Supplementary Online Content


**eMethods.** Modeling Approach

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eMethods. Modeling Approach

Estimated Number of Pregnant Women Infected With Zika Virus

Let $B$ be the number of births occurring in a given 12 month period. If we assume that all pregnancies resulting in these births are uniformly distributed across months, we would expect $n = B/12$ pregnancies to begin in any given month. Under this assumption, there would be $9n$ pregnant women at risk for Zika infection in any given month of the epidemic, $n$ women in each of 9 possible months of gestation. In addition, the $n$ women who become pregnant during each month of the epidemic are assumed to have experienced the same time at risk for Zika infection as the women who are already pregnant. For example, women who become pregnant in the third month of the epidemic are assumed to have experienced two months at risk for Zika infection prior to their pregnancy. Suppose the epidemic lasts $k$ months. If $p_i$ is the risk for Zika infection among pregnant women in month $i$ of the epidemic, then the total number of pregnant women infected in the course of the epidemic, say $TI$, is given by

$$TI = 9n \cdot p_1 + 9n \cdot p_2 \cdot (1 - p_1) + 9n \cdot p_3 \cdot (1 - p_2) \cdot (1 - p_3) + \cdots$$

or

$$TI = 9n \left[ p_1 + \sum_{i=2}^{k} p_i \cdot \prod_{j=2}^{i-1} (1 - p_j) \right]. \quad [1]$$

In equation [1],

$$p_1 + \sum_{i=2}^{k} p_i \cdot \prod_{j=2}^{i-1} (1 - p_j)$$

corresponds to the final attack Zika infection rate for the entire population. If this attack rate is designated as $P$, then, for any values of $p_i, i = 1, 2, \ldots k$ and $k$, the total number of infected pregnant women is given by

$$TI = 9n \cdot P .$$

or, after substituting for $n$,

$$TI = \frac{9B}{12} \cdot P = \frac{3}{4}B \cdot P . \quad [2]$$

Under the assumption that pregnancies are uniformly distributed across gestation months, the number of pregnant women exposed to the Zika virus during each trimester of pregnancy is given by

$$\frac{3}{4}B \cdot \frac{1}{3} = \frac{B}{4} .$$

Therefore, the expected number of Zika infections occurring among women in trimester $j$ can be estimated as

$$Tl_j = \frac{B}{4} \cdot P .$$

To reflect sampling variability associated with the number of annual births, we assume $B$ to be a random sample from the binomial distribution

$$B \sim Bin\left(N, br\right) \quad [3]$$

with expected value $N \cdot br$ where $N$ is the 2015 population of Puerto Rico and $br$ is the corresponding birth rate (Table 1). We used available information to construct an uncertainty distribution for the Zika virus attack rate, $P$, to reflect current knowledge on the true value of this parameter (Table 1). Monte Carlo simulation was used to propagate the assumed uncertainty about $P$ to the estimator for the expected total number of pregnant women infected with Zika in equation [2]. In each simulation, a value for $P$ was drawn from the assumed uncertainty distribution for this parameter and combined with the value for $B$ sampled from the distribution in equation [3] to produce a realization for $TI$ under the assumption that

$$TI \sim Bin\left(\frac{3B}{4}, P\right) .$$
Given a sampled value for $T_I$, estimates for the number of pregnant women infected with Zika virus in each trimester of pregnancy were derived as

$$T_I = \frac{T_I}{3}, \ j = 1, 2, 3$$

The Monte Carlo process was repeated 100,000 times and the resulting uncertainty distributions for the estimates are summarized using the median, the interquartile range and a 95% uncertainty interval defined as the range between the 2.5th and 97.5th percentiles of the generated values.

**Estimated Number of Microcephaly Cases**

The number of background microcephaly cases, $MC^B$, that is, the number of cases estimated to occur in the absence of the Zika outbreak, was assumed to have expected value

$$B \ast MC^B$$

where $MC^B$ is the background risk of having a live born child with microcephaly. A realization for $MC^B$ was sampled from an assumed uncertainty distribution for this parameter given in Table 1 for each Monte Carlo simulation. Realizations for the background number of microcephaly cases were then generated under the assumption that

$$MC^B \sim \text{Bin}(B, MC^B)$$

Let $MC^B_1, MC^B_2, \text{ and } MC^B_3$ be realizations for the risk of microcephaly given maternal Zika infection in trimester 1, 2 or 3 drawn from the uncertainty distributions for these parameters listed in Table 1. Given a sampled value for the trimester-specific number of infected pregnant women, $T_I$, the estimated microcephaly case counts associated with the Zika outbreak, $MC^Z_1, j = 1, 2, 3$, were generated under the assumption that

$$MC^Z_1 \sim \text{Bin}( T_I, MC^B_1)$$

The estimated total number of Zika-related microcephaly cases was generated by summing the trimester-specific estimated case counts. Finally, the total number of microcephaly cases was estimated as the sum of the background and Zika-related case count estimates.