Zika Virus Associated Neurologic Illness Case Control Study

Request for Emergency OMB approval of a new ICR

Supporting Statement B.

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1. Respondent Universe and Sampling Methods

SEVERE NEUROLOGIC ILLNESS patients at participating hospitals are being identified prospectively through surveillance conducted by PRDH. Cases will be selected from residents of Puerto Rico with a diagnosis of any SEVERE NEUROLOGIC ILLNESS since January 1, 2016.

Control ascertainment
A minimum of two controls will be pair-matched to each case by age group (<5, 5–20, 21–39, 40–64, and >65 years). Controls will be randomly selected from households within a one kilometer radius of the matching case-patient's residence. A wireless device (e.g., tablet, IPhone) will be brought to the case-patient toward identifying the place of residence using GoogleEarth. A one kilometer radius will be drawn around the case-patient's residence, and a random number generator will be used to calculate a direction (i.e., between 0 and 360 degrees) from the case-patient household as well as a random distance (i.e., between 0 and 1,000 meters) away from the case-patient household. Selected locations that are clearly uninhabited (e.g., forests, industrial areas, ocean) will be excluded. The process will be repeated until an apparent household is selected. If no age-matched control is available on the day of investigation, the field team will spin a one-sided object (e.g., bottle, pen) and proceed to the closest household in which the one-sided object points. This process will be repeated until either all households immediately adjacent to the randomly selected household have been visited or an age-matched control can be ascertained. If an age-matched control is identified but is not willing to participate in the investigations or all households that are immediately adjacent to the randomly selected household are visited and an age-matched control is not identified, another household will be visited by random selection using the described method toward finding a control. Only one control will be enrolled per randomly selected household. The team will continue until at least two age-matched controls per case are enrolled. All cases and controls may be revisited one month after the initial visit to collect a second blood specimen to assist in interpretation of diagnostic test results.

2. Procedures for the Collection of Information

Retrospective medical record review

SEVERE NEUROLOGIC ILLNESS patient identification and description

SEVERE NEUROLOGIC ILLNESS patients at participating hospitals will be identified prospectively through surveillance that is being conducted by PRDH. Case reporting will require submission of a serum specimen and a case report form that collects descriptive demographic, epidemiologic, and clinical data. SEVERE NEUROLOGIC ILLNESS patients will be contacted by project field epidemiologists, who will explain the purpose of the investigation. For those that give written consent to participate in the investigation (Attachment D), remaining clinical specimens (e.g., cerebrospinal fluid (CSF), urine, stool or rectal swabs) will be collected, and retrospective medical chart review will be performed to collect detailed information on clinical characteristics (Attachment F).

Case definition

A case will be defined as a person that resided in Puerto Rico continuously for the two months prior to onset of SEVERE NEUROLOGIC ILLNESS and presented or was transferred to a participating institution in 2016.

Case and control enrollment

Potential participants will be introduced to the investigation following a script that explains the reasons the investigation is being conducted, the activities involved in the evaluation, and the risks and benefits of participation (Attachment D). Written consent will be obtained from all participants for the following: 1) participation in the survey and collection of blood specimen on the day of the survey; 2) storage of specimens for future diagnostic testing; 3) retrieval of clinical specimens and review of medical records from any illness for which the individual sought medical care in the previous two months; and 4) willingness to be contacted in the future depending on test results or if additional studies are proposed. If a second specimen is needed one month after the initial investigation visit, a second consent form will be obtained (Attachment E). For participants meeting the definition of a minor in Puerto Rico (i.e., individuals <21 years of age, unmarried, without children, and living with their parents), written permission to participate will be obtained from a parent or guardian. Verbal assent will be obtained from participants 8–12 years of age.

Data collection and analysis

Case and control interviews will be conducted using the questionnaire developed by the investigation team (Attachment C). All cases and controls will be asked questions about activities, antecedent signs and symptoms of illness, and exposures in the two months prior to onset of neurologic illness for cases and the same time period for their matched controls. A calendar will be used to orient cases and controls to the time period of interest.

Sera, urine, and saliva will be collected from cases and controls at the time of interview using standard techniques. The sera will be tested for antibodies against suspected infectious pathogens, such as ZIKV, dengue virus, chikungunya virus, influenza virus, human immunodeficiency virus, and Leptospira species bacteria. Urine specimens will be tested by rRT-PCR to identify ZIKV, dengue virus, or chikungunya virus. Serum will also be tested for anti-GM1 antibodies that have been previously associated with type of SEVERE NEUROLOGIC ILLNESS.

If any residual specimens are available from cases, those will also be obtained and undergo testing for infectious pathogens. It is not expected that matched controls will have any previously collected clinical specimens; however, in cases where controls had specimens collected while seeking medical care for an acute illness experienced within two months of SEVERE NEUROLOGIC ILLNESS symptom onset of the matching case, these specimens will also be collected and tested for evidence of infection with the

aforementioned pathogens. Residual samples will be stored after infectious testing is complete at the U.S. CDC with an identification number for possible additional testing for SEVERE NEUROLOGIC ILLNESS-associated biological markers or other infectious pathogens as clinically indicated. If a participant does not provide consent to store the specimens, all specimens for that participant will be destroyed once testing for infectious disease pathogens has been completed. As with cases, written consent will also be obtained to review controls' medical records, where applicable and available, using a standardized chart abstraction form (Attachment F). Diagnostic test results will be securely transmitted from CDC to PRDH, which will then transmit diagnostic test results to participants by telephone or mail, as they prefer.

3. Methods to Maximize Response Rates and Deal with No Response

None

4. Tests of Procedures or Methods to be Undertaken

No pilot testing will be done for either project.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

No individuals were consulted on statistical aspects of these proje