January 2009 and December 2015.

Results: LMTs comprised 16% of all travellers. More LMTs than non-LMTs travelled for business or to visit friends and relatives (VFR) (26% vs 16% and 15% vs 8%, respectively; $P < 0.0001$). More LMTs also travelled for longer than 1 month (27% vs 21%; $P < 0.0001$) and visited only urban areas (40% vs 29%; $P < 0.0001$). At least one travel vaccine was deferred by 18% of LMTs because of insufficient time before departure. Vaccines that required multiple vaccinations, such as Japanese encephalitis and rabies, were the most likely to be deferred because of time constraints.

Conclusion: Interventions to improve the timing of pre-travel health consultations should be developed, particularly for business and VFR travellers. Recently endorsed accelerated vaccine schedules for Japanese encephalitis and rabies may help some LMTs receive protection against these infections despite late presentation for pre-travel health care.

Key words: last-minute traveler, vaccines, Japanese encephalitis vaccine, rabies vaccine

Introduction

International tourist arrivals reached 1.3 billion in 2017 and are expected to exceed 1.6 billion by 2020.[1] The spread of infections such as Zika virus and Middle East respiratory syndrome coronavirus and the importation of yellow fever (YF) and drug-resistant typhoid into non-endemic countries have shown how travel can facilitate the global spread of previously geographically confined infections.[2–5] Recently, travel-associated outbreaks

of measles have also significantly increased.[6–8] Consultation with a health care provider prior to travel can help reduce the risk of travel-related illness and mitigate the spread of infectious diseases.

Immunizations are a key component of the pre-travel health consultation. The pre-travel consult provides an opportunity to update routine immunizations as well as vaccinate against infections that are endemic in the traveller's destinations. Hepatitis A and typhoid are the most commonly administered travel vaccines.[9,10] However, the uptake of vaccines with multi-dose schedules such as rabies and Japanese encephalitis (JE) is low for a variety of reasons, including travellers' lack of concern regarding these rare infections, cost and insufficient time for vaccination before departure.[11–13]

The US Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) recommend that international travellers have a pre-travel health consultation at least 4–6 weeks before departure.[14,15] This time frame allows travellers to receive appropriate pre-travel health care, including vaccines that may require a series of administrations. Previous studies have shown that travellers present to specialized travel clinics for health advice a median of 3–4 weeks before departure.[9,10,] However, up to one-fourth of travellers present 2 weeks or fewer from the time of departure, including some who receive consultations on the day of departure.[16]

'Last-minute' travellers (LMTs) (defined by WHO as travellers whose departure is 2 weeks or less from the time of consultation[15]) may be at increased risk of travel-associated infections because of insufficient time to complete recommended vaccinations or to start prophylactic medications before departure. This study analyses the demographics, travel characteristics and vaccine utilization of LMTs presenting to Global TravEpiNet (GTEN), a network of US clinical practices that provide pre-travel health care. To our knowledge, this is the first study to analyse a large group of LMTs. A better understanding of LMTs may help travel medicine providers to develop improved strategies to decrease the number of LMTs and potentially reduce travel-related morbidity.

Methods

GTEN is a CDC-sponsored consortium of clinical practices that provide pre-travel health care. It is composed of academic practices, health care consortia, health maintenance organizations and pharmacy-based and public health clinics that are distributed across the USA.[10] Data collected at 25 GTEN sites between January 2009 and December 2015 were analysed. An institutional review board at each participating site approved the study or exempted it from review.

For our analysis, we defined an LMT as a traveller who had a pre-travel consult 7 days or fewer before departure. We chose this definition instead of the WHO definition because most single vaccines take at least 7 days for the development of immunity, so these travellers, if vaccinated, would be at risk of acquiring vaccine-preventable infections early in their trip. In addition, vaccines with administrative requirements such as YF or meningococcal vaccination (for the Hajj) should be given at least 10 days prior to arrival,[15,17] and travellers receiving these vaccines a week or less before arrival would not be in compliance with these regulations.

For each pre-travel consultation, travellers provided information regarding their itinerary, reason for travel, reason for seeking pre-travel health care and medical history via a secure online tool. Travellers were able to select more than one purpose of travel. Travellers were classified as visiting friends and relatives (VFR) if they were returning to their country of origin and were visiting a low or low–middle-income country. If business was listed as a reason for travel, it was considered the primary purpose of travel. If a traveller selected leisure in addition to another reason for travel, then the second reason was considered the main purpose of travel.

Clinicians confirmed all traveller-provided information and entered data on immunization history, immunizations administered, medications prescribed and advice given. Clinicians were asked to consider rabies vaccine for all travellers to rabies-endemic high-risk countries[12] and to consider JE vaccine for travellers visiting a country deemed endemic by CDC.[14] If a vaccine was not administered, the clinician gave a reason why [vaccine not indicated, pre-existing immunity (based on positive serology, vaccination history or if the clinician determined the traveller was immune based on past illness), medical contraindication, insufficient time (either inadequate time to complete a vaccination series before departure or late vaccination would not provide protection during the trip), patient declined, vaccine not available or referred to another provider]. If a vaccine was not indicated, if it was contraindicated or if the traveller had pre-existing immunity, then the vaccine was excluded from the analysis of vaccinations deferred because of insufficient time.

Statistical analysis

Summary statistics (proportions and medians) were obtained for all variables of interest. Difference in the (continuous) age distribution between the two groups was tested using the non-parametric Wilcoxon rank sum test. Generalized linear mixed models were used to assess the significance of group differences in the distribution of categorical variables accounting for the clustering of patients within sites. A two-sided P value of <0.05 was considered significant. All analyses were conducted in SAS 9.4 (SAS Institute Inc., Cary, NC, USA.)

Results

Of the 76 281 GTEN travellers in the study period, 12 494 (16%) met our definition of an LMT (Table 1). More LMTs than non-LMTs travelled for business (26% vs 16%; $P < 0.0001$) or to VFRs (15% vs 8%; $P < 0.0001$). More LMTs travelled for 29 or more days (27% vs 21%; $P < 0.0001$) and travelled exclusively to urban destinations (40% vs 29%; $P < 0.0001$) compared to their non-LMT counterparts.

Only 17 of 12 494 (0.1%) LMTs in the study had pre-existing immunity to all indicated vaccines (including routine and travel-specific vaccines such as typhoid, YF, JE and rabies). Of the remaining 12 477 LMTs, 2 278 (18%) had at least one travel vaccine deferred because of insufficient time. Among non-LMTs, 43 of 63 787 (0.1%) had pre-existing immunity to all recommended

Table 1. Demographic and travel characteristics of LMTs vs non-LMTs[1]

Characteristics	Non-LMT *N* (%) 63 787 (84)	LMT *N* (%) 12 494 (16)	*P* value[2]
Age (median)	35 (24–54)	34 (24–49)	**<0.0001**
Categories			**<0.0001**
<5 years old	1747 (3)	652 (5)	
5–19	7849 (12)	1411 (11)	
20–24	6748 (11)	1198 (10)	
25–44	23 692 (37)	5271 (42)	
45–64	17 329 (27)	3176 (25)	
65–74	5310 (8)	660 (5)	
≥75	1112 (2)	126 (1)	
Gender			**<0.0001**
Female	35 919 (56)	6390 (51)	
Male	27 868 (44)	6104 (49)	
Duration of travel			**<0.0001**
<29 days	50 470 (79)	9098 (73)	
≥29 days	13 273 (21)	3382 (27)	
Reason for travel[3]			
Leisure	31 997 (50)	4519 (36)	**<0.0001**
Business	9927 (16)	3278 (26)	**<0.0001**
VFR	4960 (8)	1834 (15)	**<0.0001**
Other	15 044 (24)	2071 (17)	**<0.0001**
Geographic destination type			**<0.0001**
Urban only	18 260 (29)	4973 (40)	
Rural only	6785 (11)	921 (7)	
Both	38 714 (61)	6594 (53)	
Reason for clinic visit[4]			
Referred by PCP	12 345 (21)	2207 (19)	**<0.0001**
Information on internet	7275 (12)	1315 (11)	0.20
Referred by travel agent	3497 (6)	396 (3)	**<0.0001**
Referred by employer	5838 (10)	1738 (15)	**<0.0001**
Family recommended	10 178 (17)	1792 (15)	**0.01**
Public health announcement	542 (1)	119 (1)	0.09
Concerned about health issues	24 142 (41)	4696 (40)	**<0.0001**

[1]Numbers might not add to total because some values are missing.
[2]Obtained for categorical variables from generalized mixed models accounting for clustering of patients within sites. Difference in the distribution of age between the groups was obtained from the non-parametric Wilcoxon rank sum test.
[3]Reflects hierarchical characterization: if purpose included 'Business' then categorized as 'Business'. If not, then if purpose included 'VFR' (based on United Nations Human Development Index definition) then categorized as 'VFR' travellers. If not, if purpose included 'Leisure' then considered as 'Leisure'. If not, then considered as 'Other' travellers.
[4]Could answer more than one reason.
Abbreviations: VFR, visiting friends and relatives; PCP, primary care provider.

vaccines, and 4114 (6.5%) of the remaining 63 74 non-LMTs had at least one vaccine deferred because of insufficient time. Travel vaccinations that were deferred due to insufficient time are shown in Table 2. Not unexpectedly, the number of travellers who did not receive a travel vaccine because of insufficient time was greatest for vaccines that required a series to complete. JE vaccine was indicated for 1004 LMTs. Of these, 526 (52%) did not receive the JE vaccine because of insufficient time to complete the series before departure, and 151 (15%) received one dose. Rabies vaccine was considered indicated for 5579 LMTs. Data on reasons for not administering rabies vaccine were collected beginning in 2012 and were available for 3458 LMTs.

Table 2. Vaccinations deferred due to insufficient time

Vaccine	LMTs		Non-LMTs	
	Vaccine indicated	Vaccine deferred	Vaccine indicated	Vaccine deferred
Hepatitis A	6784	66 (1%)	35 523	190 (1%)
Hepatitis B	3314	482 (15%)	14 667	1144 (8%)
Influenza	5962	57 (1%)	28 068	85 (<1%)
Typhoid	10 185	263 (3%)	52 778	38 (<1%)
Rabies	3458	1411 (41%)	26 207	2433 (9%)
JE	1005	526 (52%)	4965	1093 (22%)
YF	3541	13 (<1%)	18 465	9 (<1%)

Note: If a vaccine was indicated but the traveller had a contraindication to the vaccine, it was not included in the analysis. Abbreviations: Last minute travellers, LMTs; Japanese encephalitis, JE; yellow fever, YF.

Of these, 1411 (41%) did not receive the rabies vaccine because of insufficient time to complete the series before departure, and 151 (4%) received a single dose.

A total of 51% of LMTs and 58% of non-LMTs visiting YF-endemic countries received the YF vaccine. Among those travelling to YF-endemic countries, the most common reason for not receiving the YF vaccine was pre-existing immunity (23% of LMTs and 16% of non-LMTs). Less than 1% of both LMTs and non-LMTs travelling to YF countries did not receive the YF vaccine because of insufficient time.

The most common destination countries for both LMTs and non-LMTs were India, Thailand, South Africa, China and Kenya. Within the subgroup of VFR travellers, the most visited countries were India, Ghana, Nigeria, Ethiopia and Guinea for LMTs and India, Ghana, Nigeria, Ethiopia and Vietnam for non-LMTs.

Discussion

In our analysis of a large network of pre-travel clinics in the USA, we found that 16% of international travellers sought pre-travel health care within 7 days of departure, and 18% of these LMTs had at least one recommended vaccine deferred because of insufficient time. A higher proportion of LMTs were business and VFR travellers compared to those who had a consultation more than 7 days before travel. Business travellers may need to take unexpected trips that make timely pre-travel consultation difficult, and VFRs may seek care at the last minute for a variety of reasons including family emergencies.[18]

Although the majority of travellers were able to receive at least one recommended travel vaccine, nearly one in five LMTs had a vaccine deferred because they presented for consultation too close to departure, leaving them vulnerable to vaccine-preventable infections. This was especially true for high-consequence infections with high morbidity or mortality, such as JE and rabies—over half of LMTs for whom JE vaccination was indicated and 41% of LMTs for whom rabies vaccination was indicated did not receive the respective vaccination series because of insufficient time. In this study, many LMTs received a single vaccination against JE or rabies. Single-dose vaccination for a multi-administration vaccine may be adequate for boosting pre-existing immune responses but is not recommended for primary immunization. It is not known whether the single doses of JE or rabies were the initial vaccine of a series that would be completed

after return or were intended to complete an incomplete series. For frequent travellers, the cumulative lifetime risk of exposure to infections such as JE and rabies should be considered and may warrant commencing a vaccine series (to be completed upon return) even if it does not provide protection for the immediate trip.[19]

Our findings highlight that LMTs would be an appropriate target group for increased consideration of accelerated vaccination series.[20–22] In 2018 the US Food and Drug Administration (FDA) approved an accelerated 7-day primary immunization series for the inactivated JE vaccine (Ixiaro).[23] In addition, a two-dose series of intradermal rabies vaccination given over 7 days was found to be non-inferior to the traditional three-dose intramuscular vaccination given over 3 or 4 weeks,[24] and 2018 WHO guidelines for rabies pre-exposure prophylaxis now include accelerated vaccination regimens with two doses given at Days 0 and 7.[25] However, the accelerated rabies schedule is not FDA approved in the USA and has not yet been endorsed by the CDC, which may limit its use in the USA.

One-half of all LMTs travelling to YF-endemic countries received the YF vaccine, while <1% of both LMTs and non-LMTs had the YF vaccine deferred due to insufficient time. This low percentage of deferred vaccination is likely because the YF vaccine is a single-dose vaccine and may have also been required for entry at the destination country. Among GTEN travellers, three of the five most frequently visited countries for VFR LMTs were holoendemic for YF (Ghana, Nigeria and Guinea) so some of these LMTs may not have had immunity by the time they arrived at their destination. Notably, late vaccination was found to be associated with YF infection in some Chinese workers who acquired YF in Angola.[26] If YF vaccination was a country entry requirement, the traveller may not have been in compliance with the WHO International Health Regulations, thereby putting the traveller at risk of refused entry or quarantine. Late vaccination against YF would also mean that serious adverse vaccine reactions such as YF vaccine-associated neurotropic and viscerotropic disease may not present until after the traveller arrived at his or her destination, where accessing medical care may be more challenging than in the traveller's home country.

Overall, LMTs travelled longer than non-LMTs in our study. This finding appears to be largely due to the higher proportion of VFRs among LMTs, since VFRs have been shown to travel longer than other types of travellers.[27,28] This observation is a concern because the risk of infections increases with travel duration, and LMTs may not be optimally prepared if they fail to complete travel vaccine series. The greater proportion of LMTs travelling exclusively to urban areas is likely a reflection of the fact that VFR and business travellers are more likely to visit urban rather than rural areas.[29,30]

Although 18% of GTEN travellers were unable to receive a travel vaccine due to time constraints, many LMTs received at least one recommended travel vaccine, thus demonstrating that travellers still benefit from a late pre-travel consultation. Vaccination series that provide long-term protection can also be started and completed upon return if the anticipated lifetime risk of exposure is sufficiently high. A consult close to departure also provides opportunities to discuss risk-reduction measures such as the use of mosquito repellents, avoiding animals and the need to urgently seek post-exposure prophylaxis for potential rabies exposures. This information is especially relevant for travellers to rabies- or JE-endemic areas who could not be vaccinated against these infections before departure.

Clinicians, public health practitioners and employers should collaborate to improve timely pre-travel health preparation of business travellers. Airline reservations for US business travellers are made a median of 24 days before departure, and 40% are made by corporate travel agents.[31] Because of this short time and process for pre-travel preparation, it may be useful for employers to encourage routine (e.g. semiannual) pre-travel consultations for employees who travel internationally. Employers could also require those in charge with arranging business travel to schedule a pre-travel clinic appointment at the time travel plans are made.

International business travellers often make multiple trips within one or more years, and the number of trips has been found to be associated with serious health problems requiring hospitalization or evacuation in business travellers.[32] In addition, a cost–benefit analysis of JE vaccination for business travellers concluded that the benefits of vaccination outweigh the costs when multiple trips to endemic areas are planned.[33] Therefore, the cumulative risk of vaccine-preventable disease exposure should be factored in the risk assessment.[19] The potential for disruption of the business trip due to illness or the need to emergently seek rabies post-exposure prophylaxis should also be considered.

Travellers visiting friends and relatives (VFRs) could also benefit from strategies to help improve the timing of their pre-travel consultations. Primary care providers are the most common source of pre-travel health advice for VFRs,[34,35] so providing them with resources (e.g. Pre-Travel Providers' Rapid Evaluation Portal (PREP), a free Web-based tool based on CDC travel guidelines; https://gten.travel/prep/prep) to help them deliver pre-travel health advice may improve the timely preparation of VFRs. For practices that care for large immigrant or migrant populations, including a routine screening question such as 'Do you plan on traveling out of the country within the next 6 months?' at each visit may identify early on those who could benefit from a pre-travel consultation.[36] It should be noted that VFRs are not a homogenous group, and their pre-travel health needs may differ based on their countries of origin,[37] so approaches to improve their pre-travel care may also vary accordingly.

GTEN is the largest consortium of pre-travel clinics in the USA. The large number of LMTs in our analysis and the diversity of GTEN practice types are strengths of this study. However, the large sample size leads to small *P* values making small differences significant. Hence, in our results, we have attempted to highlight clinically meaningful differences. Other limitations include the fact that GTEN sites are specialized travel clinics so GTEN travellers may not be representative of all travellers. In addition, travellers were able to select more than one reason for travel, and our purpose of travel hierarchy may have resulted in travellers being categorized as business or VFR travellers even if most of the trip time was spent for leisure.

Although GTEN sites have the capacity to accommodate travellers who request a consultation on short notice, some travellers might have been seen at the last minute because of access issues rather than traveller-dependent factors—i.e. the traveller might have requested an appointment more than 7 days

before departure but could not be accommodated until 7 or fewer days. Furthermore, we did not collect information on whether consultations were for new or repeat travellers. Those who had previous pre-travel consults might have delayed seeking health advice because they believed they were already adequately prepared. It is also possible that travellers who had prior consults did not seek an appointment at all because they believed they were sufficiently educated about preventative measures, and this may have biased our study population towards travellers with less exposure to pre-travel health advice. We also did not include analysis of prescription use since the distribution of prescriptions was thought to be less time dependent, except if the traveller would have insufficient time to fill the prescription.

Lastly, we acknowledge that any general definition of an LMT may not be generalizable to all travellers. Some travellers, such as those taking immune-suppressing medications and for whom a live virus vaccine may be indicated, should ideally be seen several months before travel so that there is time to stop immune-modulating medications prior to receiving a live vaccine such as YF.[38] For these travellers, presenting within the generally recommended 4–6 weeks before departure may be considered late because of the inability to receive an indicated vaccine due to time constraints.

In conclusion, LMTs are at risk of acquiring vaccine-preventable diseases if they are unable to receive adequate pre-travel vaccinations, particularly those that require a series to complete. Our findings suggest that business and VFR travellers should particularly be targeted by strategies to improve timely pre-travel health consultation, with the goal of decreasing travel-related infections in the individual traveller as well as in the traveller's home community. Newly approved accelerated vaccination schedules may also be considered.

Funding

This work was supported by US Centers for Disease Control and Prevention grants U19CI000514, U01CK000175 and U01CK000490. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Acknowledgements

Members of the Global TravEpiNet Consortium (in alphabetical order) include George M. Abraham, Saint Vincent Hospital (Worcester, MA); Salvador Alvarez, Mayo Clinic (Jacksonville, FL); Vernon Ansdell and Johnnie A. Yates, Travel Medicine Clinic, Kaiser Permanente (Honolulu, HI); Elisha H. Atkins, Chelsea HealthCare Center (Chelsea, MA); Holly K. Birich and Dagmar Vitek, Salt Lake Valley Health Department (Salt Lake, Utah); John Cahill, Travel and Immunization Center, St. Luke's—Roosevelt (New York, NY); Lin Chen, Mount Auburn Hospital (Cambridge, MA); Bradley A. Connor, New York Center for Travel and Tropical Medicine, Cornell University (New York, NY); Roberta Dismukes, Jessica Fairley, Phyllis Kozarsky and Henry Wu, Emory TravelWell, Emory University (Atlanta, GA); Ronke Dosunmu, JourneyHealth (Maywood, NJ); Jeffrey A. Goad and Edith Mirzaian, International Travel Medicine Clinic, University of Southern California (Los Angeles, CA); Nelson Iván Agudelo Higuita, University of Oklahoma Health Sciences Center, Oklahoma City, OK; Karl Hess, Hendricks Pharmacy International Travel Clinic, Claremont, CA; Noreen A. Hynes, John Hopkins Travel and Tropical Medicine, Division of Infectious Diseases, John Hopkins School of Medicine (Baltimore, MD); Frederique Jacquerioz and Susan McLellan, Tulane University (New Orleans, LA); Jenn Katsolis, Jacksonville Travel Clinic-St. Vincents, Jacksonville, FL; Paul Kelly, Bronx Lebanon Medical Center (New York, NY); Mark Knouse, Keystone Travel Medicine, Lehigh Valley Health Network (Allentown, PA); Jennifer Lee, Northwestern Medical Group-Travel Medicine, Northwestern Memorial Hospital (Chicago, IL); Daniel Leung, Brian Kendall and DeVon Hale, International Travel Clinic, University of Utah (Salt Lake City, UT); Alawode Oladele and Hanna Demeke, DeKalb County Board of Health Travel Services-DeKalb North and Central-T.O. Vinson Centers (Decatur, GA); Alawode Oladele and Althea Otuata, DeKalb County Board of Health Travel Services-DeKalb East (Decatur, GA); Roger Pasinski and Amy E. Wheeler, Revere HealthCare Center (Revere, MA); Adrienne Showler, Laura Coster and Jessica Rosen, Infectious Diseases and Travel Medicine, Georgetown University (Washington, DC); Brian S. Schwartz, Travel Medicine and Immunization Clinic, University of California (San Francisco, CA); William Stauffer and Patricia Walker, HealthPartners Travel Medicine Clinics (St. Paul, Minnesota); and Joseph Vinetz, Travel Clinic, Division of Infectious Diseases, Department of Medicine, University of California—San Diego School of Medicine (La Jolla, CA).

Conflict of interest: None declared.

References

1. World Tourism Organization. *World Tourism Highlights 2018 Edition*. https://www.e-unwto.org/doi/pdf/10.18111/9789284419876. (1 April 2019, date last accessed).
2. Fauci AS, Morens DM. Zika virus in the Americas—yet another arbovirus threat. *N Engl J Med* 2016; **374**:601–4.
3. Gostin LO, Lucey D. Middle East respiratory syndrome: a global health challenge. *JAMA* 2015; **314**:771–1.
4. Chatham-Stephens K, Medalla F, Hughes M *et al.* Emergence of extensively drug-resistant *Salmonella Typhi* infections among travelers to or from Pakistan–United States, 2016–1208. *MMWR Morb Mortal Wkly Rep* 2019; **68**:11–3. http://dx.doi.org/10.15585/mmwr.mm6801a3.
5. Ling Y, Chen J, Huang Q *et al.* Yellow fever in a worker returning to China from Angola, March 2016. *Emerg Infect Dis* 2016; **22**: 1317–8.
6. Han G, Batra N, Vallejo A, Schecther R, Zipprich J, Harriman K. Notes from the field: measles outbreak in an era of stricter immunization requirements—California, March 2018. *MMWR Morb Mortal Wkly Rep* 2019; **68**:201–2. http://dx.doi.org/10.15585/mmwr.mm6801a3.
7. Centers for Disease Control and Prevention. *Measles. Cases and Outbreaks. Measles Cases in 2019*. https://www.cdc.gov/measles/cases-outbreaks.html (1 April 2019, date last accessed).
8. Sotir MJ, Esposito DH, Barnett ED *et al.* Measles in the 21st century, a continuing preventable risk to travelers: date from the GeoSentinel Global Network. *Clin Infect Dis* 2016; **62**:210–2.
9. Boubaker R, Meige P, Mialet C *et al.* Traveller's profile, travel patterns and vaccine practices—a 10-year prospective study in a Swiss travel clinic. *J Travel Med* 2016; **23**:1–9.

10. RC LR, Rao SR, Lee J *et al*. Global TravEpiNet: a national consortium of clinics providing care to international travelers—analysis of demographic characteristics, travel destinations, and pretravel healthcare of high-risk US international travelers, 2009–2011. *Clin Infect Dis* 2012; **54**:455–62.
11. Deshpande BR, Rao SR, Jentes ES *et al*. Use of Japanese encephalitis vaccine in US travel medicine practices in Global TravEpiNet. *Am J Trop Med Hyg* 2014; **91**:694–8.
12. Dolan SB, Jentes ES, Sotir MJ *et al*. Pre-exposure rabies vaccination among US international travelers: findings from the Global TravEpiNet Consortium. *Vector Borne Zoonotic Dis* 2014; **14**:160–7.
13. Walker XJ, Barnett ED, Wilson ME *et al*. Characteristics of travelers to Asia requiring multidose vaccine schedules: Japanese encephalitis and rabies prevention. *J Travel Med* 2015; **22**:403–9.
14. Centers for Disease Control and Prevention. *CDC Health Information for International Travel 2018*. New York: Oxford University Press, 2018.
15. World Health Organization. *International Travel and Health 2012*. http://who.int/ith/ITH_EN_2012_WEB_1.2.pdf?ua=1 (30 March 2019, date last accessed).
16. Buhler S, Ruegg R, Steffen R, Hatz C, Jaeger VK. A profile of travelers—an analysis from a large Swiss travel clinic. *J Travel Med* 2014; **21**:324–31.
17. Ministry of Health of Saudi Arabia. Health Regulations. 2016. http://www.moh.gov.sa/en/hajj/pages/healthregulations.aspx (22 May 2016, date last accessed).
18. Savage RD, Rosella LC, Crowcroft NS *et al*. How can we keep immigrant travelers health? Health challenges experienced by Canadian South Asian travelers visiting friends and relatives. *Qual Health Res* 2018; **28**:610–23.
19. Leder K, Chen LH, Wilson ME. Aggregate travel vs. single trip assessment: arguments for cumulative risk analysis. *Vaccine* 2012; **30**:2600–4.
20. Zuckerman JN, Van Damme P, Van Herck K, Loscher T. Vaccination options for last-minute travelers in need of travel-related prophylaxis against hepatitis A and B and typhoid fever. A practical guide. *Travel Med Infect Dis* 2003; **1**:219–26.
21. Jelinek T, Burchard G, Dieckmann S *et al*. Short-term immunogenicity and safety of an accelerated pre-exposure prophylaxis regimen with Japanese encephalitis vaccine in combination with rabies vaccine: a phase III multicenter, observer-blind study. *J Travel Med* 2015; **22**:225–31.
22. Cramer JP, Jelinek T, Paulke-Korinek M *et al*. One-year immunogenicity kinetics and safety of a purified chick embryo cell rabies vaccine and an inactivated Vero cell-derived Japanese encephalitis vaccine administered concomitantly according to a new, 1-week, accelerated primary series. *J Travel Med* 2016; **23**:1–8.
23. U.S. Food and Drug Administration. *Package Insert and Patient Information—Ixiaro*. https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142569.pdf (18 February 2019, date last accessed).
24. Soentjens P, Andries P, Aerssens A *et al*. Preexposure intradermal rabies vaccination: a noninferiority trial in healthy adults on shortening the vaccination schedule from 28 to 7 days. *Clin Infect Dis* 2019; **68**:607–614 . https://doi.org/10.1093/cid/ciy513.
25. WHO Expert Consultation on Rabies, third report. *WHO Technical Report Series, No. 1012*. Geneva: World Health Organization, 2018
26. Song R, Guan S, Lee SS *et al*. Late or lack of vaccination linked to importation of yellow fever from Angola to China. *Emerg Infect Dis* 2018; **24**:13831386.
27. Rowe K, Chaves N, Leder K. Challenges to providing pre-travel care for travellers visiting friends and relatives: an audit of a specialist travel medicine clinic. *J Travel Med* 2017; **24**:1–4. doi: 10.1093/jtm/tax038.
28. LaRocque RC, Deshpande B, Rao SR *et al*. Pre-travel health care of immigrants returning home to visit friends and relatives. *Am J Trop Med Hyg* 2013; **88**:376–80.
29. Khan NM, Jentes ES, Brown C *et al*. Pre-travel medical preparation of business and occupational travelers. An analysis of the Global TravEpiNet Consortium, 2009 to 2012. *J Occup Environ Med* 2016; **58**:76–82.
30. Pavli A, Lymperi I, Minitsios T *et al*. Changing trends and pretravel preparation of business travelers from Greece during the financial crisis. *Public Health* 2019; **168**:168–71.
31. National Travel and Tourism Office. U.S. Department of Commerce. *Profile of U.S. Resident Travelers Visiting Overseas Destinations: 2015 Outbound*. http://travel.trade.gov/outreachpages/download_data_table/2015_Outbound_Profile.pdf (30 September 2016, date last accessed).
32. Druckman M, Harber P, Liu Y, Quigley RL. Assessing the risk of work-related international travel. *J Occup Environ Med* 2014; **56**:1161–6.
33. Rogers WH, Bunn WB, Lerner D. Analysis of the full economic cost for Japanese encephalitis under different risk scenarios for business travelers to Asia. *J Occup Environ Med* 2019; **61**:16–20.
34. LaRocque RC, Rao SR, Tsibris A *et al*. Pre-travel health advice-seeking behavior among US international travelers departing from Boston Logan International Airport. *J Travel Med* 2010; **17**:387–91.
35. Van Herck K, Castelli F, Zuckerman J *et al*. Knowledge, attitudes and practices in travel-related infectious diseases: the European airport survey. *J Travel Med* 2004; **11**:3–8.
36. Heywood AE, Zwar N. Improving access and provision of pre-travel healthcare for travelers visiting friends and relatives: a review of the evidence. *J Travel Med* 2018;**25**:1–8. doi: https://doi.org/10.0193/jtm/tay010.
37. Baggett HC, Graham S, Kozarsky PE *et al*. Pretravel health preparation among US residents traveling to India to VFRs: importance of ethnicity in defining VFRs. *J Travel Med* 2009; **16**:112–8.
38. Hall V, Johnson D, Torresi J. Travel and biologic therapy: travel-related infection risk, vaccine response and recommendations. *J Travel Med* **2018**:1–17. doi:10.1093/jtm/tay018.