



# HHS Public Access

## Author manuscript

*Obstet Gynecol.* Author manuscript; available in PMC 2018 April 20.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Published in final edited form as:

*Obstet Gynecol.* 2017 December ; 130(6): 1357–1365. doi:10.1097/AOG.0000000000002360.

## Travel Characteristics and Pretravel Health Care Among Pregnant or Breastfeeding U.S. Women Preparing for International Travel

**Stefan H. F. Hagmann, MD, MSc, Sowmya R. Rao, PhD, Regina C. LaRocque, MD, MPH, Stefanie Erskine, MPH, Emily S. Jentes, PhD, MPH, Allison T. Walker, PhD, MPH, Elizabeth D. Barnett, MD, Lin H. Chen, MD, Davidson H. Hamer, MD, Edward T. Ryan, MD, and for the Global TravEpiNet Consortium and the Boston Area Travel Medicine Network\***

Division of Pediatric Infectious Diseases, Bronx Lebanon Hospital Center, Bronx, New York; the Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, New York; the Department of Surgery, Boston University Medical Center, Boston, Massachusetts; MGH Biostatistics Center and the Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts; the Department of Medicine, Harvard Medical School, Boston, Massachusetts; the Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, Atlanta, Georgia; the Department of Pediatrics and the Section of Infectious Diseases, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts; the International Clinic, Boston Medical Center, Boston, Massachusetts; the Division of Infectious Diseases and Travel Medicine, Mount Auburn Hospital, Cambridge, Massachusetts; and the Department of Global Health, Boston University School of Public Health, Boston, Massachusetts

### Abstract

**OBJECTIVE**—To study characteristics and preventive interventions of adult pregnant and breastfeeding travelers seeking pretravel health care in the United States.

**METHODS**—This cross-sectional study analyzed data (2009–2014) of pregnant and breastfeeding travelers seen at U.S. travel clinics participating in Global TravEpiNet.

Nonpregnant, nonbreastfeeding adult female travelers of childbearing age were used for comparison. We evaluated the prescription of malaria chemoprophylaxis and antibiotics for this population as well as the administration of three travel-related vaccines: hepatitis A, typhoid, and yellow fever. We also evaluated use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis and influenza vaccines, because these are widely recommended in pregnancy.

---

Corresponding author: Stefan H. F. Hagmann, MD, MSc, Division of Pediatric Infectious Diseases, Steven and Alexandra Cohen Children's Medical Center of New York, 269-01 76th Avenue, New Hyde Park, NY 11040; shagmann@northwell.edu.

\*For a list of members of the Global TravEpiNet Consortium and the Boston Area Travel Medicine Network who contributed data to this study, see Appendix 1, available online at <http://links.lww.com/AOG/B30>.

Stefan H. F. Hagmann is presently affiliated with the Steven and Alexandra Cohen Children's Medical Center of New York, New Hyde Park, New York; and Hofstra Northwell School of Medicine, Hempstead, New York.

Presented in part at the 14th Conference of the International Society of Travel Medicine, May 24–28, 2015, Quebec City, Canada.

**Financial Disclosure:** Dr. Chen has been an advisor for Shoreland, Inc, and has received speaker travel support and an honorarium from GlaxoSmithKline. The other authors did not report any potential conflicts of interest.

**RESULTS**—Of 21,138 female travelers of childbearing age in Global TravEpiNet, 170 (0.8%) were pregnant and 139 (0.7%) were breastfeeding. Many traveled to destinations endemic for mosquito-borne illnesses, including malaria (pregnant: 95%; breastfeeding: 94%), dengue (pregnant: 87%; breastfeeding: 81%), or yellow fever (pregnant: 35%; breastfeeding: 50%). Compared with nonpregnant, nonbreastfeeding adult female travelers, eligible pregnant travelers were less likely to be vaccinated against hepatitis A (28% compared with 51%,  $P<.001$ ) and typhoid (35% compared with 74%,  $P<.001$ ). More than 20% of eligible pregnant travelers did not receive influenza vaccination. Yellow fever vaccine was occasionally provided to pregnant and breastfeeding travelers traveling to countries entirely endemic for yellow fever (6 [20%] of 30 pregnant travelers and 18 [46%] of 39 breastfeeding travelers). Half of pregnant travelers and two thirds of breastfeeding travelers preparing to travel to malaria-holoendemic countries received a prescription for malaria prophylaxis.

**CONCLUSION**—Most pregnant and breastfeeding travelers seen for pretravel health consultations traveled to destinations with high risk for vector-borne or other travel-related diseases. Destination-specific preventive interventions were frequently underused.

Of 74 million international trips in 2015 among U.S. residents, approximately half (50.3%) were made by females.<sup>1</sup> The proportion of these who are pregnant or breastfeeding is largely unmeasured, and little is known about the pretravel medical care that they receive. A retrospective analysis of a Swiss travel clinic showed that 1.3% of 9,005 women between 15 and 49 years of age presenting for pretravel care between 2010 and 2012 were either pregnant or breastfeeding.<sup>2</sup>

Pregnant and breastfeeding travelers require special considerations during a pretravel visit.<sup>3,4</sup> Pregnant women are more susceptible to, and experience increased severity of, certain infectious diseases. Intrauterine infections, as the experience with Zika virus shows, may result in adverse pregnancy outcomes.<sup>5–7</sup> Safety concerns related to live vaccinations and certain antimicrobials for the fetus and breastfed infant also affect pretravel health care interventions.<sup>3,4</sup>

We aimed to investigate the demographic and clinical characteristics, destinations, and pretravel interventions of U.S. pregnant and breastfeeding travelers seeking pretravel health care. The ongoing epidemic of Zika virus has increased the importance of pretravel health preparation of the pregnant traveler. Although our data were collected before the Zika virus epidemic, our findings may help inform preventive efforts and inform public health recommendations for this vulnerable group of travelers.<sup>6,7</sup>

## MATERIALS AND METHODS

Data used in this cross-sectional analysis were collected by clinicians who are members of the Global TravEpiNet, a national consortium of U.S. travel clinics that systematically collect demographic and clinical information on people who plan to travel internationally.<sup>8</sup> The Global TravEpiNet data collection protocol was approved or considered exempt by the institutional review boards of all 24 participating sites. Female travelers were included if they were of childbearing age (aged 18–49 years) when they visited a Global TravEpiNet

clinical site for pretravel health consultation between January 1, 2009, and December 31, 2014.

Global TravEpiNet clinicians use a secure internet-based tool to collect during the clinical visit: anonymous data on medical history, itinerary, travel purpose, immunization history, vaccines administered, and prescriptions provided for persons receiving pretravel health advice.<sup>8</sup> Because data are being entered and submitted automatically into a secure database during the clinical visit, no separate data transcription and respective validation step have been deemed necessary. Vaccine recommendations for pregnant or breastfeeding individuals as well as destination-specific vaccine recommendations were used according to guidelines of the Advisory Committee on Immunization Practices and the Centers for Disease Control and Prevention (CDC) that were current at the time of the pretravel encounter.<sup>9</sup> For each vaccine, clinicians were required to record if it was found indicated and administered, indicated but declined by the traveler, not indicated for this traveler and itinerary, medically contraindicated, or not needed as a result of pre-existing immunity.

We evaluated adult female travelers who self-identified as pregnant or actively breastfeeding while receiving pretravel care at a Global TravEpiNet site. We randomly selected five nonpregnant, nonbreastfeeding female travelers of childbearing age (aged 18–49 years) for each pregnant or breastfeeding traveler within each Global TravEpiNet site as a comparison group.<sup>10</sup> Destination countries were classified in accordance with the 2015 U.N. Human Development Index.<sup>11</sup> According to the CDC definition, patients traveling to visit friends or relatives in a region of origin of self or family, provided the destination was a low-income or low-middle-income country, were considered visiting friends and relatives travelers.<sup>12</sup> Vaccines of interest in this analysis resulting from their critical importance during pregnancy and during pretravel preparation to tropical and subtropical destinations were tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap), influenza, hepatitis A, typhoid fever, and yellow fever. The utilization of other vaccines was summarized within the appendices (see Appendix 2, available online at <http://links.lww.com/AOG/B30>). Other travel health interventions assessed were the use of malaria chemoprophylaxis and the provisional prescription of standby antibiotics for the treatment of travelers' diarrhea.

We used separate random intercept regression models with clinical site as the random effect to evaluate measures of association and statistical significance accounting for the clustering of patients within sites.<sup>13</sup> Fisher exact tests were used when sample sizes were small. A two-sided  $P$  value  $<.05$  was considered statistically significant. Data analyses were performed using SAS 9.2.

Because the number of pregnant or breastfeeding travelers is low, we performed a descriptive analysis of pretravel health care using data from the Boston Area Travel Medicine Network to confirm our findings. These results are presented within the appendices (see Appendix 3, available online at <http://links.lww.com/AOG/B30>).

## RESULTS

Of 63,321 travelers who visited a Global TravEpiNet clinic for pretravel care during the study period, 34,908 (55%) were female travelers and 21,138 (33%) were adult female travelers of childbearing age (18–49 years). Of those, 170 (0.8%) were pregnant and 139 (0.7%) were breastfeeding; 1,545 nonpregnant, nonbreastfeeding women were selected for comparison (Table 1). Leisure was the leading reason for travel in all groups (Table 1). Compared with nonpregnant, nonbreastfeeding travelers, more pregnant (25% compared with 17%,  $P<.05$ ) and breastfeeding travelers (28% compared with 17%,  $P<.01$ ) were traveling for business or were visiting friends and relatives (19% compared with 11%,  $P<.01$  and 36% compared with 11%,  $P<.01$ , respectively). The intended median travel duration was between 2 weeks (pregnant and nonpregnant, nonbreastfeeding travelers) and 3 weeks (breastfeeding travelers); 43% of breastfeeding travelers intended to travel for greater than 28 days compared with 18% of pregnant and 26% of nonpregnant, nonbreastfeeding travelers (pregnant compared with nonpregnant, nonbreastfeeding travelers,  $P<.05$ ; breastfeeding compared with nonpregnant, nonbreastfeeding travelers,  $P<.01$ ; Table 1).

Almost all pregnant (95%) and breastfeeding travelers (94%) intended to travel to a country with reported year-round malaria transmission (holoendemic). Likewise, many traveled to dengue-endemic countries (pregnant traveler: 87%; breastfeeding traveler: 81%). One third of pregnant (35%) and half of breastfeeding travelers (50%) planned to travel to a country with regions of yellow fever transmission, whereas a minority (pregnant travelers: 18%; breastfeeding travelers: 28%) were planning travel to an entirely yellow fever-endemic country.

Of vaccines to be administered routinely during or after each pregnancy, almost all pregnant (91%) and breastfeeding travelers (99%) were noted to have Tdap vaccine–related immunity (either as a result of pre-existing immunity or vaccination during the clinic visit) (Fig. 1). A lower proportion of travelers reported influenza-related immunity: 98 (72%) of 137 pregnant and 84 (79%) of 107 breastfeeding travelers seen during the northern hemisphere influenza season (October 1–June 30; Fig. 1). Of note, 17 (12%) and nine (8%) of pregnant and breastfeeding travelers, respectively, declined the influenza vaccine (Fig. 1).

Typhoid and hepatitis A were the most commonly administered vaccines indicated for both pregnant and breastfeeding travelers (Fig. 1). In comparison with nonpregnant, nonbreastfeeding travelers, pregnant travelers were less likely to receive typhoid (35% compared with 74%,  $P<.001$ ) or hepatitis A vaccines (28% compared with 51%,  $P<.001$ ; Fig. 1). Typhoid and hepatitis A vaccines were declined by 18% and 15% of pregnant travelers and deemed as contraindicated by the practitioners in 21% and 8% of pregnant travelers, respectively (Fig. 1). Among travelers receiving typhoid vaccine, 668 (58%) nonpregnant, nonbreastfeeding travelers, 56 (95%) pregnant, and 81 (77%) breastfeeding travelers received the inactivated Vi capsular polysaccharide vaccine (pregnant compared with nonpregnant, nonbreastfeeding travelers or breastfeeding compared with nonpregnant, nonbreastfeeding travelers,  $P<.01$ ).

Among those traveling to countries entirely endemic for yellow fever, six (20%) pregnant and 18 (46%) breastfeeding travelers received the yellow fever vaccine during the pretravel consultation. Clinicians withheld vaccine as a result of medical contraindications in 12 (40%) pregnant and five (13%) breastfeeding travelers (Fig. 1). For breastfeeding travelers, health care providers justified withholding the yellow fever vaccine in two of five patients with neonates aged 1 month or less, whereas the administration was reported as being medically justified in 8 of 18 patients with infants aged older than 3 months (Fig. 1).

Among those planning a visit to a malaria-holoendemic country, 81 (50%) pregnant and 86 (66%) breastfeeding travelers were prescribed malaria chemoprophylaxis. Pregnant travelers were less likely than nonpregnant, nonbreastfeeding travelers to receive an antimalarial prescription (50% compared with 73%,  $P<.001$ ). Although atovaquone–proguanil was the most commonly used antimalarial in nonpregnant, nonbreastfeeding and breastfeeding travelers, mefloquine was most commonly prescribed in pregnant travelers (Fig. 2A).

Among those traveling to a low or medium Human Development Index country, 102 (77%) pregnant and 85 (72%) breastfeeding travelers received an antibiotic prescription for self-treatment of diarrhea. Both pregnant and breastfeeding travelers were less likely than nonpregnant, nonbreastfeeding travelers to receive such a prescription (77% compared with 87%,  $P<.001$ ; 72% compared with 87%,  $P<.001$ ). Among those receiving an antibiotic prescription, a macrolide was used almost exclusively in pregnant (94%), in most breastfeeding (79%), and in half of nonpregnant, nonbreastfeeding travelers (50%; Fig. 2B).

## DISCUSSION

We found that approximately 2% of all international female travelers of childbearing age seeking pretravel care at Global TravEpiNet or Boston Area Travel Medicine Network clinics were pregnant or breastfeeding. Our data show important opportunities for practitioners to prepare such vulnerable travelers and provide protection against infectious diseases for which some are at increased risk (Box 1).

First, most of these women were preparing for travel to tropical destinations that are endemic for malaria, dengue, or yellow fever. In addition, up to one third of pregnant travelers traveled to areas in the Americas, which, since this study, have experienced chikungunya and Zika virus epidemics.<sup>14</sup> Hence, emphasizing the use of insect repellent and other means of mosquito bite prevention as well as the prevention of sexual transmission in the context of potential Zika virus exposure of the partner becomes particularly important (Box 1).<sup>15–17</sup>

Furthermore, travel to visit friends and relatives and long-term travel were frequently noted in pregnant and breastfeeding travelers. Such travel characteristics have been previously associated with increased risk for travel-related illnesses, including malaria and typhoid.<sup>12,18</sup> Practitioners have a unique opportunity to identify such travelers who may return to their country of origin while pregnant or soon after giving birth. Their likely close contact to the local population including lack of safe food and water and not using bed nets puts them at

elevated risk of illness and can be effectively addressed during a pretravel consultation (Box 1).

Vaccination recommendations during pregnancy are evolving.<sup>19,20</sup> Regardless of travel, the Advisory Committee on Immunization Practices and the CDC recommend all pregnant women receive annual inactivated influenza virus vaccine and Tdap vaccine.<sup>9</sup> Travelers are at particular risk of influenza, occurring April to September in the southern hemisphere, September to April in the northern hemisphere, and year-round in tropical regions.

Unfortunately, even in the highly motivated population of women seeking medical care in a Global TravEpiNet clinic, approximately 1 in 10 pregnant women were not protected against influenza but declined the influenza vaccine. Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis was not frequently declined, suggesting that education regarding the importance of influenza vaccination in pregnant travelers is needed.<sup>21</sup>

Likewise, we found hepatitis A and typhoid vaccines underused by pregnant travelers either because the patient declined or the health care provider deemed those vaccines contraindicated despite destination-specific indication. Hepatitis A is a common infection in many resource-limited areas, and the CDC recommends that travelers be immune to hepatitis A. The hepatitis A vaccine is produced from inactivated virus, and the CDC recommends that use of the vaccine in pregnant women be based on a risk–benefit assessment (Box 1).<sup>3,9</sup> Two versions of the typhoid vaccine are available in the United States: an oral live attenuated vaccine that should not be used during pregnancy and an injectable purified Vi polysaccharide vaccine. The CDC states that data are inadequate on the safety of typhoid vaccine but that Vi polysaccharide may be given if needed (Box 1).<sup>3</sup> Despite this weak recommendation, the high proportion of apparently eligible pregnant travelers not receiving this vaccine is notable. Typhoid fever can be a life-threatening illness and is increasingly difficult to treat because of multidrug-resistant organisms.<sup>22</sup> This discordance on risk and concern may suggest additional guidance on use of typhoid polysaccharide vaccine in pregnant women may be useful.

Notable was the use of live attenuated yellow fever vaccine in a sizable proportion of pregnant and breastfeeding travelers. In general, live viral vaccines are contraindicated during pregnancy; however, the CDC recommends vaccinating a pregnant traveler against yellow fever if the trip cannot be postponed and the risk for yellow fever exposure is judged to be greater than the risks associated with vaccination (Box 1).<sup>3</sup> According to a recent review of 1,381 pregnant females receiving yellow fever vaccine, no excess risk of adverse events was noted.<sup>23</sup> Because immunity induced after vaccination during pregnancy has been found to be variable, the Advisory Committee on Immunization Practices recommends serologic testing to verify immune response to yellow fever vaccine or need for a yellow fever vaccine booster dose.<sup>3,24</sup> Likewise, yellow fever vaccination in breastfeeding travelers is controversial in light of three reported cases of yellow fever vaccine-associated encephalitis in exclusively breastfed neonates (aged less than 1 month) whose mothers were vaccinated with yellow fever vaccine.<sup>25</sup> The CDC lists breastfeeding as a precaution (not a contraindication) for yellow fever vaccine administration (Box 1). Our findings suggest that practitioners may have provided the vaccine to breastfeeding travelers who could not avoid travel to a yellow fever-endemic area if the breastfed infants were older (aged older than 3

months) (Fig. 2). However, excretion of vaccine in breast milk and the risk of vaccine exposure through breastfeeding need to be more carefully researched.

Practitioners provided fewer prescriptions for malaria chemoprophylaxis and antibiotics for empiric self-treatment of acute diarrhea to pregnant and breastfeeding travelers compared with nonpregnant, nonbreastfeeding travelers. Their reasoning may have been that overall evidence of effects of antimicrobial medications including malaria chemoprophylaxis taken during pregnancy and lactation is limited.<sup>26,27</sup> However, pregnant women with acute diarrhea are particularly vulnerable to dehydration. Prompt treatment with vigorous oral hydration is needed, and azithromycin may also be used because this drug has been recommended to be safe during pregnancy and lactation (Box 1).<sup>4,28</sup> Moreover, malaria during pregnancy carries a high risk for morbidity and mortality for both the mother and fetus; hence, the prevention of malaria in pregnant women constitutes a priority, albeit problematic as a result of drug safety concerns, comorbidities (eg, neuropsychiatric disorders), or exposure to multidrug-resistant strains (Box 1).<sup>3,4,29,30</sup>

Our study has a number of limitations. We do not have data on the trimester during which the pregnant women were seen, and practitioners may have given different recommendations based on trimester. Similarly, we do not have data on the age of the children of the breastfeeding women nor the exclusivity of use of breast milk, and these factors may have influenced medical practice. These data were collected before the chikungunya and Zika virus outbreaks in the western hemisphere and do not reflect recommended clinical guidance that pregnant women not travel to areas with a risk of Zika virus. Most importantly, the women seen in the Global TravEpiNet systems may not be representative of all U.S. resident pregnant or breastfeeding women traveling internationally or seeking pretravel care. Many pregnant and breastfeeding travelers may discuss their travel plans at nonspecialized practices or not seek pretravel care at all.<sup>30</sup> However, our results provide insight into the clinical challenges related to international travel in this unique group of travelers. Our data suggest that additional research, guidance, and education on use of vaccines and malaria chemoprophylaxis may be warranted for both travelers and their health care providers.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

Global TravEpiNet is supported by U01CK000490 and U01CK000175 from the U.S. Centers for Disease Control and Prevention.

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.

Each author has indicated that he or she has met the journal's requirements for authorship.

## References

1. U.S. Department of Commerce, International Trade Administration, National Travel and Tourism Office. United States resident travel abroad. 2015. Available at: [http://travel.trade.gov/outreachpages/download\\_data\\_table/2015\\_Outbound\\_Analysis.pdf](http://travel.trade.gov/outreachpages/download_data_table/2015_Outbound_Analysis.pdf). Retrieved June 18, 2017
2. Jaeger VK, Tschudi N, Rüegg R, Hatz C, Bühler S. The elderly, the young and the pregnant traveler—a retrospective data analysis from a large Swiss Travel Center with a special focus on malaria prophylaxis and yellow fever vaccination. *Travel Med Infect Dis.* 2015; 13:475–84. [PubMed: 26526774]
3. Morof, DF., Carroll, D. Pregnant travelers. In: Brunette, GW., editor. Centers for Disease Control and Prevention. CDC yellow book 2018: health information for international travel. New York (NY): Oxford University Press; 2017. p. 575-81.
4. Shealy, KR. Travel & breastfeeding. In: Brunette, GW., editor. Centers for Disease Control and Prevention. CDC yellow book 2018: health information for international travel. New York (NY): Oxford University Press; 2017. p. 546-50.
5. Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. *N Engl J Med.* 2014; 370:2211–8. [PubMed: 24897084]
6. Rasmussen SA, Jamieson DJ, Honein MA, Peterson LR. Zika virus and birth defects—reviewing the evidence for causality. *N Engl J Med.* 2016; 374:1981–7. [PubMed: 27074377]
7. Meaney-Delman D, Hills SL, Williams C, Galang RR, Iyengar P, Hennenfent AK, et al. Zika virus infection among U.S. pregnant travelers—August 2015–February 2016. *MMWR Morb Mortal Wkly Rep.* 2016; 65:211–4. [PubMed: 26938703]
8. LaRocque RC, Rao SR, Lee J, Ansdell V, Yates JA, Schwartz BS, et al. Global TravEpiNet: a national consortium of clinics providing care to international travelers—analysis of demographics, travel destinations, and pretravel health care of high-risk US international travelers, 2009–2011. *Clin Infect Dis.* 2012; 54:455–62. [PubMed: 22144534]
9. Centers for Disease Control and Prevention. Guidelines for vaccinating pregnant women. Available at: [www.cdc.gov/vaccines/pubs/preg-guide.htm](http://www.cdc.gov/vaccines/pubs/preg-guide.htm). Retrieved June 18, 2017
10. World Health Organization. Sexual and reproductive health. Available at: <http://www.who.int/reproductivehealth/topics/infertility/definitions/en/>. Retrieved June 18, 2017
11. Human Development Index. 2015. Available at: <http://hdr.undp.org/en/statistics/>. Retrieved June 18, 2017
12. Keystone, JS. Immigrants returning home to visit friends and relatives (VFRs). In: Brunette, GW.Kozarsky, PE.Magill, AJ.Shlim, DR., Whatley, AD., editors. CDC health information for international travel 2016. New York (NY): Oxford University Press; 2016. p. 569-73.
13. Rao SR, LaRocque RC, Jentes ES, Hagmann SHF, Ryan ET, Han PV, et al. Comparison of methods for clustered data analysis in a non-ideal situation: results from an evaluation of predictors of yellow fever vaccine refusal in the Global TravEpiNet (GTEN) consortium. *Int J Stat Med Res.* 2014; 3:215–23.
14. Fernández-Salas I, Díaz-González EE, López-Gatell H, Alpuche-Aranda C. Chikungunya and Zika virus dissemination in the Americas: different arboviruses reflecting the same spreading routes and poor vector-control policies. *Curr Opin Infect Dis.* 2016; 29:467–75. [PubMed: 27472289]
15. Wylie BJ, Hauptman M, Woolf AD, Goldman RH. Insect re-pellants during pregnancy in the era of Zika virus. *Obstet Gynecol.* 2016; 128:1111–15. [PubMed: 27548647]
16. U.S. Environmental Protection Agency. Find the insect repellent that is right for you. Available at: [www.epa.gov/insect-repellents/find-insect-repellent-right-you](http://www.epa.gov/insect-repellents/find-insect-repellent-right-you). Retrieved June 18, 2017
17. LaRocque RL, Ryan ET. Personal actions to minimize mosquito-borne illnesses, including Zika virus. *Ann Intern Med.* 2016; 165:589–90. [PubMed: 27399646]
18. LaRocque RC, Deshpande BR, Rao SR, Brunette GW, Sotir MJ, Jentes ES, et al. Pre-travel health care of immigrants returning home to visit friends and relatives. *Am J Trop Med Hyg.* 2013; 88:376–80. [PubMed: 23149585]
19. Guiding principles for development of ACIP recommendations for vaccination during pregnancy and breastfeeding. Available at: <http://www.cdc.gov/vaccines/acip/committee/downloads/preg-principles-2008.pdf>. Retrieved June 18, 2017

20. Keller-Stanislawski B, Englund JA, Kang G, Mangtani P, Neuzil K, Nohynek H, et al. Safety of immunization during pregnancy: a review of the evidence of selected inactivated and live attenuated vaccines. *Vaccine*. 2014; 32:7057–64. [PubMed: 25285883]

21. Chamberlain AT, Seib K, Ault KA, Orenstein WA, Frew PM, Malik F, et al. Factors associated with intention to receive influenza and tetanus, diphtheria, and acellular pertussis (Tdap) vaccines during pregnancy: a focus on vaccine hesitancy and perceptions of disease severity and vaccine safety. *PLoS Curr*. 2015; 7

22. Date KA, Newton AE, Medalla F, Blackstock A, Richardson L, McCullough A, et al. Changing patterns in enteric fever incidence and increasing antibiotic resistance of enteric fever isolates in the United States, 2008–2012. *Clin Infect Dis*. 2016; 63:322–9. [PubMed: 27090993]

23. Thomas RE, Lorenzetti DL, Spragins W, Jackson D, Williamson T. The safety of yellow fever vaccine 17D or 17DD in children, pregnant women, HIV+ individuals, and older persons: a systematic review. *Am J Trop Med Hyg*. 2012; 86:359–72. [PubMed: 22302874]

24. Staples JE, Bochini JA Jr, Rubin L, Fischer M, Centers for Disease Control and Prevention (CDC). Yellow fever vaccine booster doses: recommendations of the Advisory Committee on Immunization Practices, 2015. *MMWR Morb Mortal Wkly Rep*. 2015; 64:647–50. [PubMed: 26086636]

25. Alain S, Dommergues M, Jacquard AC, Caulin E, Launay O. State of the art: could nursing mothers be vaccinated with attenuated live virus vaccine? *Vaccine*. 2012; 30:4921–6. [PubMed: 22659446]

26. Schlagenhauf P, Blumentals WA, Suter P, Regep L, Vital-Durand G, Schaefer MT, et al. Pregnancy and fetal outcomes after exposure to mefloquine in the pre- and periconception period and during pregnancy. *Clin Infect Dis*. 2012; 54:e124–31. [PubMed: 22495078]

27. Villegas L, McGready R, Htway M, Paw MK, Pimanpanarak M, Arunjerdja R, et al. Chloroquine prophylaxis against vivax malaria in pregnancy: a randomized, double-blind, placebo-controlled trial. *Trop Med Int Health*. 2007; 12:209–18. [PubMed: 17300627]

28. LactMed: a TOXNET database. Bethesda (MD): National Library of Medicine; Available at: <http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm>. Retrieved June 18, 2017

29. Käser AK, Arguin PM, Chiodini PL, Smith V, Delmont J, Jiménez BC, et al. Imported malaria in pregnant women: a retrospective pooled analysis. *Travel Med Infect Dis*. 2015; 13:300–10. [PubMed: 26227740]

30. Roggelin L, Cramer JP. Malaria prevention in the pregnant traveller: a review. *Travel Med Infect Dis*. 2014; 12:229–36. [PubMed: 24813714]

**Box 1**

**Recommendations for Vaccines, Malaria Chemoprophylaxis, and Antibiotics for Self-Treatment of Travelers' Diarrhea in Pregnant and Breastfeeding International Travelers According to Guidelines of the Advisory Committee on Immunization Practices and the Centers for Disease Control and Prevention**

**General**

- Review in detail travel itinerary and epidemiology of vaccine-preventable infectious diseases, malaria, and other mosquito-borne infectious diseases (eg, Zika virus, dengue, chikungunya) at the destinations.\*
- Discuss whether travel can be postponed if itinerary involves high-risk destinations with potential exposure to malaria, yellow fever, Zika virus, dengue, and chikungunya virus.
- Review history of previous vaccinations; consider checking immunity to infectious diseases (eg, hepatitis A and B).
- Do not administer live vaccines to pregnant travelers with the exception of the yellow fever vaccine; see subsequently.
- Discuss prompt and vigorous oral hydration as the treatment of choice for travelers' diarrhea.<sup>†</sup>
- Discuss measures to avoid mosquito bites including bed nets, insect repellents, and protective clothing.<sup>‡</sup>
- Discuss need for sexual abstinence or use of condoms during the entire sexual act throughout the pregnancy of a pregnant woman if she or her partner cannot avoid travel to areas with exposure to Zika virus.<sup>§||</sup>

**Vaccine¶****Tdap**

- Provide Tdap vaccine to all pregnant travelers irrespective of history of receiving this vaccine.
- Tdap can be given at any time during pregnancy, but optimal timing is between 27 and 36 weeks of gestation.

\*See updated country specific information at [www.cdc.gov/travel](http://www.cdc.gov/travel) and consider referring to a travel medicine specialist.

<sup>†</sup>Bismuth subsalicylate is contraindicated in pregnant and breastfeeding travelers.

<sup>‡</sup>Environmental Protection Agency-registered repellents including those containing N,N-diethyl-m-toluamide should be used and do not require any precautions in pregnant and breastfeeding travelers.<sup>15–17</sup>

<sup>§</sup>See updated recommendations and infograms at <https://www.cdc.gov/zika/prevention/sexual-transmission-prevention.html#PregnantCouples>.

<sup>||</sup>Breastfeeding travelers to areas with exposure to Zika virus, even in the event of a Zika virus infection, are encouraged to breastfeed their infants. <https://www.cdc.gov/zika/hc-providers/infants-children/zika-in-infants-children.html>.

<sup>¶</sup>Breastfeeding is not considered a contraindication for listed vaccines; however, breastfeeding is considered a precaution for yellow fever vaccine administration and requires a careful risk–benefit assessment.

**Influenza**

- Provide the inactivated influenza vaccine to all pregnant travelers at any time during the pregnancy before and during the influenza season.<sup>#</sup>

**Hepatitis A**

- The safety of hepatitis A vaccination during pregnancy has not been studied but the theoretic risk is deemed low because the vaccine is produced from inactivated hepatitis A virus.
- Consider the hepatitis A vaccine for unvaccinated or incompletely vaccinated pregnant travelers who will visit regions with high or intermediate hepatitis A virus endemicity.\*

**Hepatitis B**

- Consider the hepatitis B vaccine for unvaccinated or incompletely vaccinated pregnant travelers who will visit regions with intermediate or high prevalence of chronic hepatitis B virus infection.\*

**Meningococcal**

- Consider a quadrivalent meningococcal conjugate vaccine for unvaccinated or 5 or more years previously vaccinated pregnant travelers to areas where *Neisseria meningitidis* is hyperendemic or epidemic.
- Hyperendemic regions include the meningitis belt in Africa during the dry season (December to June).\*

**Polio**

- Consider the inactivated polio vaccine for polio unvaccinated or incompletely vaccinated pregnant travelers who will visit regions where wild polio virus or vaccine-derived poliovirus is actively circulating.\*

**Japanese Encephalitis**

- The inactivated Vero cell culture-derived Japanese encephalitis vaccine, available in the United States, has not been studied in pregnant women.
- Consider this vaccine only after thoroughly balancing the theoretical risk of immunization against the risk of infection based on the itinerary.\*

**Rabies**

- Consider providing rabies pre-exposure immunization if the risk for exposure is considered substantial.\*

**Typhoid**

- No data have been reported on the use of typhoid fever vaccines in pregnant women.

<sup>#</sup>Consider providing the influenza vaccine (if available) to a pregnant traveler with plans to travel to the tropics or the southern hemisphere if seen after the influenza season and influenza was not received during the preceding fall and winter.

- Consider the Vi capsular polysaccharide vaccine to pregnant travelers who will visit regions with an increased risk of exposure to *Salmonella enterica* serotype Typhi.\*

### **Yellow Fever**

- Pregnancy and breastfeeding represent precautions for yellow fever vaccine administration.
- Consider the yellow fever vaccine for a pregnant traveler if travel cannot be deferred and the risk for yellow fever virus exposure is determined to be significant and outweighs the vaccination risks.\*
- If the risks for vaccination are determined to outweigh the risk for yellow fever virus exposure, the pregnant traveler should be given a medical waiver to fulfill international health regulations.
- Breastfeeding travelers should not receive the yellow fever vaccine—because encephalitis has been reported in three exclusively breastfed infants whose mothers were vaccinated with the yellow fever vaccine—unless travel to yellow fever-endemic regions cannot be avoided and after a thorough risk–benefit analysis.\*

### **Malaria Chemoprophylaxis**

#### **Chloroquine**

- Can be used if pregnant or breastfeeding traveler plans to visit destinations with chloroquine-sensitive malaria\*

#### **Mefloquine**

- Can be used if pregnant or breastfeeding traveler plans to visit destinations with chloroquine-resistant malaria\*\*††

#### **Atovaquone–Proguanil**

- Not recommended in pregnant and breastfeeding traveler (if infant weighs less than 5 kg) because of lack of safety data

#### **Doxycycline**

- Contraindicated in pregnant and breastfeeding traveler, but short-term course may be compatible with breastfeeding

#### **Primaquine**

- Contraindicated in pregnant traveler but may be used in breastfeeding travelers if mother and infant have normal G6PD levels

### **Antibiotics for Self-Treatment of Travelers' Diarrhea**

\*\*Be aware of regions in Southeast Asia with mefloquine-resistant malaria.

††Contraindicated if the patient has a history of a neuropsychiatric disorder.

**Azithromycin**

- May be used in pregnant and breastfeeding travelers

**Ciprofloxacin**

- Should be avoided in pregnant and breastfeeding travelers as a result of concern about adverse effects on the infant's developing joints

Data from Centers for Disease Control and Prevention. Guidelines for vaccinating pregnant women. Available at: [www.cdc.gov/vaccines/pubs/preg-guide.htm](http://www.cdc.gov/vaccines/pubs/preg-guide.htm). Retrieved June 18, 2017.

Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

\*See updated country specific information at [www.cdc.gov/travel](http://www.cdc.gov/travel) and consider referring to a travel medicine specialist.

†Bismuth subsalicylate is contraindicated in pregnant and breastfeeding travelers.

‡Environmental Protection Agency-registered repellents including those containing N,N-diethyl-m-toluamide should be used and do not require any precautions in pregnant and breastfeeding travelers.<sup>15-17</sup>

§See updated recommendations and infograms at <https://www.cdc.gov/zika/prevention/sexual-transmission-prevention.html#PregnantCouples>.

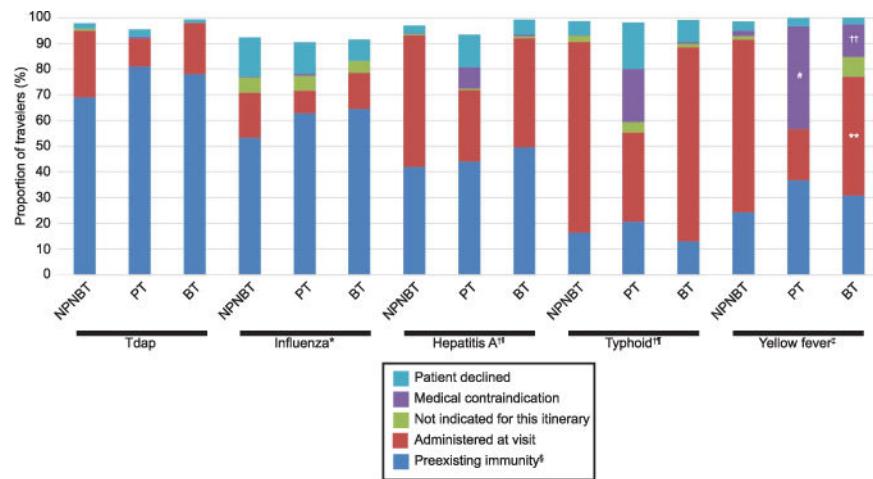
||Breastfeeding travelers to areas with exposure to Zika virus, even in the event of a Zika virus infection, are encouraged to breastfeed their infants. <https://www.cdc.gov/zika/hc-providers/infants-children/zika-in-infants-children.html>.

¶Breastfeeding is not considered a contraindication for listed vaccines; however, breastfeeding is considered a precaution for yellow fever vaccine administration and requires a careful risk–benefit assessment.

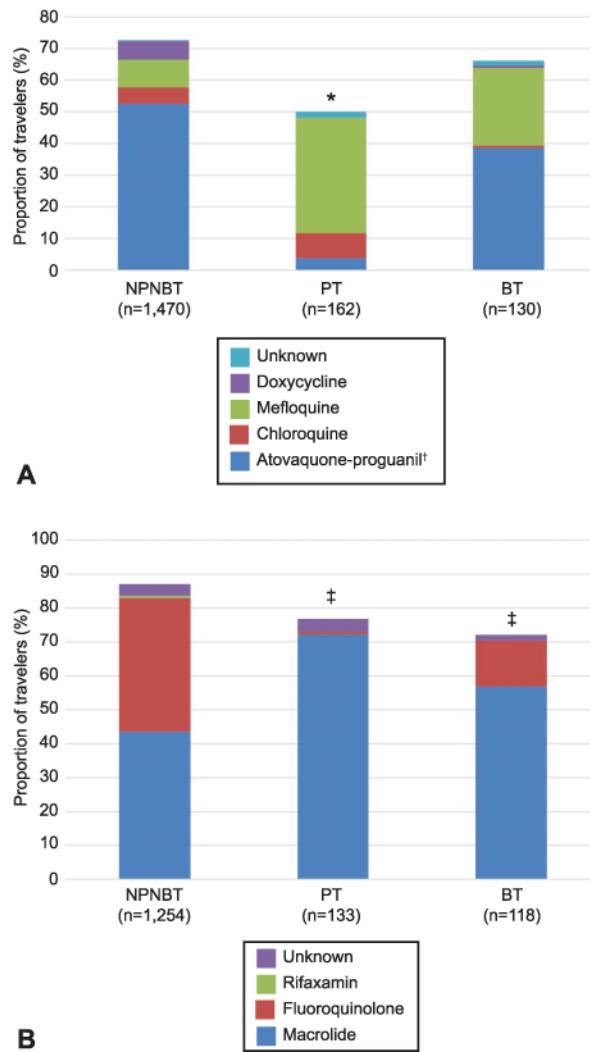
#Consider providing the influenza vaccine (if available) to a pregnant traveler with plans to travel to the tropics or the southern hemisphere if seen after the influenza season and influenza was not received during the preceding fall and winter.

\*\*Be aware of regions in Southeast Asia with mefloquine-resistant malaria.

††Contraindicated if the patient has a history of a neuropsychiatric disorder.

**Figure 1.**

Use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap), influenza, hepatitis A, typhoid, and yellow fever vaccines in pregnant and breastfeeding travelers, Global TravEpiNet Consortium, January 2009–December 2014. NPNBT, nonpregnant, nonbreastfeeding female traveler of childbearing age; PT, pregnant traveler; BT, breastfeeding traveler. \*Includes only travelers who presented during the northern hemisphere influenza season (October 1–June 30) (PT, n5137; BT, n5107; NPNBT, n51,215). †Includes all travelers (PT, n5170; BT5139; NPNBT51,545). All had indicated travel to destinations for which hepatitis A and typhoid vaccines were recommended (see [www.cdc.gov/travel](http://www.cdc.gov/travel)).<sup>3,4,9</sup> ‡Includes only travelers to entirely yellow fever-endemic countries (PT, n530; BT, n539; NPNBT, n5281). §For each vaccine, health care providers could indicate pre-existing immunity as defined by a positive serology, a history of vaccination, or clinical review. ¶Proportion receiving hepatitis A vaccine (PT compared with NPNBT,  $P < .001$ ). ¶Proportion receiving typhoid fever vaccine (PT compared with NPNBT,  $P < .001$ ). #For 3 of 12 patients, first-trimester gestation noted as the reason for contraindication. \*\*For 8 of 18 patients, infants aged older than 3 months noted as the reason for administration. ††For two of five patients, neonates aged 1 month or younger noted as the reason for contraindication.

**Figure 2.**

Cumulative proportion of antimarial drugs (A) and antibiotics for self-treatment of diarrhea (B) prescribed according to pregnancy and breastfeeding status, Global TravEpiNet Consortium, January 2009–December 2014. All travelers analyzed in A traveled to a malaria-holoendemic destination. NPNBT, nonpregnant, nonbreastfeeding female traveler of childbearing age; PT, pregnant traveler; BT, breastfeeding traveler. \*Proportion with prescription of any antimalarial drug (PT compared with NPNBT,  $P<.001$ ). †Proportion of prescription of atovaquone–proguanil (BT compared with NPNBT,  $P<.05$ ). ‡Proportion with prescription of any antibiotic for diarrhea (PT compared with NPNBT and BT compared with NPNBT,  $P<.001$ ).

**Table 1**

Demographic and Clinical Characteristics of Pregnant or Breastfeeding International Travelers Visiting Global TravEpiNet Clinics for Pretravel Consultation

| Variable                            | Global TravEpiNet Clinics 2009–2014 |                       |  |
|-------------------------------------|-------------------------------------|-----------------------|--|
|                                     | Pregnant (n=170)                    | Breastfeeding (n=139) | Nonpregnant, Nonbreastfeeding* (n=1,545) |
| Age (y)                             | 32 (29–35)                          | 33 (31–37)            | 30 (25–38)                               |
| Age groups (y)†‡                    |                                     |                       |  |
| 18–29                               | 48 (28)                             | 26 (19)               | 711 (46)                                 |
| 30–34                               | 75 (44)                             | 57 (41)               | 302 (20)                                 |
| 35–49                               | 47 (28)                             | 56 (40)               | 532 (34)                                 |
| U.S.-born‡§                         | 124 (73)                            | 81 (58)               | 1,233 (80)                               |
| Any medical condition               | 98 (58)                             | 81 (58)               | 972 (63)                                 |
| Taking medications†¶                | 137 (81)                            | 79 (57)               | 1,029 (67)                               |
| Time to departure less than 14 d    | 63 (37)                             | 57 (41)               | 500 (32)                                 |
| Travel duration greater than 28 d‡§ | 30 (18)                             | 59 (43)               | 394 (26)                                 |
| Reason for travel                   |                                     |                       |  |
| Leisure¶                            | 80 (47)                             | 53 (38)               | 759 (49)                                 |
| Business‡§                          | 43 (25)                             | 39 (28)               | 268 (17)                                 |
| Visiting friends and relatives†‡    | 33 (19)                             | 50 (36)               | 162 (11)                                 |
| Other#                              | 24 (14)                             | 18 (13)               | 344 (22)                                 |
| Destination by HDI category         |                                     |                       |  |
| Low or medium                       | 133 (78)                            | 118 (85)              | 1,254 (81)                               |
| High or very high                   | 37 (22)                             | 21 (15)               | 291 (19)                                 |
| Region of destination               |                                     |                       |  |
| Africa                              | 51 (30)                             | 64 (46)               | 584 (38)                                 |
| North America                       | 0 (0)                               | 0 (0)                 | 1 (0.1)                                  |
| Central America or Caribbean        | 35 (21)                             | 13 (9)                | 232 (15)                                 |
| South America                       | 18 (11)                             | 11 (8)                | 202 (13)                                 |
| Southeast Asia                      | 52 (31)                             | 35 (25)               | 380 (25)                                 |
| Europe§                             | 2 (1)                               | 3 (2)                 | 73 (5)                                   |
| Eastern Mediterranean               | 9 (5)                               | 7 (5)                 | 63 (4)                                   |
| Western Pacific                     | 22 (13)                             | 17 (12)               | 253 (16)                                 |

HDI, Human Development Index.

Data are median (interquartile range) or n (%).

Random intercept regression models with clinical site as the random effect were used to evaluate measures of association and statistical significance accounting for the clustering of patients within sites. Fisher exact tests were used when sample sizes were small.

\* Nonpregnant, nonbreastfeeding and nonpregnant travelers were females of childbearing age.

†  $P<.01$  pregnant traveler compared with nonpregnant, nonbreastfeeding traveler.

‡  $P<.01$  breastfeeding traveler compared with nonpregnant, nonbreastfeeding traveler.

<sup>§</sup> $P<.05$  pregnant traveler compared with nonpregnant, nonbreastfeeding traveler.

<sup>¶</sup>Use of multivitamins was reported by 83.2%, 63.3%, and 32.0% of pregnant, breastfeeding, and nonpregnant, nonbreastfeeding travelers, respectively.

<sup>¶</sup> $P<.05$  breastfeeding traveler compared with nonpregnant, nonbreastfeeding traveler.

<sup>#</sup>Health care-seeking, education or research, missionary, or volunteer.