

# **ZIKA POSTPARTUM EMERGENCY RESPONSE (ZPER) PROTOCOL**

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**Objective:** To conduct a rapid, population-based assessment of maternal behaviors and experiences related to Zika virus exposure among recently pregnant women in Puerto Rico using methodology based on previous rapid assessments conducted using the Center for Disease Control and Prevention's (CDC) Pregnancy Risk Assessment Monitoring System (PRAMS).

To conduct a follow-up phone survey about the ongoing needs of postpartum women and their infants after leaving the hospital during the early postpartum period in the context of the continued threat of Zika virus infection in Puerto Rico. To assess concerns, knowledge, behaviors, and use of Zika prevention strategies among husbands and partners of recently pregnant women in Puerto Rico using hospital-based sampling methodology based on previous rapid assessments conducted by the Puerto Rico Department of Health.

**Background:** In early 2015, an outbreak of Zika virus was identified in northeastern Brazil<sup>1</sup>. Zika is a flavivirus primarily transmitted by the bite of *Aedes* mosquitoes, which are found in much of the region of the Americas including parts of the United States, and also transmit dengue and chikungunya viruses<sup>2,3</sup>. More recently, evidence has emerged of the possibility of transmission of Zika virus through sexual contact<sup>4</sup>. As of February 2017, there has been confirmed transmission of Zika virus over many countries in the Americas and the United States<sup>5</sup>.

Clinical illness from Zika virus infection is usually mild, with symptoms including fever, rash, joint pain, and conjunctivitis lasting from several days to a week<sup>6</sup>. While there is no evidence of increased susceptibility to Zika virus infection in pregnant women or that pregnant women experience more severe disease once infected, there is evidence of a causal association between Zika virus infection in pregnancy and an increased risk for congenital microcephaly and other severe brain abnormalities in the infants of women infected during pregnancy<sup>7</sup>.

Currently no vaccine or medication exists to prevent or treat Zika virus infection. CDC issued interim guidelines for health care providers caring for pregnant women and women of reproductive age with possible Zika virus exposure<sup>8</sup>, as well as guidelines for the evaluation and testing of infants with possible congenital Zika virus infection<sup>9</sup>, and guidance for women of reproductive age on planning pregnancies and avoiding unintended pregnancies<sup>4</sup>. This guidance includes screening and testing recommendations for symptomatic and asymptomatic pregnant women; recommendations for contraception counseling, family planning, preconception health counseling; and screening and testing of infants born to mothers who traveled to or resided in areas of Zika virus transmission.

A rapid assessment of maternal-related behaviors and experiences in regard to Zika virus in Puerto Rico will provide information on prenatal experiences such as discussions with providers, testing for Zika and sources of information, as well as behaviors employed to reduce sexual and vector-based exposure to the Zika virus (**PRAMS ZPER Hospital-based survey**). A hospital father/partner survey will provide information about the concerns, behaviors, experiences, and contributions of fathers and partners to the prevention of Zika virus

transmission during pregnancy (**PRAMS ZPER Partner Survey**). A follow-up telephone survey will assess the ongoing needs of postpartum women and their infants after leaving the hospital during the early postpartum period (**PRAMS ZPER Telephone Follow-up Survey**).

### **PRAMS ZPER Hospital-based survey**

**Duration:** Project duration will be approximately 6 months for each cohort. Data collection for the first cohort of women was completed in the fall of 2016. Data collection activities for a second cohort will occur over a 3-month period in 2017. A possible tentative timeline is suggested below:

#### Month 1-2 – Set-up, hospital based survey:

Finalize protocol, finalize questionnaire, finalize sampling, CDC develops and tests data collection platform, obtain IRB and other required approvals, hire and train staff in Puerto Rico.

#### Month 2 – Pretest & Data collection initiation, hospital based-survey:

Conduct pre-test to verify protocol and questionnaire work and staff are ready to implement; make any final adjustments; data collection begins; regular submission of data to CDC begins

#### Months 3-5 Data collection implemented, hospital based survey:

Collect data; regularly conduct quality control measures; regularly submit data to CDC; CDC begins data processing and generation of preliminary results

#### Month 6 and beyond: Data analysis and dissemination:

Full dataset is weighted by CDC; data analysis and dissemination plan is executed by the Puerto Rico Department of Health (PRDH), CDC Emergency Operations Center (EOC), and CDC PRAMS. After that plan has been executed, data will be made available to other researchers for additional analyses.

**Study Design:** The Zika Postpartum Emergency Response (ZPER) will be an island-wide, stratified proportional sample of women who recently delivered a live-born infant in a hospital during the study period. The sample will be stratified by 8 geographic health regions. For the second cohort of mothers, all partners of sampled women will be eligible to participate in the father/partner survey; however, contact will be limited to those fathers/partners who are present at the hospital when the interviewers are there contacting sampled women.

**Data source:** ZPER data collection will take place in all hospitals in Puerto Rico with 100 or more births per year. According to 2015 and 2016 birth data, 36 hospitals meet this eligibility criterion for 2016 hospital surveillance and 33 hospitals for 2017 hospital surveillance representing 97.7% of all Puerto Rico births. Data collection will take place over a 3-month period in 2017. The hospital-based sampling frame is identified by the hospital's delivery log. In most hospitals, the delivery log represents a complete and accurate account of all births occurring in the hospital. It will be important to ensure that the delivery log in each

participating hospital is reliable and kept up-to-date. A more detailed description of sampling can be found in **Appendix A**.

**Sample size:** Approximately 3,000 women for each of two cohorts; for the second cohort, the partner of all participants also will be eligible for the father/partner survey, but availability for sampling depends on their being present in the hospital at the time of maternal interview. It is anticipated that 60% of the partners may be available (approximately 1,800 partners).

**Survey Instrument:** Questions were initially developed with input from subject matter experts from CDC's National Center for Birth Defects and Developmental Disabilities, the National Center for Immunization and Respiratory Disease, and the National Center for Emerging and Zoonotic Infections. Questions were finalized in collaboration with subject matter experts from the Puerto Rico Department of Health, and for the second cohort were updated on the basis changes in clinical recommendations and experience from the first season of the Zika outbreak, with careful review to ensure questions do not duplicate information being collected from postpartum women through other efforts. Topics covered include interactions between women and their providers regarding Zika virus, counseling and testing for Zika virus by prenatal care providers, other sources of information that women consult regarding Zika virus, and use of preventive measures to prevent Zika exposure and transmission. Proposed questions can be found in **Appendix B**.

Likewise, the questions for the father/partner survey for the second cohort were developed with input from subject matter experts from CDC's National Center for Birth Defects and Developmental Disabilities, CDC's National Center for Chronic Disease Prevention and Health Promotion, Northwestern University, and the Puerto Rico Department of Health, with careful review and pretesting in Puerto Rico to ensure questions are appropriate for the population and setting. Topics covered include interactions between partners and health care providers regarding Zika virus, sources of information consulted regarding Zika virus, use of preventive measures to prevent Zika exposure and transmission, and involvement in the pregnancy of the wife or partner. Proposed questions can be found in **Appendix G**.

**Proposed Data Collection Plan:**

Details of the data collection procedures will be developed in collaboration with the Puerto Rico Department of Health based on the infrastructure and experience of the group from the existing Maternal and Infant Health Survey of Puerto Rico (ESMIPR) study. An initial proposal is for health department to hire and/or train staff who will become the field staff. Field staff will visit each hospital on the designated day, select the sample from the hospital birth log, and [enter the information onto a data form (or directly into a tablet/laptop) for each sampled mother.] This is the manner in which study participants are recruited. Each sampled mother would be assigned a unique study ID that could later be used to link information from the birth log to information from the questionnaire. Health department staff would then visit each mother individually and offer her the opportunity to complete the interview on a paper form or

using a tablet. Paper surveys forms would then need to be collected, tracked, and passed on for data entry and verification following the interviews each day.

For the second cohort, fathers/partners will be offered the opportunity to participate in the partner survey if they are in the hospital at the time when the interviewer is present to administer the maternal survey. Each partner will also be assigned a unique study ID that is linked to the mother's ID number. The partner survey will also be available on a paper form or using the tablet, and the partner can complete the survey before, after, or at the same time as the mother (although there will only be 1 tablet per interviewer, so if completing simultaneously, one person will complete on the paper form).

**Staffing:** In addition to a principal investigator, a project coordinator will oversee project start-up activities, field work, and closeout activities. The coordinator position will likely be a full-time position for the duration of the project. Based on the required sample size, it is estimated that approximately 12 full-time interviewers would be needed for the 3-month data collection period. This assumes that 1 worker can collect, on average, 8 surveys/day (~1 hour per mom), and each worker collects data 5 days per week (regular work week). However, this estimate may need to be adjusted, taking into account the distance and time needed to travel between hospitals, the actual amount of time it takes to complete each interview, and other factors. A more detailed explanation can be found in Appendix A.

For the implementation of the father survey, it is anticipated that 30 staff, including interviewers and regional coordinators, will be needed to collect all information from both mothers and partners during the 3-month data collection period.

**Proposed Data Management Plan:** CDC will provide a secure data collection platform. Data entry and data entry verification will be conducted in Puerto Rico by staff or contractors as determined by the Puerto Rico Department of Health. Data will be uploaded by Puerto Rico staff daily to CDC. CDC will perform data management functions and assist Puerto Rico staff with addressing data questions. At the conclusion of data collection activities, CDC will weight the data and provide a final dataset to Puerto Rico.

**Data Analysis & Data Dissemination:** Given the emergency nature of this rapid assessment, a preliminary dissemination plan will be developed, along with the analysis plan, at the outset of the project. The plan will be developed through a collaboration between CDC and the Puerto Rico Department of Health, and will focus on quickly sharing important findings through the appropriate channels to inform programs and policies. Once developed, the analysis plan will be included in **Appendix C**.

**Data Sharing:** The final weighted dataset will reside at both CDC and the Puerto Rico Department of Health. CDC and the Puerto Rico Department of Health will draft and sign a data sharing agreement specifying the terms through which data can be released to researchers within each agency, as well as to external researchers who may request the data. After CDC EOC, CDC/DRH and PRAMS, and PRDH have completed analytic objectives, CDC will coordinate

the release of the data to external researchers as part of the existing PRAMS data release process, or researchers may contact the Puerto Rico Department of Health directly for access to the data. A sample data sharing agreement is provided in **Appendix D**.

**Human Subjects Protections:** All project staff will complete human subjects training using a curriculum identified by CDC, in addition to fulfilling requirements of the Puerto Rico Department of Health. Each survey participant will be read or provided with written informed consent materials prior to beginning the questionnaire. Details regarding human subjects protections and informed consent are provided in **Appendix E**.

ZPER does not specifically target children. ZPER is a population-based sample of women who have recently given birth, thus all sectors of the birth population are represented and minors may be included in the sample if they meet other eligibility criteria. The PRAMS protocol (CDC #2233) approved in 1999 allows for waiving of parental permission for minors where the parental permission is not required by state law or the local IRB. If the state is required to obtain parental consent, the state has the option of requesting a waiver of parental consent, excluding minors, or obtaining written parental consent.

The Puerto Rico Department of Health (local IRB) has approved the parental waiver for ZPER and it attached (**Appendix J**). The assent form header approved by the local IRB is boiler plate language used for minor participation in research. We have also added language to the amendment requesting approval for parental waiver of permission by CDC IRB.

**IRB Approval:** CDC will obtain IRB approval for ZPER. The Puerto Rico Department of Health will determine if additional local IRB approval is needed.

**Funding:** The proposed funding mechanism would be a supplement to the new PRAMS Cooperative Agreement RFA-DP-16-001. Puerto Rico will submit a budget for the project. Requested funding would cover initial start-up cost (training, staffing, planning, and development of survey materials) and implementation of project activities (i.e. staff travel, data collection, data processing, analysis and reporting).

### **PRAMS ZPER Telephone Follow-up Survey**

**Objective:** To conduct a rapid, population-based assessment of maternal behaviors, experiences, and receipt of services for postpartum women and their infants in the context of the Zika virus outbreak in Puerto Rico using a methodology based the Center for Disease Control and Prevention's (CDC) Pregnancy Risk Assessment Monitoring System (PRAMS).

**Background:** The hospital-based component of the PRAMS-ZPER survey reaches women shortly after delivery during their hospital stay, and collects critical information on concerns, behaviors, and experiences during pregnancy related to Zika virus counseling, testing, and use of measures to prevent infection during pregnancy. However, given the timing of

administration of the hospital-based component of the PRAMS-ZPER survey, no information is collected beyond the first few days after delivery. Little is known about the ongoing needs of postpartum women and their infants during the early postpartum period after leaving the hospital in the context of the continued threat of Zika virus infection in Puerto Rico. The PRAMS-ZPER telephone follow-up survey will collect information on postpartum experiences. This will include women from the first cohort of the PRAMS-ZPER hospital-based survey who delivered live-born infants in the fall of 2016, and women from the second cohort who delivered live-born infants in the fall of 2017. Only participants in the hospital survey are eligible for the telephone follow-up survey. All Zika positive women will be included in the follow-up sample. The purpose is to gain an understanding of postnatal experiences including: interactions between women and their postpartum health care providers regarding Zika virus, maternal postpartum health and well-being; infant health, well-being, and access to services for potentially exposed infants; and use of preventive measures to prevent Zika exposure and transmission, need for support services, and postpartum contraceptive use among women who may have had Zika-affected pregnancies and infants, and those who did not.

**Duration:** Project duration will be approximately 6 months for each cohort. Data collection activities will occur over a 3-month period. A tentative timeline is suggested below:

Month 1-2 – Set-up:

Finalize protocol, finalize questionnaire, finalize sampling, CDC develops and tests data collection platform, obtain IRB and OMB approvals, hire and train staff in Puerto Rico.

Month 2 – Pretest & Data collection initiation:

Conduct pre-test to verify protocol and questionnaire work and staff are ready to implement; make any final adjustments; data collection begins; regular submission of data to CDC begins

Months 3-5 - Data collection implemented:

Collect data; regularly conduct quality control measures; regularly submit data to CDC; CDC begins data processing and generation of preliminary results

Month 6 and beyond: Data analysis and dissemination:

Full dataset is weighted by CDC; data analysis and dissemination plan is executed by the Puerto Rico Department of Health (PRDH), CDC Emergency Operations Center (EOC), and CDC PRAMS. After that plan has been executed, data will be made available to other researchers for additional analyses.

**Study Design:** The Zika Postpartum Emergency Response (ZPER) Telephone follow-up survey will sample women who completed the initial hospital-based survey proportionally by region and include all women who indicated they were diagnosed with Zika on the hospital survey.

**Data source:** Data collection for the ZPER Telephone Follow-up Survey will be conducted by calling women on the telephone (landline or cell phone) using contact information obtained from the Puerto Rico Demographic Registry Office. Data collection for the first cohort will take

place over a 3-month period in the summer of 2017, and data collection for the second cohort will take place starting in the spring of 2018. The sampling frame is identified from the list of respondents from the PRAMS-ZPER 2017 study. A more detailed description of sampling can be found in **Appendix A**.

**Sample size:** Approximately 1,500 women for each of 2 cohorts.

**Survey Instrument:** Questions have been taken from the regular PRAMS survey on maternal postpartum health care, health, and infant care. Questions on use of measures to prevent Zika virus infection have been taken from the PRAMS-ZPER hospital-based survey instrument used in 2016. Additional questions have been developed in collaboration with subject matter experts from CDC, the Puerto Rico Department of Health, and the Human Resources and Services Agency (HRSA) with careful review to ensure questions do not duplicate information being collected from postpartum women through other efforts. Topics covered may include: interactions between women and their postpartum health care providers regarding Zika virus, maternal postpartum health and well-being, infant health and well-being, and use of preventive measures to prevent Zika exposure and transmission, need for support services, and postpartum contraceptive use. The survey instrument can be found in **Appendix F**.

**Proposed Data Collection Plan:**

Data collection will be conducted in accordance with selected elements of standard PRAMS operational procedures. A list of eligible women in a specified file format will be uploaded into the PRAMS Integrated Data Collection System (PIDS). Each woman will receive a preletter informing her that she has been selected to participate (**Appendix G, Part 1**). The letter will include a pre-paid postage card and a phone number, either of which she can use to decline participation or any further contact. Women who do not opt-out, will be grouped into batches based on the birth date of their infant. Women with the oldest infants will be called first. A call sheet will be generated for each sampled mother. On the designated start date, the interviewers will begin calling the first batch of women, and will record information about call attempts on the call sheet. An introductory script is read when the phone is answered (**Appendix G, Part 2**). No information about the study is revealed until the person speaking is confirmed to be the intended respondent. A separate script is used when leaving messages with a family member or on voicemail (**Appendix G, Part 3**). Once the participant is on the phone, a consent script is read before initiating the questionnaire (**Appendix H**). If the mother agrees to participate, her responses will be captured on a paper form. Follow-up for a batch of women ends 30 days after the date of initiation. Telephone interviewers can make up to 15 call attempts to each working telephone number for each sampled women. Women who participate will be offered a nominal reward for their time that will be sent to them via the postal service. Women who decline to participated are removed from the call list for further follow-up. Ten percent of the calls that each interviewer makes will be monitored by the project coordinator or other designated staff person. Survey responses that are collected on the paper form are data entered into PIDS.

**Staffing:** In addition to a principal investigator, a project coordinator will oversee the project activities. Based on the required sample size, it is estimated that approximately 2-4 phone interviewers will be needed for the duration of the 3-month data collection period, and potentially for several additional months to finalized data entry activities following the period of active data collection. ZPER Telephone Follow-up study telephone interviewers may also support regular Puerto Rico PRAMS interviewing and data collection activities.

**Proposed Data Management Plan:** CDC will provide a secure data collection platform. Data entry and data entry verification will be conducted in Puerto Rico by staff or contractors as determined by the Puerto Rico Department of Health. CDC will perform data management functions and assist Puerto Rico staff with addressing data questions. At the conclusion of data collection activities, CDC will weight the data and provide a final dataset to Puerto Rico.

**Data Analysis & Data Dissemination:** Given the emergency nature of this rapid assessment, a preliminary dissemination plan will be developed, along with the analysis plan, at the outset of the project. The plan will be developed through a collaboration between CDC and the Puerto Rico Department of Health, and will focus on quickly sharing important findings through the appropriate channels to inform programs and policies **Appendix C**.

**Data Sharing:** The final weighted dataset will reside at both CDC and the Puerto Rico Department of Health. CDC and the Puerto Rico Department of Health will draft and sign a data sharing agreement specifying the terms through which data can be released to researchers within each agency, as well as to external researchers who may request the data. After the CDC Emergency Operation Center (EOC), CDC Division of Reproductive Health (DRH) and PRAMS, and Puerto Rico Department of Health (PRDH) have completed analytic objectives, CDC will coordinate the release of the data to external researchers as part of the existing PRAMS data release process, or researchers may contact the Puerto Rico Department of Health directly for access to the data. A proposed data sharing plan is in **Appendix D**.

**Human Subjects Protections:** All project staff will complete human subjects training using a curriculum identified by CDC, in addition to fulfilling requirements of the Puerto Rico Department of Health. Participants will be given the opportunity to opt out of the follow-up telephone survey (**Appendix G**), and each survey participant will be read a consent script at the beginning of the survey (**Appendix H**).

**IRB and OMB Approval:** CDC will obtain IRB and OMB approval for the ZPER Telephone Follow-Up Survey. The Puerto Rico Department of Health will also obtain local IRB approval.

**Funding:** The proposed funding mechanism will be the PRAMS Cooperative Agreement RFA-DP-16-001. Puerto Rico will submit a budget for the project. Requested funding would cover initial start-up cost (training, staffing, planning, and development of survey materials) and implementation of project activities (i.e. staff travel, data collection, data processing, analysis and reporting).



## References

1. Schuler-Faccini L, Ribeiro EM, Feitosa IM, et al. Possible Association Between Zika Virus Infection and Microcephaly — Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65:59–62. DOI: <http://dx.doi.org/10.15585/mmwr.mm6503e2>.
2. Estimated range of *Aedes albopictus* and *Aedes aegypti* in the United States, 2016 <https://www.cdc.gov/zika/pdfs/zika-mosquito-maps.pdf>.
3. Staples JE, Dziuban EJ, Fischer M, et al. Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection — United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:63–67. DOI: <http://dx.doi.org/10.15585/mmwr.mm6503e3>.
4. Petersen E, Meaney-Delman D, Neblett-Fanfair R, et al. Update: Interim Guidelines for Preconception Counseling Prevention of Sexual Transmission of Zika Virus for Persons with Possible Zika Virus Exposure — United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65(39):1077–1081: <https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6539e1.pdf>.
5. All Countries and Territories with Active Zika Virus Transmission: <https://www.cdc.gov/zika/geo/active-countries.html>.
6. CDC. Zika virus. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <http://www.cdc.gov/zika/index.html>.
7. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika Virus and Birth Defects - Reviewing the Evidence for Causality. N Engl J Med. 2016 374(20):1981-7.
8. Oduyebo T, Igbinsola I, Petersen E, et al. Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States, July 2016. MMWR Morb Mortal Wkly Rep 2016;65(29):739-744: <https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6529e1.pdf>.
9. Russell K, Oliver S, Lewis L, et al. Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016. MMWR Morb Mortal Wkly Rep 2016;65(33): 879-878.