

Published in final edited form as:

JAMA Pediatr. 2020 February 01; 174(2): e194515. doi:10.1001/jamapediatrics.2019.4515.

Missed opportunities for measles-mumps-rubella (MMR) vaccination among US pediatric international travelers

Emily P. Hyle, MD^{a,b,c,d}, Sowmya R. Rao, PhD^{e,f}, Audrey C. Bangs, BA^b, Paul Gastañaduy, MD MPH^g, Amy Parker Fiebelkorn, MSN MPH^h, Stefan H.F. Hagmann, MD MSc^{i,j}, Allison Taylor Walker, PhD, MPH^k, Rochelle P. Walensky, MD MPH^{b,c,d}, Edward T. Ryan, MD^{a,c,d}, Regina C. LaRocque, MD MPH^{a,c,d}

^aTravelers' Advice and Immunization Center, Massachusetts General Hospital, Boston, MA

^bMedical Practice Evaluation Center, Department of Medicine, Massachusetts General Hospital, Boston, MA

^cDivision of Infectious Diseases, Massachusetts General Hospital, Boston, MA

^dHarvard Medical School, Boston, MA

eMGH Biostatistics Center, Massachusetts General Hospital, Boston, MA

Department of Global Health, Boston University School of Public Health, Boston, MA

⁹Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA

^hImmunization Services Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA

ⁱDivision of Pediatric Infectious Diseases, Steven and Alexandra Cohen Children's Medical Center of New York, New Hyde Park, NY

Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY

^kDivision of Global Migration and Quarantine, Centers for Disease Control and Prevention, Atlanta, GA

Abstract

Importance: The United States is experiencing a resurgence of measles, with more than 1000 cases in the first six months of 2019. Imported measles cases among returning international travelers are the source of most US measles outbreaks, and such importations can be reduced with pretravel measles-mumps-rubella (MMR) vaccination. Although children account for less than 10% of US international travelers, pediatric travelers account for almost half of all measles importations.

Objective: To examine clinical practice regarding MMR vaccination of pediatric international travelers and to identify reasons for nonvaccination of those identified as MMR-eligible.

Design: Observational study (2009–2018).

Setting: 29 sites associated with Global TravEpiNet (GTEN), a Centers for Disease Control and Prevention-supported consortium of clinical sites that provide pretravel consultations.

Participants: Pediatric travelers (6 months and <18 years of age) attending pretravel consultation.

Main Outcomes: MMR vaccination among MMR-eligible pediatric travelers.

Results: Of 14 602 pretravel consultations for pediatric international travelers, 2864 travelers (20%) were eligible to receive pretravel MMR vaccination at the time of the consultation: 365 of 398 (92%) infants (6 to <12 months), 2161 of 3623 (60%) preschool-aged travelers (1 to <6 years), and 338 of 10 581 (3%) school-aged travelers (6 to <18 years). MMR-eligible travelers were frequently not vaccinated (1682 of 2864 [59%]) including: 161 of 365 (44%) infants, 1222 of 2161 (57%) preschool-aged travelers, and 299 of 338 (88%) school-aged travelers. We observed a diversity of clinical practice at different GTEN sites. In multivariable analysis, MMR-eligible pediatric travelers were less likely to be vaccinated at the pretravel consultation if they were school-aged or evaluated at specific GTEN sites. The most common reasons for nonvaccination were provider decision not to administer MMR vaccination (37%) and guardian refusal (36%).

Conclusions and Relevance: Although most infant and preschool-aged travelers evaluated at GTEN sites were eligible for pretravel MMR vaccination, fewer than half were vaccinated during pretravel consultation, mostly due to provider decision or guardian refusal. Strategies are needed to improve MMR vaccination among pediatric travelers that will reduce measles importations and resultant outbreaks in the United States.

Introduction

The United States (US) has had a resurgence of measles. More than 1000 cases were reported from 28 states within the first six months of 2019, which is the greatest number of cases in the US since 2000. Measles is a viral illness associated with fever, cough, coryza, and conjunctivitis followed by rash that can result in hospitalization, severe neurologic disease, and death. A safe and effective measles-mumps-rubella (MMR) vaccine is included in the routine childhood vaccination schedule in the US, and widespread vaccine coverage has ensured maintenance of measles elimination (ie, lack of sustained measles transmissions for more than 12 months) in the US since 2000. Although MMR vaccination rates are stable at the national level, refused or delayed MMR vaccination among healthy children has increased, and communities with large numbers of incompletely vaccinated children are highly susceptible to outbreaks. This major public health concern jeopardizes the elimination of measles in the US. 1,10

Since elimination in 2000, measles outbreaks in the US are due to international importation. More than half of all measles importations occur among US residents who are infected during international travel. However, the risk of measles exposure during international travel is often under-recognized by health care providers and travelers. At pretravel consultations in the Global TravEpiNet (GTEN) Consortium from 2009 through 2014, providers identified 16% of US adult international travelers born after 1956 as eligible for pretravel MMR vaccination prior to travel, yet only 47% of these were vaccinated. 13

Pediatric travelers are a particularly important group for pretravel MMR vaccination. Although pediatric travelers comprise less than 10% of US international travelers annually, ¹⁴ they accounted for 47% of measles importations among returning US travelers from 2001

through 2016.^{11,12} The Advisory Committee on Immunization Practices (ACIP) recommends that US children without other evidence of immunity receive two lifetime MMR doses as part of routine vaccination; the first dose is given between 12 and 15 months and a second dose between 4 and 6 years (Table 1).⁶ Since 1989, ACIP has recommended a specific schedule of MMR vaccination among pediatric international travelers.^{15,16} Infants (6 to <12 months) should receive one MMR vaccination before international travel that does not count towards the two lifetime doses. Preschool-aged travelers (1 to <6 years) should receive both lifetime MMR doses before departure and at least 28 days apart. ACIP recommendations for international travelers do not differ from the routine immunization schedule for school-aged children (6 to <18 years), who should have already received two MMR doses during routine care.¹⁵

The objective of this multisite observational study was to characterize clinical practice regarding MMR vaccination of pediatric travelers seen for pretravel consultation. We characterized how frequently providers identified pediatric travelers eligible for MMR vaccination. We then examined whether MMR vaccination was administered during the pretravel consultation and reasons for nonvaccination.

Methods

Study setting

Global TravEpiNet (GTEN) is a consortium of US clinical sites, supported by the Centers for Disease Control and Prevention (CDC), where providers evaluate travelers in anticipation of upcoming travel; data have been prospectively collected since 2009 regarding clinical practice patterns. ¹⁷ Twenty-nine sites contributed data to this analysis from four US Census regions: Northeast (9 sites), Midwest (2 sites), West (8 sites), and South (10 sites). ¹⁸ Nineteen sites were academic centers, and 10 were other types of health facilities, including primary care practices, pharmacies, and public health clinics.

Study population and eligibility criteria

Travelers were eligible for inclusion if they were <18 years when they attended a GTEN site from January 1, 2009, through December 31, 2018. We excluded data on pediatric travelers whose itineraries were restricted to the US or who were younger than 6 months at the pretravel consultation because they would not be eligible for ACIP-recommended pretravel MMR vaccination. How characterized pediatric travelers into three age groups given agestratified ACIP guidelines for MMR vaccination (Table 1): infants (6 to <12 months), preschool-aged (1 to <6 years), and school-aged (6 to <18 years).

Data collection

Providers used a structured, online questionnaire during pretravel consultations to confirm details entered by the traveler/guardian regarding demographics, medical conditions, and travel itinerary (eg, region, purpose, and duration of travel). Providers entered data about immunization history as per traveler/guardian report or written documentation, as well as health advice provided, vaccines administered, and medications prescribed. Incomplete answers were not allowed.

Assessment of MMR eligibility

We reviewed the data that providers entered in the GTEN structured questionnaire to classify travelers as "MMR-eligible" according to our age-stratified study definition: infants (6 to <12 months), if providers noted no prior MMR vaccination and no alternative evidence of immunity; children 1 year (ie, preschool-aged and school-aged travelers), if providers did not elicit a history of two MMR vaccinations or other evidence of immunity. ^{15,16} We considered pediatric travelers to be MMR-ineligible if they had evidence of preexisting measles immunity, contraindications to MMR vaccination (ie, immunosuppression), or had received a dose of MMR less than 28 days before the pretravel consultation.

Clinical management

Providers assessed travelers' past MMR vaccination status and administered MMR vaccine according to their clinical practice. When providers identified travelers as MMR-eligible, the structured questionnaire prompted providers to consider MMR vaccination and to select one reason for nonvaccination from a list of possibilities available for any travel-related vaccination: not indicated for this patient/itinerary; insufficient time before departure; guardian refusal; or referral to another provider for vaccination. ¹³ If providers failed to identify travelers who were MMR-eligible, the structured questionnaire did not prompt providers to provide a reason for nonvaccination.

We grouped reasons for nonvaccination into three categories: provider decision; guardian refusal; or referral to another provider. Because MMR vaccination is indicated for all MMR-eligible international travelers regardless of itinerary and at any time prior to departure, we categorized encounters as provider decision if the provider: failed to identify an MMR-eligible traveler (ie, traveler met the study definition of MMR-eligibility but the provider misclassified as ineligible) or selected the answers, "not indicated for this traveler/itinerary," or "insufficient time before departure." Before 2012, guardian refusal of MMR vaccination was recorded without a more specific reason. In 2012 and afterward, providers recorded one of three reasons for guardian refusal: lack of concern about illness; concerns about vaccine safety; or concerns about cost. Providers could also note that the MMR vaccine was not available at the pretravel consultation.

Statistical analyses

We grouped destinations into six geographic regions as defined by the World Health Organization (WHO). ¹⁹ The most common purposes of pediatric travel were 1) leisure, 2) visiting friends and relatives (VFR), or 3) non-medical service work or education. We defined VFR travelers according to CDC guidelines: "traveling to region of origin of self or family to visit friends or relatives" or who reported residing with relatives in a low- or middle-income country. ^{17,20} We grouped additional reasons for travel (eg, business) as "other" because they were infrequent. We calculated the time between pretravel consultation and departure.

We obtained distributions of traveler and site characteristics among all pediatric travelers and MMR-eligible travelers, stratified by age group. We examined whether the distribution

of characteristics varied by whether vaccine was administered to MMR-eligible travelers or by reasons for nonvaccination among the MMR-eligible not vaccinated.

We obtained odds ratios with 95% confidence intervals from two separate multivariable logistic regressions to assess the relationship of vaccination of MMR-eligible pediatric travelers with traveler sex, age group, region, purpose and duration of travel, and time to departure. Model 1 also included type of site, whereas Model 2 included US census region. Although vaccination rates varied by the type of site and census region, we were unable to include both variables in a single model or study the interaction of these two variables due to the unequal distribution of academic and nonacademic sites across the US census regions and insufficient sample sizes. The multivariable models used Taylor linearization methods to adjust for the clustering of patients within sites. Analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC) and SUDAAN version 11.0.3 (RTI, NC). We considered a two-sided P < 0.05 to be significant.

IRB Approval

The study was approved or found to be exempt by an institutional review board at each participating site.

Results

Of the 121 295 pretravel consultations at 29 GTEN sites from 2009 through 2018, pediatric travelers comprised 14 802 (12%) consultations (eFigure 1). We excluded 12 pediatric travelers reporting destinations only within the US or associated territories and 188 travelers younger than 6 months. Demographics of these 14 602 pediatric travel consultations are presented in Table 2 and stratified by age group in eTable 1.

MMR-eligible pediatric travelers

Among 14 602 pretravel consultations, we identified 11 708 (80%) pediatric travelers who were not MMR-eligible, and 2864 (20%) who were MMR-eligible. Fewer than 1% of travelers had medical contraindications or received the first dose of MMR within past 28 days (eFigure 1).

MMR eligibility varied substantially by age group (eFigure 1). Infants were most frequently MMR-eligible (365 of 398 [92%] travelers), while 2161 of 3623 (60%) preschool-aged travelers were MMR-eligible. School-aged travelers were rarely MMR-eligible (338 of 10 581 [3%] travelers).

Nonvaccination of MMR-eligible pediatric travelers

MMR-eligible pediatric travelers were not vaccinated at 1682 of 2864 (59%) GTEN pretravel consultations (Figure 1): 161 of 365 (44%) MMR-eligible infants, 1222 of 2161 (57%) MMR-eligible preschoolers, and 299 of 338 (88%) MMR-eligible school-aged travelers were not vaccinated.

Reasons for nonvaccination of 1682 MMR-eligible travelers included: provider decision (37%), guardian refusal (36%), referral to another provider (26%), and vaccine unavailable (1%) (Figure 1). Among the 621 consultations in which providers decided not to vaccinate MMR-eligible travelers, providers failed to identify MMR-eligibility in 475 (76%) consultations, incorrectly endorsed that MMR vaccine was not indicated in 104 (17%) consultations, and incorrectly cited insufficient time for vaccination in 42 (7%) consultations. Most guardians (>75%) who refused MMR vaccination cited a lack of concern about measles illness and rarely expressed concerns about MMR safety or cost. Provider decision occurred most often among infants (70 of 161 [43%]) and preschool-aged travelers (497 of 1222 [41%]), whereas guardians refused most frequently for school-aged travelers (187 of 299 [63%]). Referral to another provider occurred for 63 of 161 (39%) infants, 314 of 1222 (26%) preschoolers, and 56 of 299 (19%) school-aged travelers who were MMR-eligible but not vaccinated.

Characteristics of MMR-eligible travelers vaccinated and not vaccinated

We examined the traveler and site characteristics of all pretravel consultations where MMR-eligible pediatric travelers were vaccinated, compared to those not vaccinated (Table 2; eTable 2). MMR-eligible travelers were less likely to be vaccinated if they were school-aged, traveling within the Americas, traveling fewer than 14 days, or evaluated at a nonacademic center or in the South or West. MMR-eligible travelers were more likely to be vaccinated if VFR or traveling to Africa.

In both multivariable models (Table 3), MMR-eligible travelers were more likely to be vaccinated if traveling to Africa and were less likely to be vaccinated if they were schoolaged; they were also more likely to be vaccinated if VFR and less likely if evaluated at nonacademic centers (Model 1, left) or at GTEN sites in the South or West (Model 2, right).

Specific reasons for nonvaccination among MMR-eligible travelers were also associated with traveler and site characteristics (Table 2; eTable 2). Provider decision to not vaccinate was more common in evaluation of travelers with one prior MMR vaccination or at academic centers or in the Northeast. Guardians were more likely to refuse MMR vaccination for school-aged travelers, travel to Africa, itineraries 14 days, or at nonacademic centers or in the South. Guardians of preschool-aged and school-aged travelers with zero prior MMR vaccinations were also more likely to refuse MMR vaccination. Referral to another provider occurred more frequently when departure was 14 days after pretravel consultation among infants or preschool-aged travelers or at sites in the West.

A wide range of clinical practice was evident among the GTEN sites (Figure 2; eTable 3). At nonacademic centers in the Northeast and South or at academic centers in the West, more than 90% of MMR-eligible travelers were not vaccinated, compared to nonvaccination of 36–59% of MMR-eligible travelers at other sites. The most common reasons for nonvaccination varied by site: provider decision (nonacademic centers in the Northeast and Midwest); guardian refusal (nonacademic centers in the South); referral to another provider (academic centers in the West).

Discussion

These data from the largest US consortium of providers offering pretravel consultations demonstrate that at least 20% of pediatric international travelers were eligible for pretravel MMR vaccination, yet almost 60% were not vaccinated during the consultation despite evaluation by providers experienced in pretravel consultations. These missed opportunities were due in similar proportions to provider decision not to vaccinate and guardian refusal. A better understanding of the benefits of MMR vaccination and the risks of measles illness is essential among providers and guardians to improve measles immunity among pediatric international travelers prior to travel and reduce measles importations to the US.

In more than 40% of pretravel consultations with MMR-eligible infant and preschool-aged travelers who were not vaccinated, providers had not recommended MMR vaccination, which underscores major knowledge gaps even among this group of providers with expertise in travel medicine and vaccinations. Infants and preschool-aged travelers are at high risk for serious disease with measles infection and are unlikely to have had appropriate prior MMR vaccinations. Although MMR vaccination is safe for children 6 to <12 months, it is not routinely recommended because of the low likelihood of measles exposure in the US and its lower effectiveness when given to children younger than 12 months (ie, 85% instead of 93% with one dose) due to potential interference by maternal antibodies and immaturity of the immune system. However, infants at high risk for measles exposure, such as international travelers, should be offered early MMR vaccination, followed by the standard two MMR vaccinations after 12 months of age. 15,16 An investigation of reasons why providers did not identify MMR-eligible travelers or did not administer MMR vaccination is needed to educate providers and to improve implementation of ACIP recommendations for MMR vaccination of pediatric travelers.

Only 3% of school-aged travelers were MMR-eligible in this study, reflecting the overall high uptake of routine vaccines in the US.^{23,24} However, those identified as MMR-eligible were usually not vaccinated at the pretravel consultation due to guardian refusal. Vaccinehesitant guardians are commonly noted to minimize concerns about vaccine-preventable disease, ^{25,26} which is notable because the study period included major measles outbreaks with robust media coverage.^{27–29} Providers should preemptively discuss beliefs regarding the risks of becoming infected with measles and the realities of clinical illness with measles. Because school-aged travelers should already have received two MMR vaccinations routinely, it is notable that 12% of the 338 MMR-eligible school-aged travelers in this study were successfully vaccinated at the pretravel consultation. Providers are trusted sources of information about vaccinations and must take advantage of every opportunity to address vaccine effectiveness, even in the setting of past vaccine refusal.

Referral to another provider for MMR vaccination was common among pediatric travelers of all age groups in our study, particularly when there were 14 days or more between the pretravel consultation and departure. Past GTEN analyses have demonstrated that routine vaccinations are less likely to be administered at pretravel consultations than travel-related vaccinations, ³⁰ which may reflect providers' concerns that routine vaccinations can prompt higher out-of-pocket costs for the traveler and family or might not be recorded in the

travelers' permanent medical record if given at pretravel consultations. However, missed opportunities for MMR vaccination remain likely because families may not pursue another health care appointment before travel.

These data from GTEN sites likely underestimate the percentage of MMR-eligible pediatric travelers. Providers followed their typical clinical practice and were not required to accept only written documentation of past MMR vaccinations or other evidence for immunity. If strict ACIP criteria had been required, an even greater proportion of pediatric travelers may have been considered MMR-eligible. Additionally, primary care practices may be less likely to consider and recommend pretravel MMR vaccination for eligible pediatric travelers, in contrast to GTEN providers who are travel medicine specialists. This is of particular concern for travelers to Europe, who are rarely referred for pretravel consultation (ie, only 3% of the pediatric travelers evaluated at GTEN sites had itineraries restricted to Europe). Measles remains wide-spread in Europe, and travelers returning from Europe accounted for 30% of imported measles cases to the US from 2001–2016. 12,31 Ensuring measles immunity among international travelers is essential and can only be improved if primary care pediatricians also discuss pretravel MMR recommendations with pediatric travelers and their guardians at routine visits.

These data are from a large, prospective, multisite study, but our analysis has limitations. Although the observed patterns of reported vaccination are consistent with US coverage levels, our estimates of MMR-eligibility may be under- or over-estimates as we did not have access to written documentation of past immunizations. ^{8,23,24} Health-seeking behavior may be more likely among travelers and families who pursue pretravel consultation, who may be more likely to be up to date on routine vaccines and to follow recommendations about additional vaccinations. An even greater proportion of US travelers might lack measles immunity or refuse vaccination if recommended. These GTEN data demonstrate diverse clinical practices at different types of sites in different regions of the US that may not be representative of any specific region; the uneven distribution of the types of sites across the US census regions and relatively small sample sizes precluded accounting for both variables simultaneously in the multivariable models. Our data are not representative of travelers to international settings who did not attend specialized pretravel consultation.

In conclusion, we observed extensive missed opportunities for MMR vaccination among eligible pediatric travelers. Profound misunderstandings remain. Providers often did not administer pretravel MMR vaccination, even for vulnerable infants and preschool-aged travelers, and guardians did not recognize measles as a serious illness. Strategies are needed to improve provider and guardian knowledge of measles as a serious travel-related illness and the benefits of MMR vaccination, particularly in the setting of ongoing US measles outbreaks.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

Members of the Global TravEpiNet Consortium (in alphabetical order) are George M. Abraham, Saint Vincent Hospital (Worcester, MA); Salvador Alvarez, Mayo Clinic (Jacksonville, FL); Vernon Ansdell, Johnnie A. Yates, Travel Medicine Clinic, Kaiser Permanente (Honolulu, HI); Elisha H. Atkins, Chelsea HealthCare Center (Chelsea, MA); Holly K. Birich, Dagmar Vitek, Salt Lake Valley Health Department (Salt Lake, UT); John Cahill, Travel and Immunization Center, St. Luke's-Roosevelt (New York, NY); Lin Chen, Mount Auburn Hospital (Cambridge, MA); Marina Rogova, Bradley A. Connor, New York Center for Travel and Tropical Medicine, Cornell University (New York, NY); Roberta Dismukes, Jessica Fairley, Phyllis Kozarsky, Henry Wu, Emory TravelWell, Emory University (Atlanta, GA); Jeffrey A. Goad, 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, 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, DeVon Hale, International Travel Clinic, University of Utah (Salt Lake City, UT); Alawode Oladele, Hanna Demeke, DeKalb County Board of Health Travel Services-DeKalb North and Central-T.O. Vinson Centers (Decatur, GA); Alawode Oladele, Althea Otuata, DeKalb County Board of Health Travel Services-DeKalb East (Decatur, GA); Roger Pasinski, Amy E. Wheeler, Revere HealthCare Center (Revere, MA); Adrienne Showler, Laura Coster, 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, Patricia Walker, HealthPartners Travel Medicine Clinics (St. Paul, MN); and Joseph Vinetz, Travel Clinic, Division of Infectious Diseases, Department of Medicine, University of California-San Diego School of Medicine (La Jolla, CA).

Role of the Funding Sources: This work was supported by US Centers for Disease Control and Prevention [U19CI000514; U01CK000175; U01CK000490], the National Institutes of Health [K01HL123349 (EPH)], the Claflin Distinguished Scholars Award (EPH), and the Steve and Deborah Gorlin MGH Research Scholars Award (RPW). The content is solely the responsibility of the authors, and the study's findings and conclusions do not necessarily represent the official position of the CDC, the NIH, or the MGH Executive Committee on Research.

References

- 1. Measles cases and outbreaks. Centers for Disease Control and Prevention. https://www.cdc.gov/measles/cases-outbreaks.html. Published 6 20, 2019 Accessed September 12, 2019.
- Wendorf KA, Winter K, Zipprich J, et al. Subacute sclerosing panencephalitis: the devastating measles complication that might be more common than previously estimated. Clin Infect Dis 2017;65(2):226–232. doi:10.1093/cid/cix302 [PubMed: 28387784]
- Moss WJ, Griffin DE. Measles. Lancet 2012;379(9811):153–164. doi:10.1016/ S0140-6736(10)62352-5 [PubMed: 21855993]
- Sukumaran L, McNeil MM, Moro PL, Lewis PW, Winiecki SK, Shimabukuro TT. Adverse events
 following measles, mumps, and rubella vaccine in adults reported to the Vaccine Adverse Event
 Reporting System (VAERS), 2003–2013. Clin Infect Dis 2015;60(10):e58–e65. doi:10.1093/cid/
 civ061 [PubMed: 25637587]
- Jain A, Marshall J, Buikema A, Bancroft T, Kelly JP, Newschaffer CJ. Autism occurrence by MMR vaccine status among US children with older siblings with and without autism. JAMA 2015;313(15):1534–1540. doi:10.1001/jama.2015.3077 [PubMed: 25898051]
- 6. Advisory Committee on Immunization Practices. Recommended child and adolescent immunization schedule for ages 18 years or younger, United States, 2019. Centers for Disease Control and Prevention. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html. Published 2 2019 Accessed September 12, 2019.
- Papania MJ, Wallace GS, Rota PA, et al. Elimination of endemic measles, rubella, and congenital rubella syndrome from the Western hemisphere: the US experience. JAMA Pediatr. 2014;168(2):148–155. doi:10.1001/jamapediatrics.2013.4342 [PubMed: 24311021]
- 8. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19–35 months United States, 2017. MMWR Morb Mortal Wkly Rep 2018;67(40):1123–1128. doi:10.15585/mmwr.mm6740a4 [PubMed: 30307907]

 Olive JK, Hotez PJ, Damania A, Nolan MS. The state of the antivaccine movement in the United States: A focused examination of nonmedical exemptions in states and counties. PLOS Med 2018;15(6):e1002578. doi:10.1371/journal.pmed.1002578 [PubMed: 29894470]

- Majumder MS, Cohn EL, Mekaru SR, Huston JE, Brownstein JS. Substandard vaccination compliance and the 2015 measles outbreak. JAMA Pediatr 2015;169(5):494–495. doi:10.1001/ jamapediatrics.2015.0384 [PubMed: 25774618]
- 11. Fiebelkorn AP, Redd SB, Gastañaduy PA, et al. A comparison of post-elimination measles epidemiology in the United States, 2009–2014 versus 2001–2008. J Pediatr Infect Dis Soc 2017;6(1):40–48. doi:10.1093/jpids/piv080
- Lee AD, Clemmons NS, Patel M, Gastañaduy PA. International importations of measles virus into the United States during the postelimination era, 2001–2016. J Infect Dis 2018. doi:10.1093/infdis/ jiy701
- Hyle EP, Rao SR, Jentes ES, et al. Missed opportunities for measles, mumps, rubella vaccination among departing U.S. adult travelers receiving pretravel health consultations. Ann Intern Med 2017;167(2):77. doi:10.7326/M16-2249 [PubMed: 28505632]
- 14. 2017 Profile of U.S. resident travelers visiting overseas destinations (outbound). 2017 http://tinet.ita.doc.gov/outreachpages/outbound.general_information.outbound_overview.asp. Accessed September 12, 2019.
- 15. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS, Centers for Disease Control and Prevention. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2013;62(RR-04):1–34. [PubMed: 23302815]
- 16. Centers for Disease Control (CDC). Measles prevention. MMWR Suppl 1989;38(9):1–18.
- 17. LaRocque RC, 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(4):455–462. doi:10.1093/cid/cir839 [PubMed: 22144534]
- Census regions and divisions of the United States. https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf. Accessed September 12, 2019.
- WHO regional offices. World Health Organization. http://www.who.int/about/regions/en/. Accessed September 12, 2019.
- 20. Centers for Disease Control and Prevention. CDC Yellow Book 2018: Health Information for International Travel. New York, NY: Oxford University Press; 2017.
- 21. Gastañaduy PA, Goodson JL. Measles (Rubeola) In: CDC Yellow Book 2018: Health Information for International Travel. New York, NY: Oxford University Press; 2017 https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/measles-rubeola. Accessed September 12, 2019.
- 22. Woo EJ, Winiecki SK, Arya D, Beeler J. Adverse events after MMR or MMRV vaccine in infants under nine months old. Pediatr Infect Dis J 2016;35(8):e253. doi:10.1097/INF.000000000001201 [PubMed: 27167117]
- Mellerson JL, Choppell MB, Knighton CL, Kriss JL, Seither R, Black CL. Vaccination coverage for selected vaccines and exemption rates among children in kindergarten — United States, 2017– 18 school year. MMWR Morb Mortal Wkly Rep 2018;67(40):1115–1122. doi:10.15585/ mmwr.mm6740a3 [PubMed: 30307904]
- 24. Walker TY, Elam-Evans LD, Yankey D, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years United States, 2017. MMWR Morb Mortal Wkly Rep 2018;67(33):909–917. doi:10.15585/mmwr.mm6733a1 [PubMed: 30138305]
- 25. Salmon DA, Dudley MZ, Glanz JM, Omer SB. Vaccine hesitancy: causes, consequences, and a call to action. Am J Prev Med 2015;49(6, Supplement 4):S391–S398. doi:10.1016/j.amepre.2015.06.009 [PubMed: 26337116]
- 26. Blaisdell LL, Gutheil C, Hootsmans NAM, Han PKJ. Unknown risks: parental hesitation about vaccination. Med Decis Making. 2016;36(4):479–489. doi:10.1177/0272989X15607855 [PubMed: 26506958]

27. Gastañaduy PA, Budd J, Fisher N, et al. A measles outbreak in an underimmunized Amish community in Ohio. N Engl J Med 2016;375(14):1343–1354. doi:10.1056/NEJMoa1602295 [PubMed: 27705270]

- Zipprich J, Winter K, Hacker J, Xia D, Watt J, Harriman K. Measles outbreak California, December 2014–February 2015. MMWR Morb Mortal Wkly Rep 2015;64(6):153–154. [PubMed: 25695321]
- 29. Hall V, Banerjee E, Kenyon C, et al. Measles outbreak Minnesota April–May 2017. MMWR Morb Mortal Wkly Rep 2017;66(27):713–717. doi:10.15585/mmwr.mm6627a1 [PubMed: 28704350]
- 30. Hagmann S, LaRocque RC, Rao SR, et al. Pre-travel health preparation of pediatric international travelers: analysis from the Global TravEpiNet consortium. J Pediatr Infect Dis Soc 2013;2(4):327–334. doi:10.1093/jpids/pit023
- 31. Angelo KM, Gastañaduy PA, Walker AT, et al. Spread of Measles in Europe and implications for US travelers. Pediatrics. 6 2019:e20190414. doi:10.1542/peds.2019-0414 [PubMed: 31209161]

Key Points

Question:

Are there missed opportunities for measles-mumps-rubella (MMR) vaccination at pretravel consultations for US pediatric international travelers?

Findings:

We evaluated >14 000 pretravel consultations of pediatric travelers. At least 92% of infants, 60% of preschool-aged travelers and 3% of school-aged travelers were eligible for MMR vaccination. However, 44% of MMR-eligible infants, 57% of MMR-eligible preschool-aged travelers, and 88% of MMR-eligible school-aged travelers were not vaccinated at the consultation. Provider decision and guardian refusal were the most common reasons for nonvaccination.

Meaning:

To combat the resurgence in measles, providers should ensure that all US pediatric travelers are appropriately vaccinated with MMR. Additional education of providers and guardians is essential.

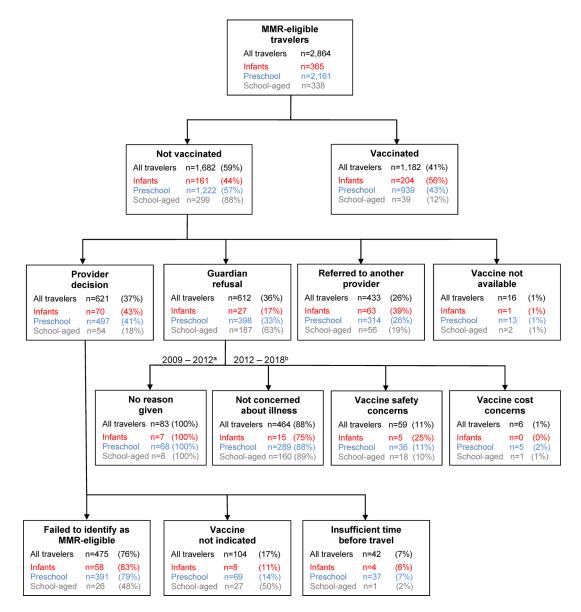


Figure 1.

Reasons for nonvaccination among MMR-eligible pediatric travelers at 29 GTEN clinic sites from 2009 through 2018. All travelers (black) included all MMR-eligible pediatric travelers, regardless of age. Infants (red) included travelers aged 6 to <12 months, preschool (light blue) included travelers aged 1 to <6 years, and school-aged (gray) were travelers aged 6 to <18 years. Abbreviations: MMR, measles-mumps-rubella; GTEN, Global TravEpiNet ^a From 2009 through 2012, providers did not collect reasons for guardian refusal of MMR vaccination; therefore, no reason was given in 100% of pretravel consultations in which guardians refused MMR vaccination during this timeframe.

^b From 2012 through 2018, providers were prompted to ask guardians to specify one of three reasons for MMR refusal.

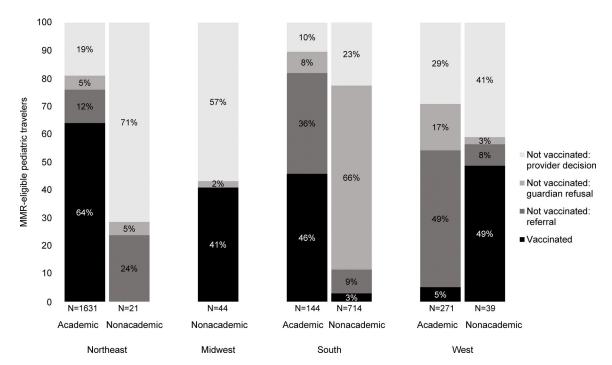


Figure 2.

MMR vaccination and reasons for nonvaccination among MMR-eligible pediatric travelers at academic sites and nonacademic sites, stratified by US census region of GTEN site. The absolute number of MMR-eligible travelers is shown below each bar. Travelers not vaccinated because of unavailability of MMR vaccine were included with those who were referred to another provider. No pediatric travelers evaluated at academic centers in the Midwest were MMR-eligible.

Abbreviations: MMR: measles-mumps-rubella, GTEN: Global TravEpiNet

Table 1.

Differences between the routine MMR vaccination schedule and the MMR vaccination recommendations for US pediatric international travelers

	Infants (6 to <12 months)	Preschool-aged (1 to <6 years)	School-aged (6 to <18 years)
,		1 dose MMR ^a	2 doses MMR ^a
Routine vaccination ⁶	None	1st dose: 12–15 months	1st dose: 12-15 months
			2 nd dose: 4–6 years
International travelers15	1 dose MMR b	2 doses MMR c	2 doses MMR $^{\it c}$

^aFor children 1 to 4–6 years old who have not received one dose MMR after 12 months of age, the catchup immunization schedule recommends 1 dose of MMR. For children 4–6 to <18 years who have not received MMR after 12 months of age, the catchup immunization schedule recommends two doses of MMR administered at least 28 days apart.

b total of three lifetime doses of MMR vaccination is recommended for those children who received a dose of MMR before 12 months of age.

 $^{^{}c}_{\mathrm{The}}$ second dose of MMR vaccination should be given at least 28 days after the first dose.

Abbreviation: MMR: Measles-mumps-rubella

Table 2.

Distribution of traveler and site characteristics of GTEN pretravel consultations for MMR-eligible pediatric travelers from 2009 through 2018

		MMR-elig	MMR-eligible travelers			M	MMR-eligible travelers not vaccinated	s not vaccinated	
Characteristics	Total N=2834	Vaccinated N=1182	Not vaccinated N=1682	P value	Total N=1682	Provider decision N=621	Guardian refusal N=612	Referred to another provider N=449	P value
		Z	N (Col %)				N (Col %)	(
Sex				0.08					0.91
Female	1389 (49)	576 (49)	813 (48)		813 (48)	295 (48)	296 (48)	222 (49)	
Male	1475 (52)	606 (51)	869 (52)		869 (52)	326 (52)	316 (52)	227 (51)	
Age group				0.05					<0.001
Infants (6 to <12mo)	365 (13)	204 (17)	161 (10)		161 (10)	70 (11)	27 (4)	64 (14)	
Preschool-aged (1 to <6y)	2161 (76)	939 (79)	1222 (73)		1222 (73)	497 (80)	398 (65)	327 (73)	
School-aged (6 to <18y)	338 (12)	39 (3)	299 (18)		299 (18)	54 (9)	187 (31)	58 (13)	
Past MMR vaccinations				0.12					<0.001
0 MMR	891 (31)	334 (28)	557 (33)		557 (33)	120 (19)	285 (47)	152 (35)	
1 MMR	1973 (70)	848 (72)	1125 (67)		1125 (67)	501 (81)	327 (53)	297 (69)	
Region of travel $^{\mathcal{C}}$									
Africa	1634 (57)	739 (63)	895 (53)	0.007	895 (53)	324 (52)	392 (64)	179 (40)	0.01
Americas	469 (16)	166 (14)	303 (18)	0.006	303 (18)	113 (18)	92 (15)	98 (22)	0.00
Eastern Mediterranean	136 (5)	46 (4)	90 (5)	0.41	90 (5)	34 (5)	33 (5)	23 (5)	0.88
Europe	59 (2)	24 (2)	35 (2)	0.97	35 (2)	12 (2)	7 (1)	16 (4)	0.78
Southeast Asia	463 (16)	183 (15)	280 (17)	0.00	280 (17)	109 (18)	73 (12)	98 (22)	0.62
Western Pacific	223 (8)	(9) 89	155 (9)	0.11	155 (9)	60 (10)	35 (6)	60 (13)	0.59
Duration of travel				0.03					<0.001
<14 days	386 (14)	111 (9)	275 (16)		275 (16)	75 (12)	124 (20)	76 (17)	
14 days	2478 (87)	1071 (91)	1407 (84)		1407 (84)	546 (88)	488 (80)	373 (83)	
Purpose of travel				0.004					<0.001
VFR	1752 (61)	848 (72)	904 (54)		904 (54)	373 (60)	322 (53)	209 (47)	
Leisure	782 (27)	247 (21)	535 (32)		535 (32)	186 (30)	187 (31)	162 (36)	
Service or education	132 (5)	13 (1)	(7)		(7)	17 (3)	68 (11)	34 (8)	
Other	198 (7)	74 (6)	124 (7)		124 (7)	45 (7)	35 (6)	44 (10)	

ript	
Author Manuscript	
Author Manuscript	

		MMR-elig	AMR-eligible travelers			WIN	MMR-eligible travelers not vaccinated	not vaccinated	
Characteristics	Total N=2834	Vaccinated N=1182	Not vaccinated N=1682	P value	Total N=1682	Provider decision N=621	Guardian refusal N=612	Referred to another provider $N=449$	P value
) N	N (Col %)				N (Col %)		
Time until departure				0.23					<0.001
<14 days	1236 (43)	503 (43)	733 (44)		733 (44)	287 (46)	297 (49)	149 (33)	
14 days	1628 (57)	(24) (24)	949 (56)		949 (56)	334 (54)	315 (51)	300 (67)	
Type of site				<0.001					<0.001
Academic center	2046 (71)	1124 (95)	922 (55)		922 (55)	404 (65)	138 (23)	380 (85)	
Nonacademic center	818 (29)	58 (5)	760 (45)		760 (45)	217 (35)	474 (78)	69 (15)	
US census region				<0.001					<0.001
Northeast	1652 (58)	1044 (88)	(98) (39)		608 (36)	325 (52)	83 (14)	200 (45)	
Midwest	44 (2)	18 (2)	26 (2)		26 (2)	25 (4)	1 (<1)	0 (0)	
South	858 (30)	(7) 28	771 (46)		771 (46)	176 (28)	482 (79)	113 (25)	
West	310 (11)	33 (3)	277 (16)		277 (17)	95 (15)	46 (8)	136 (30)	

^aFor categorical variables: p-values were obtained from the Cochran-Mantel-Haenszel test and indicate whether the association of the characteristic and the outcome is statistically significant after adjusting for clinic site. P-values for testing the association of type of site or US census region were obtained from Chi-Square test of independence. For continuous variables, p-values were obtained from the Wilcoxon/Kruskal-Wallis test and indicate whether the distribution of the variable is significantly different in the outcome groups.

b. The 16 pediatric travelers not vaccinated because of vaccine unavailability were included with those referred to another provider for demographic analysis.

cColumn percentages may not sum to 100% because more than one selection was allowed.

 $d_{\mbox{\footnotesize Midwest}}$ excluded from this comparison given low sample size.

Abbreviations: GTEN: Global TravEpiNet, MMR: Measles-mumps-rubella, mo: months, y: years, VFR: Visiting friends and relatives

Table 3.

Odds ratios (OR) and 95% confidence intervals (CI) obtained from multivariable logistic regressions^a evaluating the association of traveler and site characteristics with MMR vaccination at GTEN sites among MMR-eligible pediatric travelers from 2009 through 2018

Variable				
aram in t	OR (95% CI)	P value	OR (95% CI)	P value
Sex				
Male	REF	0.74	REF	0.13
Female	1.04 (0.83, 1.29)		1.14 (0.95, 1.37)	
Age group				
Infants (6 to <12mo)	REF	<0.001	REF	<0.001
Preschool-aged (1 to <6y)	0.77 (0.53, 1.11)		0.83 (0.58, 1.20)	
School-aged (6 to <18y)	0.32 (0.24, 0.42)		0.26 (0.14, 0.47)	
Region of travel				
Africa	1.86 (1.15, 3.01)	0.008	1.74 (1.17, 2.58)	0.004
Americas	1.07 (0.63, 1.80)	0.80	1.17 (0.66, 2.07)	0.56
Eastern Mediterranean	0.77 (0.45, 1.33)	0.33	0.70 (0.41, 1.21)	0.18
Europe	0.91 (0.61, 1.36)	0.62	1.05 (0.78, 1.40)	0.75
Southeast Asia	0.97 (0.48, 1.95)	0.93	1.26 (0.68, 2.32)	0.44
Western Pacific	0.76 (0.44, 1.30)	0.29	0.90 (0.56, 1.45)	99.0
Duration of travel				
<14 days	REF	0.36	REF	0.24
14 days	1.17 (0.82, 1.67)		1.19 (0.88, 1.62)	
Purpose of travel				
VFR	REF	0.002	REF	0.22
Leisure	0.49 (0.26, 0.94)		0.64 (0.38, 1.08)	
Service or education	0.18 (0.07, 0.48)		0.47 (0.16, 1.34)	
Other	0.60 (0.36, 1.00)		0.77 (0.49, 1.19)	
Time until departure				
<14 days	REF	0.34	REF	0.24
14 days	1.13 (0.87, 1.48)		1.18 (0.88, 1.59)	
Type of site				

	Model 1		Model 2	2
Variable	OR (95% CI) P value	P value	OR (95% CI) P value	P value
Academic center	REF	<0.001		
Nonacademic center	0.04 (0.01, 0.20)		1	
US census region				
Northeast/Midwest	1	,	REF	<0.001
South	•		0.06 (0.01, 0.52)	
West			0.10 (0.02, 0.47)	

Hyle et al.

^aModels used Taylor Linearization methods, a form of Generalized Estimating Evaluations, to adjust for the clustering of patients within sites. Abbreviations: GTEN: Global TravEpiNet, MMR: measles, mumps, rubella, mo: Months, y: Years, VFR: Visiting friends and relatives.

Page 19