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Travelers and travel vaccines at six health care systems in the Vaccine Safety Datalink

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Abstract

Background: Studying the safety of travel vaccines poses challenges since recipients may be traveling during the risk window for adverse events and the identification of a suitable comparison group can also be difficult. The examination of traveler characteristics, travel vaccination patterns, and health care utilization using electronic health record (EHR) data can inform the feasibility of future travel vaccine safety studies.

Methods: We performed a retrospective cohort study of health plan members aged 9 months and older who had a travel-related encounter or received a travel vaccine from 2009 to 2018. Travel regions visited, travel duration, type of travel vaccine received (typhoid, yellow fever, Japanese encephalitis, rabies, and cholera), and timing of vaccination date before departure date were described. Sociodemographic information, clinical characteristics, and health care utilization were compared between travelers who received travel vaccines and travelers who did not.

Results: A total of 1,026,822 unique travelers were identified; 612,795 travelers received 898,196 doses of travel vaccines. The most commonly administered travel vaccine was typhoid vaccine and 77% of all travel vaccines were given more than one week prior to departure. Compared with travelers without travel vaccines, travelers with travel vaccines were overall similar but as a group were slightly younger, healthier, and had lower Hispanic representation. Health care utilization dramatically decreased during travel. Outpatient visits decreased from

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294.8 visits per 10,000 person-days before travel to 24.2 visits per 10,000 person-days during reported travel dates.

Conclusions: Through the EHR information from almost a million travelers, a departure date and duration of travel were successfully captured for the majority of travelers with corresponding health care utilization data. Time after vaccination and prior to departure can potentially be used to compare travelers who receive travel vaccines with travelers who do not receive travel vaccines when looking at adverse events of interest after vaccination.

Keywords

traveler; travel vaccine; vaccine safety; travel information

Background:

Prior to the COVID-19 pandemic, the number of travelers every year departing the United States (US) for international destinations had increased annually. Over 87 million US citizens traveled to international destinations in 2017, compared to just over 40 million US citizens in 2007.[1] At a pre-travel health consultation, recommendations often include vaccines on the routine adult and child / adolescent immunization schedules, as well as travel-specific vaccines against typhoid fever, yellow fever, Japanese encephalitis, rabies, and cholera.[2] Travel vaccines have been an area of robust development over the last decade, addressing diseases endemic in countries outside the US. There have been changes in schedules, such as the accelerated dosing of Japanese encephalitis vaccine with 2 doses one week apart in adults aged 19 to 64 years old and a new 2-dose rabies vaccine pre-exposure prophylaxis schedule completed in one week without requiring a third dose 21 to 28 days after the first dose, both allowing more people to complete the vaccination series before departure. New products have also been introduced to the US market, including the Yellow Fever Vaccine Live (Stamaril®) and Cholera Vaccine Live Oral (CVD 103-HgR, Vaxchora®).[3–7] However, compared to vaccines on the routine adult and child / adolescent immunization schedules, there have been fewer large observational safety studies performed on travel vaccines.[8–11]

Studying the safety of travel vaccines poses specific challenges since recipients may be traveling during the risk window of adverse events of interest, leading to under-ascertainment of medically attended adverse events.[12] Consideration must also be given to the selection of an appropriate comparator group. A review of travelers seen at the travel clinics in the Global TravEpiNet Consortium between 2009 and 2015 found that 16% of their travelers were considered last minute travelers departing within 7 days but there was variability depending on the type of travel.[13–15] Additionally, the travel encounter may have the potential of coadministration of more vaccines than at other health encounters. This encounter can be an opportunity for catch up of routine vaccines, especially for healthy persons who may not otherwise visit a doctor.[16,17] Adults may also be vaccinated against location-specific diseases such as measles, hepatitis A and meningococcal meningitis, especially if they did not receive their full vaccination series as children.[18]

Prior assessments of the safety of travel vaccines involved only limited studies done looking at electronic data extraction of traveler health information. Past studies were done mainly to either enhance public health surveillance or study the timing of vaccination prior to departure to identify opportunities for increased vaccination rates.[19,20] The extraction of data from pre-travel patient visits from electronic health records (EHR) offers the opportunity to understand baseline characteristics of travelers.

To this end, we conducted a descriptive study of traveler characteristics, travel vaccination patterns, and health care utilization before and after travel using EHR data from several US health care systems. This analysis can help inform the feasibility of conducting large, multi-site observational safety studies of travel vaccines using EHR.

Methods:

Study Setting

We performed a retrospective cohort study within six health care organizations participating in the Vaccine Safety Datalink (VSD) Project[21] (Kaiser Permanente: Southern California, Northern California, Northwest, Washington, and Colorado; HealthPartners) that provide travel medicine services. The VSD is a collaborative project between the Centers for Disease Control and Prevention's Immunization Safety Office and nine integrated health care systems representing approximately 3.6% of the US population. Each participating site creates standardized data sets with information on demographic characteristics, membership enrollment, vaccination history, and medical encounters in the outpatient, emergency department, and inpatient setting. The Institutional Review Board at each study site approved the study and determined that informed consent was not required given the data-only retrospective research activities.

Study population

The study included health plan members aged 9 months and older who had a travel-related encounter or received a travel vaccine of interest during 2009–2018. Individuals were required to have at least 6 months of continuous membership (allowing a 31-day gap) prior to a travel-related encounter or vaccination. Nine months of age was chosen for inclusion criteria as that is the minimum recommended age for yellow fever vaccine, while the other vaccines have older minimum or typical ages of vaccination.

Identification of travel encounters/episodes

Travel-related encounters were identified by clinician diagnosis codes related to travel (e.g., travel counseling, travel immunization counseling), reason for visit listed as travel (e.g., travel medication and immunization), a visit in an identified travel medicine department/clinic, or other site-specific methods (e.g., pre-travel questionnaire). Office, telephone, and email encounters were captured, and persons may have had multiple encounters for one trip. Encounters related to each trip were consolidated into discrete episodes such that travel-related encounters within 60 days of each other were defined as one episode of care. The first encounter with traveler information was defined as the index date for the episode. Multiple travel episodes per traveler were allowed during the study period.

Identification of travel information

The trip itinerary was typically recorded as structured text in the EHR during a pre-travel consultation encounter, although the patterns and keywords varied across sites and over the years of the study. We first identified text patterns and keywords in the clinic notes by reviewing a sample of travel encounter charts. Then, information about the nature of the travel including countries/regions visited, departure date, and length of travel was retrieved from structured text using the SAS Perl regular expression functions.[22]

Travel vaccines of interest

Vaccines against typhoid fever (both injectable and oral), yellow fever, Japanese encephalitis, rabies and cholera were chosen as they were not part of the routine child/adolescent or adult immunization schedules and were only rarely indicated for non-travel purposes such as immunization of laboratory workers. Rabies vaccine could also be indicated for non-travel exposures such as veterinary occupation, so only rabies immunizations within 60 days of a travel encounter were included in the analysis. All injectable vaccines were identified by CVX codes and oral typhoid vaccine was identified by NDC codes. Travelers who received at least one of these travel vaccines were considered vaccinated travelers; others who had travel-related encounters but did not receive any of these travel vaccines were considered unvaccinated travelers.

Analysis

The number of travel episodes and uptake of travel vaccines among the VSD population by year were plotted. Travel episodes were assessed for the availability of travel information. Among those with any travel information, the distributions of travel regions, travel duration, type of travel vaccine received, and timing of vaccination date before travel departure date were described.

Sociodemographic and clinical characteristics including age, sex, VSD site, socioeconomic status (e.g., neighborhood median household income and education, Medicaid status), Charlson comorbidity score and health care utilization (e.g., number of outpatient visits, emergency department [ED] visits, and hospitalizations) in the 12 months prior to index date, concomitant vaccination (any vaccine administered concomitantly, yes or no), season (northern hemisphere) of travel, time interval between index date and travel departure date, and travel regions were summarized by frequency and percentage, and compared using Chi-square tests between vaccinated and unvaccinated travelers. Absolute standardized differences (ASD) were calculated to assess the difference of covariate distribution. ASD ≤ 0.1 was considered a negligible difference. For travelers who received travel vaccine, the index date was the vaccination injection/dispense date. For travelers who did not receive any travel vaccines after a travel counseling visit, the index date was the date of the travel counseling visit.

Health care utilization (calculated as encounter rate per 10,000 person-days) after the index date (before, during, and after travel) was assessed overall, by setting (outpatient, ED, and inpatient), as well as whether the encounter occurred inside or outside the health plan. All analyses were conducted using SAS EG version 9.4 (SAS Institute, Cary, NC).

Results:

A total of 1,026,822 unique travelers were identified either through travel encounters, receipt of a travel vaccine, or both (Figure 1). The mean age of the study population was 42 years, the majority were female (56%), and 42% of the cohort were non-Hispanic white. Among them, 989,416 travelers identified by travel encounters contributed 1,558,776 travel episodes; 31% of travelers had 2 or more travel episodes during the study period; 75% of travel episodes had travel information; and 44% of travel episodes had a travel vaccine within 60 days after a travel encounter. A total of 612,795 travelers received 898,196 doses of travel vaccines during the study period; 92% of vaccines were administered within 60 days after a travel encounter.

Both the number of travel episodes and travel vaccinations increased during the study period (Figure 2). From 2009 through 2018, the number of travel episodes and travel vaccinations increased 87% and 58%, respectively. Among travel episodes with travel information, the two most commonly visited regions were Asia/Pacific islands (45%) and South/Latin America (31%) (Figure 3). Almost half of all trips were less than 2 weeks in duration and a third of trips were 15-30 days in duration. The most commonly administered travel vaccine was typhoid vaccine (55% injectable and 26% oral). Around 23% of travel vaccinations were given within one week prior to travel departure and 47% of vaccines were given between 8-30 days prior to travel departure.

Characteristics of vaccinated and unvaccinated travelers are presented in Table 1 and Supplementary Table 1. Compared with unvaccinated travelers, vaccinated travelers were as a group slightly younger, healthier (lower Charlson comorbidity scores, fewer inpatient visits), and had lower Hispanic representation. More than half of travelers lived in an area with median household income $80,000 and above. The distributions of neighborhood median household income and education were similar between travelers with and without travel vaccination. Summer (June–August) was the season with the most travel encounters/vaccinations, although the seasonal variation was not strong. The time between index date and departure date was longer for travelers who received Japanese encephalitis vaccine or rabies vaccine than for travelers without travel vaccination. Approximately 20% of unvaccinated travelers and 24% of travelers vaccinated with injectable typhoid vaccine were last minute travelers departing within 7 days of their travel encounter/vaccination date. Travel regions were highly associated with the type of travel vaccines received. Travelers vaccinated with yellow fever vaccine more commonly visited Africa, while travelers with Japanese encephalitis vaccine more commonly visited Asia/Pacific Islands. Among injectable travel vaccines, around 70% of travel vaccines were co-administered with other vaccines, whether travel-specific or routine.

Overall health care utilization dramatically decreased during travel (Table 2, Supplementary Figure 1). Outpatient visits decreased from 294.8 visits per 10,000 person-days before travel to 24.2 visits per 10,000 person-days during reported travel dates. Inpatient visits had the smallest change, decreasing from 1.0 visits per 10,000 person-days before travel to 0.7 visits per 10,000 person-days during reported travel dates. Inpatient visits occurring outside the

health plan (captured via claims) increased from 0.1 visits per 10,000 person-days before travel to 0.4 visits per 10,000 person-days during reported travel dates.

Discussion:

Given the large number of travelers and travel vaccines administered within the VSD sites studied, this population can provide significant information on the assessment of safety outcomes for travel vaccines. Traveler information, including departure date, travel location, and travel duration, was successfully extracted from the EHR for the majority of travelers through the retrieval of structured clinic notes. A risk window for vaccine adverse events of interest between vaccination and travel departure can be established and person-time can be calculated when looking at event rates prior to departure. This could potentially avoid the underestimation of event rates that would occur using a fixed risk window if the adverse event risk window and the travel period were to overlap. The large drop in overall utilization rates after reported departure dates suggests that an accurate departure date is being captured from the EHR for the majority of travelers. Likewise, overall inpatient utilization decreased during the reported travel period, but there was a small increase in inpatient utilization occurring outside the health plan which suggests at least partial capture of serious health events while traveling through retrieval of outside claims data.

The ability to capture unvaccinated travelers as the comparator group helps minimize bias by using similar person-time while accessible to care. This group was similar overall to those travelers who received travel vaccines, although there was a higher proportion of those over 65 years of age who did not receive travel vaccines when compared to the younger age groups. This might be partially explained by travel destination and historical receipt of travel vaccines.

The majority of travel vaccines were given more than 7 days before departure, allowing significant follow-up time for adverse events with access to care. Similar to data from the Global TravEpiNet Consortium, 16% of travelers in this cohort with departure date information were last minute travelers departing within 7 days of their travel encounter, while approximately 66% contacted the travel clinic 2 weeks or more in advance of their trip (Supplementary Table 2).

This study was also able to provide information on the appropriateness of vaccination or lack of vaccination, based on vaccination criteria for some travel vaccines.[23] Only 92 persons received cholera vaccine which has a very limited indication for use, mainly in relief workers deployed to an active outbreak zone. Interestingly, over 70 % of persons who did not receive typhoid vaccine could be explained by one of the following reasons: receipt of historical dose of vaccine, too young to receive vaccine, not going to high risk area, or had travel encounter within 14 days prior to departure.

The VSD represents approximately 3.6% of the US population and is geographically and ethnically diverse.[24,25] Certain groups, such as Asians and Hispanics, have a larger representation in the VSD than the US as a whole. Within our cohort of travelers, persons identified as Asian were over-represented while persons identified as Hispanic were under-

represented compared to the total VSD population. This could represent the true volume of travel or usage of the travel clinics, which is influenced by awareness of travel clinic services availability, type of travel, and perceived need of pre-travel medical evaluation.[26]

There were several limitations uncovered by the study including the lack of traveler-specific information for 25% of persons with a travel episode. The absence of travel information may be due to travel episodes identified by encounters with limited information or information recorded as unstructured free text. Travel vaccines given outside the health plan and retrieved through immunization information systems would likely not be associated with a travel episode; furthermore, only 8% of travel vaccinations were not associated with a travel episode. Low risk trips, for which persons did not have a travel encounter or receive a travel vaccine, would also not be captured and would likely be underrepresented. In a study of international travelers embarking from Boston Logan International Airport, 46% of travelers to low or low-middle income countries did not pursue pre-travel health information of any type. Less than a third of those that did seek advice visited a travel medicine specialist.[14] However, in the VSD, members of the health plans have travel medicine coverage, as well as travel vaccine coverage without additional charge in the California locations. One benefit to using the EHR of VSD sites is that the barrier to travel medicine services is low, leading to high patient volumes and comprehensive data within the EHR of these integrated health care systems. This study only evaluated travel-specific vaccines and not vaccines commonly given for travel but also on the routine adult and child/adolescent immunization schedules for other indications such as hepatitis A vaccine, measles vaccine, meningitis vaccine, and influenza vaccine.[27,28] The results of this study might not be applicable to other vaccines given for travel not included in this study. New travel vaccines, including Ebola Zaire Vaccine Live (*rVSVΔG-ZEBOV-GP*, Ervebo), Tick-Borne Encephalitis Vaccine (Tikovac®), and Dengue Tetravalent Vaccine, Live (Dengvaxia®), have received recent FDA approval and the methods used in this study may be applied to the study of these and other new travel vaccines in the future.[29–31]

Conclusion:

In this large cohort of almost a million travelers, an accurate departure date and duration of travel was successfully captured for the majority of travelers with matching corresponding health care utilization data. Time after vaccination and prior to departure can potentially be used to compare vaccinated travelers with unvaccinated travelers when looking at adverse events of interest after vaccination. Studies of the safety of travel vaccines may be facilitated through the use of data from the EHR.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of Interest:

LQ received funding from Moderna, GlaxoSmithKline, and Dynavax for work unrelated to this manuscript. LSS received funding from Moderna, GlaxoSmithKline, Dynavax, and Seqirus for work unrelated to this manuscript. RH received funding from Dynavax for work unrelated to this manuscript. ALN received funding from Pfizer and Vir Biotechnology for work unrelated to this manuscript.

Disclaimer:

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. Mention of a product or company name is for identification purposes only and does not constitute endorsement by the CDC.

References:

1. U.S. Department of Commerce ITA, National Travel and Tourism Office (NTTO). U.S. Citizen Traffic to Overseas Regions, Canada & Mexico. 2007–2017.
2. CDC. CDC Yellow Book 2020: Health Information for International TravelHealth Information for International Travel. 2019.
3. Hills SL, Walter EB, Atmar RL, Fischer M. Japanese Encephalitis Vaccine: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports. 2019;68(2):1–33.
4. Rao A Summary of Evidence to Recommendations Framework for Rabies Pre-Exposure Prophylaxis Vote. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/04-Rabies-Rao-508.pdf. Accessed January 17, 2022.
5. 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(6):403–409. [PubMed: 26420372]
6. Gershman MD, Angelo KM, Ritchey J, et al. Addressing a Yellow Fever Vaccine Shortage - United States, 2016–2017. MMWR Morbidity and mortality weekly report. 2017;66(17):457–459. [PubMed: 28472025]
7. Wong KK, Burdette E, Mahon BE, Mintz ED, Ryan ET, Reingold AL. Recommendations of the Advisory Committee on Immunization Practices for Use of Cholera Vaccine. MMWR Morbidity and mortality weekly report. 2017;66(18):482–485. [PubMed: 28493859]
8. Nordin JD, Parker ED, Vazquez-Benitez G, et al. Safety of the yellow Fever vaccine: a retrospective study. J Travel Med. 2013;20(6):368–373. [PubMed: 24118538]
9. Porter CK, Sorrell T, Mitra I, Riddle MS. Vaccination of active component US military personnel against Salmonella Typhi. Vaccine. 2017;35(14):1742–1748. [PubMed: 28268075]
10. Lindsey NP, Rabe IB, Miller ER, Fischer M, Staples JE. Adverse event reports following yellow fever vaccination, 2007-13. J Travel Med. 2016;23(5).
11. Moro PL, Lewis P, Cano M. Adverse events following purified chick embryo cell rabies vaccine in the Vaccine Adverse Event Reporting System (VAERS) in the United States, 2006-2016. Travel medicine and infectious disease. 2019;29:80–81. [PubMed: 31203930]
12. World Health O. Causality assessment of an adverse event following immunization (AEFI): user manual for the revised WHO classification. 2nd ed., 2019 update ed. Geneva: World Health Organization; 2019.
13. 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. Journal of occupational and environmental medicine. 2016;58(1):76–82. [PubMed: 26479857]
14. LaRocque RC, Deshpande BR, Rao SR, et al. Pre-travel health care of immigrants returning home to visit friends and relatives. The American journal of tropical medicine and hygiene. 2013;88(2):376–380. [PubMed: 23149585]

15. Stoney RJ, Jentes ES, Sotir MJ, et al. Pre-travel preparation of US travelers going abroad to provide humanitarian service, Global TravEpiNet 2009-2011. The American journal of tropical medicine and hygiene. 2014;90(3):553–559. [PubMed: 24445203]
16. Lin LH, Hochberg NS. Chapter 2: Preparing International Travelers. In: CDC, Brunette GW, Nemhauser JB, eds. CDC Yellow Book. New York: Oxford University Press; 2020.
17. Boubaker R, Meige P, Mialet C, et al. Travellers' profile, travel patterns and vaccine practices--a 10-year prospective study in a Swiss Travel Clinic. J Travel Med. 2016;23(1).
18. Sanford CA, Jong EC. Immunizations. The Medical clinics of North America. 2016;100(2):247–259.
19. Peterson KS, Lewis J, Patterson OV, et al. Automated Travel History Extraction From Clinical Notes for Informing the Detection of Emergent Infectious Disease Events: Algorithm Development and Validation. JMIR public health and surveillance. 2021;7(3):e26719. [PubMed: 33759790]
20. Bandali M, Schultz J, Than K, et al. Ensuring the Safety of Yellow Fever Vaccination in Travelers-The Experience at a Large U.S. Academic Medical Center in Colorado. Tropical medicine and infectious disease. 2020;5(3).
21. McNeil MM, Gee J, Weintraub ES, et al. The Vaccine Safety Datalink: successes and challenges monitoring vaccine safety. Vaccine. 2014;32(42):5390–5398. [PubMed: 25108215]
22. Cody R An Introduction to Perl Regular Expressions in SAS 9. SUGI 29:265–29:https://support.sas.com/resources/papers/proceedings/proceedings/sugi29/265-29.pdf. Accessed February 22, 2022.
23. Steinberg EB, Bishop R, Haber P, et al. Typhoid fever in travelers: who should be targeted for prevention? Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2004;39(2):186–191. [PubMed: 15307027]
24. Klein NP, Lewis N, Goddard K, et al. Surveillance for Adverse Events After COVID-19 mRNA Vaccination. Jama. 2021;326(14):1390–1399. [PubMed: 34477808]
25. Sukumaran L, McCarthy NL, Li R, et al. Demographic characteristics of members of the Vaccine Safety Datalink (VSD): A comparison with the United States population. Vaccine. 2015;33(36):4446–4450. [PubMed: 26209836]
26. Hill DR, Ericsson CD, Pearson RD, et al. The practice of travel medicine: guidelines by the Infectious Diseases Society of America. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2006;43(12):1499–1539. [PubMed: 17109284]
27. Angelo KM, Libman M, Gautret P, et al. The rise in travel-associated measles infections-GeoSentinel, 2015-2019. J Travel Med. 2019;26(6).
28. Boggild AK, Castelli F, Gautret P, et al. Vaccine preventable diseases in returned international travelers: results from the GeoSentinel Surveillance Network. Vaccine. 2010;28(46):7389–7395. [PubMed: 20851081]
29. Choi MJ, Cossaboom CM, Whitesell AN, et al. Use of Ebola Vaccine: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports. 2021;70(1):1–12.
30. FDA. BLA Approval Letter - Tick Borne Encephalitis Vaccine, Ticovac. August 13, 2021. https://www.fda.gov/media/151516/download. Accessed January 17, 2022.
31. Paz-Bailey G, Adams L, Wong JM, et al. Dengue Vaccine: Recommendations of the Advisory Committee on Immunization Practices, United States, 2021. MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports. 2021;70(6):1–16.

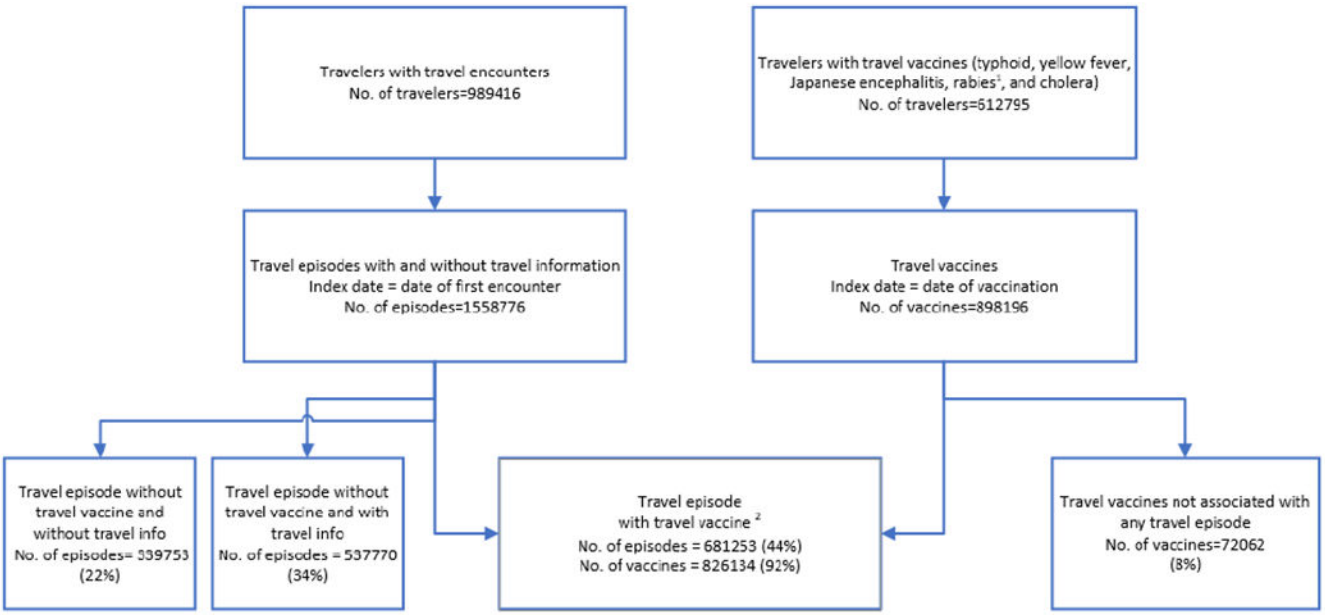

Figure 1.

Study cohort diagram

[1] Rabies vaccines within 60 days after a travel encounter were included

[2] Had a travel vaccine within 60 days after a travel encounter

Travel information consists of information on countries/regions visited, departure date, or length of travel

The total number of unique travelers N=1026822

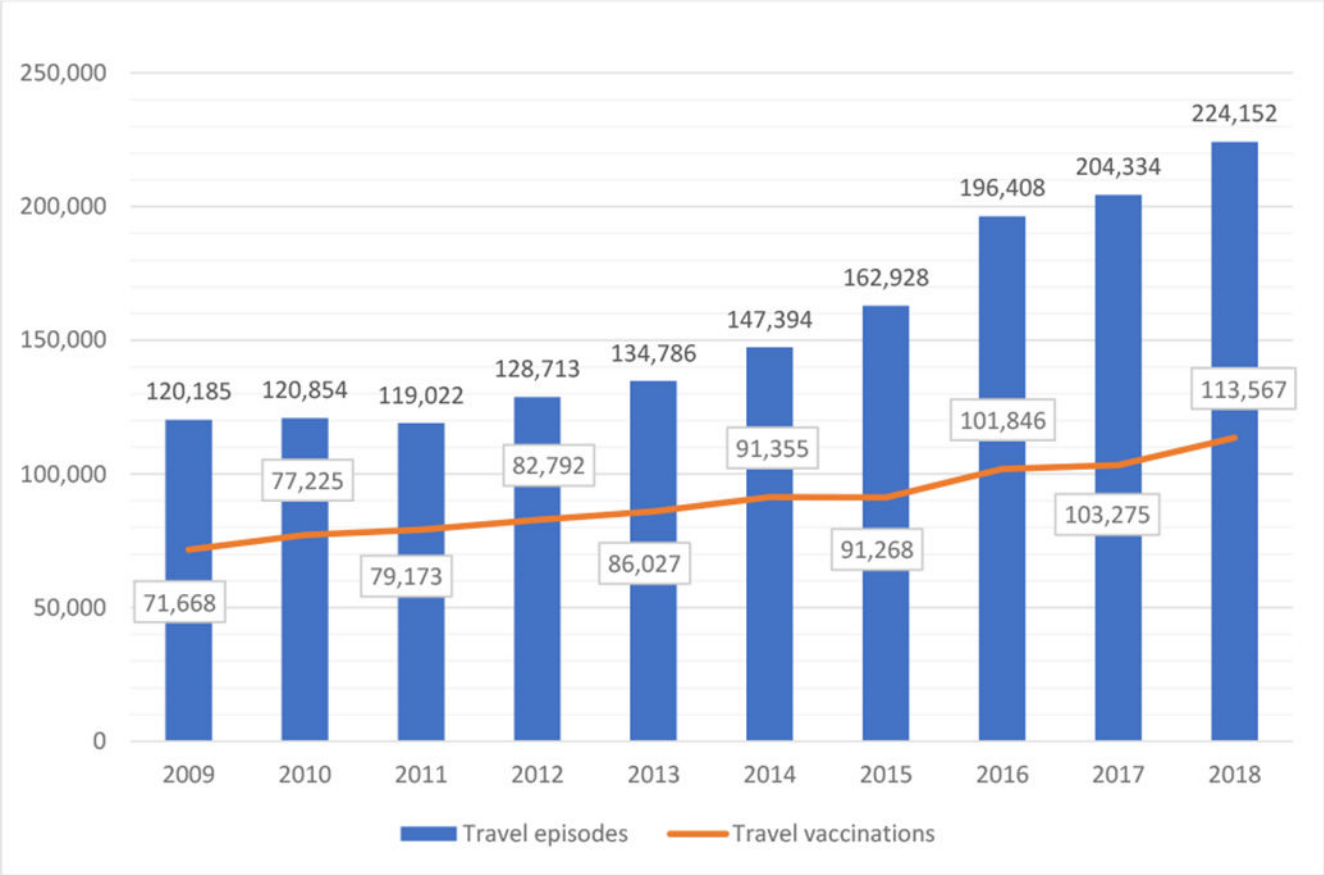

Figure 2.
Number of travel episodes and travel vaccinations by year

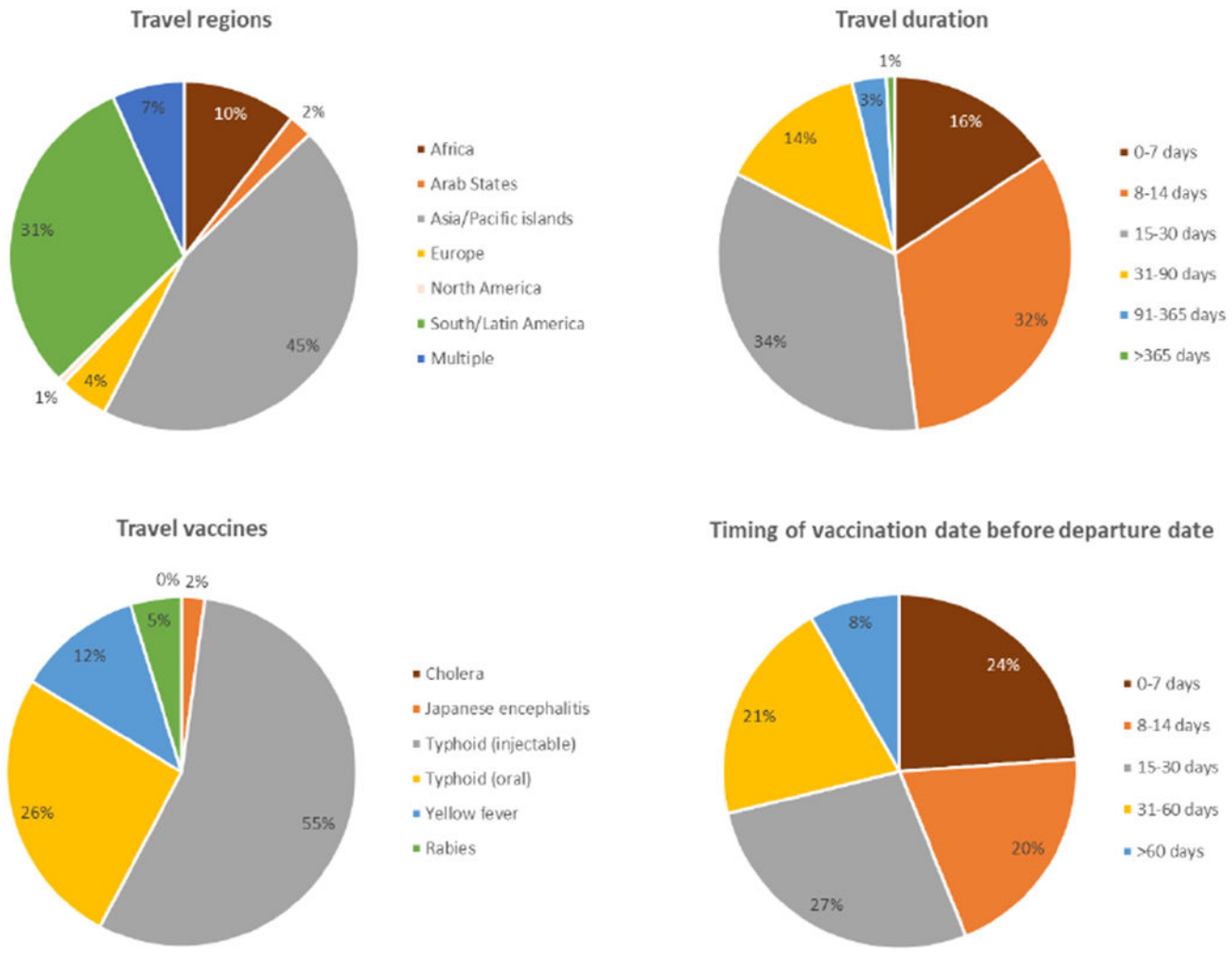

Figure 3.

Travel regions, travel duration, type of travel vaccine, and timing of vaccination date before departure date among those who received a travel vaccine or had a travel encounter.

Among travel episodes, 29% of travel episodes were missing travel regions, and 34% of travel episodes were missing travel duration. Among travel vaccinations, 14% were missing travel departure date.

Table 1.

Characteristics of travelers with and without travel vaccine(s).

	Travelers without travel vaccine[1]	Travelers with					Travelers with travel vaccine	ASD
		Typhoid (injectable)	Typhoid (oral)	Yellow fever	Japanese encephalitis	Rabies		
	N = 537770	N = 469352	N = 204174	N = 93248	N = 16957	N = 42378	N=826109	
Age at index date, year								0.259
0–17	90497(16.8%)	107154(22.8%)	23277(11.4%)	13681(14.7%)	1907(11.2%)	7521(17.7%)	153540(18.6%)	
18–29	56811(10.6%)	66350(14.1%)	35472(17.4%)	19173(20.6%)	4777(28.2%)	11012(26%)	136784(16.6%)	
30–49	142444(26.5%)	129889(27.7%)	62198(30.5%)	26587(28.5%)	4597(27.1%)	11590(27.3%)	234861(28.4%)	
50–64	129056(24%)	96911(20.6%)	52725(25.8%)	22849(24.5%)	3563 (21%)	8118(19.2%)	184166(22.3%)	
≥65yr	118962(22.1%)	69048(14.7%)	30502(14.9%)	10958(11.8%)	2113(12.5%)	4137(9.8%)	116758(14.1%)	
Sex [2]								0.037
Female	233822(57%)	221097(55%)	96905(55.8%)	51674(55.5%)	5189(54.5%)	9542(56.4%)	311716 (55.2%)	
Male	176156(43%)	181017(45%)	76852(44.2%)	41509(44.5%)	4324(45.5%)	7384(43.6%)	253060 (44.8%)	
Race/ethnicity [2]								0.136
Hispanic	58090(14.2%)	47681(11.9%)	15551(8.9%)	9058(9.7%)	455 (4.8%)	1242(7.3%)	62986 (11.2%)	
Non-Hispanic Asian	112035(27.3%)	137241(34.1%)	42964(24.7%)	9204(9.9%)	2467(25.9%)	3288(19.4%)	173414 (30.7%)	
Non-Hispanic Black	20132(4.9%)	28674(7.1%)	8418(4.8%)	17289(18.6%)	161 (1.7%)	941(5.6%)	36898 (6.5%)	
Non-Hispanic White	178571(43.6%)	142680(35.5%)	89798(51.7%)	48969(52.5%)	5476(57.6%)	9836(58.1%)	229701 (40.7%)	
Other	41161(10%)	45844(11.4%)	17035(9.8%)	8666(9.3%)	954 (10%)	1621(9.6%)	61791 (10.9%)	
Charlson score								0.121
0	406804(75.6%)	364835(77.7%)	166631(81.6%)	77679(83.3%)	13856(81.7%)	35480(83.7%)	658481(79.7%)	
1–2	119335(22.2%)	96339(20.5%)	35613(17.4%)	14913(16%)	2968(17.5%)	6666(15.7%)	156499(18.9%)	
3+	11631(2.2%)	8178 (1.7%)	1930(0.9%)	656(0.7%)	133 (0.8%)	232(0.5%)	11129(1.3%)	
Neighborhood median household income								0.042
<$40,000	17916(3.3%)	18574 (4%)	6794(3.3%)	4517(4.8%)	702 (4.1%)	1762(4.2%)	32349(3.9%)	
$40,000-$59,999	67648(12.6%)	60685(12.9%)	25834(12.7%)	13305(14.3%)	2384(14.1%)	5527(13%)	107735(13%)	
$60,000-$79,999	108596(20.2%)	94832(20.2%)	40815(20%)	19553(21%)	3655(21.6%)	8903(21%)	167758(20.3%)	

	Travelers without travel vaccine[1]	Travelers with					Travelers with travel vaccine	ASD
		Typhoid (injectable)	Typhoid (oral)	Yellow fever	Japanese encephalitis	Rabies		
	N = 537770	N = 469352	N = 204174	N = 93248	N = 16957	N = 42378	N=826109	
$80,000-$99,999	109792(20.4%)	95224(20.3%)	41291(20.2%)	18173(19.5%)	3372(19.9%)	8552(20.2%)	166612(20.2%)	
$100,000+	200335(37.3%)	169687(36.2%)	75629(37%)	30684(32.9%)	5988(35.3%)	15249(36%)	297237(36%)	
Missing	33483(6.2%)	30350(6.5%)	13811(6.8%)	7016(7.5%)	856 (5%)	2385(5.6%)	54418(6.6%)	
Neighborhood education								0.022
≤high school	52394(9.7%)	55663(11.9%)	15460(7.6%)	8688(9.3%)	1250 (7.4%)	2979(7%)	84040 (10.2%)	
>high school	451856(84%)	383280(81.7%)	174890(85.7%)	77532(83.1%)	14851(87.6%)	37010(87.3%)	687563(83.2%)	
Missing	33520(6.2%)	30409(6.5%)	13824(6.8%)	7028(7.5%)	856 (5%)	2389(5.6%)	54506 (6.6%)	
Season of index date								0.030
Spring (March-May)	135736(25.2%)	115833(24.7%)	51116(25%)	25646(27.5%)	4348(25.6%)	12459(29.4%)	209402(25.3%)	
Summer (June-August)	145640(27.1%)	132850(28.3%)	53010(26%)	28975(31.1%)	5083 (30%)	12562(29.6%)	232480(28.1%)	
Fall (September-November)	133606(24.8%)	110287(23.5%)	53222(26.1%)	18762(20.1%)	4440(26.2%)	9713(22.9%)	196424(23.8%)	
Winter (December-February)	122788(22.8%)	110382(23.5%)	46826(22.9%)	19865(21.3%)	3086(18.2%)	7644 (18%)	187803(22.7%)	
Timing of index date before planned travel departure date								0.156
Missing	42542(7.9%)	49621(10.6%)	N/A	10376(11.3%)	2952 (17.5%)	6252(14.8%)	69201 (11.2%)	
0–7 days	106533(19.8%)	113621(24.2%)	N/A	11949(12.8%)	2137 (12.6%)	3464(8.2%)	131171(21.2%)	
8–14 days	92134(17.1%)	92081(19.7%)	N/A	13781(15%)	1506 (8.9%)	2730(6.5%)	110098(17.8%)	
15–30 days	132666(24.7%)	111910(23.9%)	N/A	23854(25.9%)	3100 (18.4%)	10962(26%)	149826(24.2%)	
31–60 days	108679(20.2%)	73551(15.7%)	N/A	21583(23.4%)	4888 (29%)	12632(29.9%)	112654 (18.2%)	
61+ days	55216(10.3%)	26623(5.7%)	N/A	10594(11.5%)	2249 (13.4%)	6167(14.6%)	45633 (7.4%)	
Travel Regions								0.557
Africa	37958(7.1%)	49770(10.6%)	24601(12.4%)	37241(40.4%)	88 (0.5%)	6214(14.7%)	117914(14.4%)	
Arab States	12234(2.3%)	9219 (2%)	3475(1.8%)	435(0.5%)	14 (0.1%)	404 (1%)	13547(1.7%)	
Asia/Pacific islands	192783(35.8%)	226944(48.6%)	84510(42.7%)	554(0.6%)	12645(75.1%)	18097(42.9%)	342750(42%)	
Europe	43576(8.1%)	4767 (1%)	2209(1.1%)	456(0.5%)	75 (0.4%)	419 (1%)	7926(1%)	
North America	5003(0.9%)	1404 (0.3%)	461(0.2%)	551(0.6%)	38 (0.2%)	124(0.3%)	2578(0.3%)	

	Travelers without travel vaccine[1]	Travelers with					Travelers with travel vaccine	ASD
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	N = 537770	N = 469352	N = 204174	N = 93248	N = 16957	N = 42378	N=826109	
South/Latin America	188953(35.1%)	98916(21.2%)	46515(23.5%)	33657(36.5%)	170 (1%)	7516(17.8%)	186774(22.9%)	
Multiple/Unknown	57263(10.6%)	76387(16.4%)	36266(18.3%)	19243(20.9%)	3802(22.6%)	9433(22.3%)	145131(17.6%)	
Concomitant vaccine								N/A
Yes	N/A	322596(68.7%)	N/A	76769(82.3%)	11005(64.9%)	19741(46.6%)	430111(69.2%)	

1. Including travel episodes with travel information

2. Sex and race/ethnicity are shown in patient level

All p values were <0.001

ASD = absolute standardized difference

Table 2.

Encounter rate per 10,000 person-days before, during, and after travel among travelers with reported travel dates

	Overall			Inside Health Plan			Outside Health Plan		
	Before	**During**	**After**	**Before**	**During**	**After**	**Before**	**During**	**After**
Outpatient	294.8	24.2	158.3	282.5	21.2	147.7	12.3	3.0	10.6
ER	4.4	1.6	5.6	3.9	1.2	4.9	0.5	0.4	0.7
Inpatient	1.0	0.7	1.8	0.9	0.3	1.6	0.1	0.4	0.2

Limited to those with departure date and return date within 42 days post index date