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ESTIMATING SEROTYPE-SPECIFIC DENGUE VIRUS FORCE OF INFECTION AND TEMPORARY CROSS IMMUNITY USING LONGITUDINAL SEROLOGICAL DATA

Bobby Reiner[1]

[1]School of Public Health, Indiana University, USA

rcreiner@indiana.edu

ABSTRACT

Dengue, which is caused by any of four related but antigenically distinct virus serotypes, has increased its incidence and geographic range considerably in the past 50 years. The utility of disease models for planning public health interventions and policy relies on accurate estimates of key transmission parameters. Infection with a DENV serotype induces lifelong immunity to that serotype and a short-term, temporary cross-immunity (TCI) to the other serotypes. Despite a century of research, the strength and duration of TCI remains uncertain because it is difficult to estimate using disease surveillance data. Further, the inherent difficulty in quantifying the absence of infections is confounded by poor estimates of the background risk of infection, or force of infection (FoI). Using a 12-year longitudinal DENV dataset from Iquitos, Peru we simultaneously estimate serotype-specific, time-varying FoIs as well as serotype/serotype-specific strength and durations of TCI in an endemic population. The dataset contained information on 14,335 individuals (38,416 total samples) and 23,989 serotype-specific DENV infections. Of these, 3,854 occurred during the study period, which enabled estimation of when the infections took place. Considered independently and depending on year and serotype, yearly force of infection varied from 0 to 0.33. We identified periods of synchronization between serotypes, but there was no consistent pattern in which serotypes experienced simultaneous outbreaks.

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As an extension of our approach we calculated time-varying serotype-specific estimates of the basic reproductive number (R0)for DENV, which varied from less than 1 to 5.43, depending on year and serotype. For TCI, we found considerable variation in both the duration and strength of protection, with some serotype combinations conferring essentially no protection, while others providing relatively strong protection for months. Our results provide important new insights into DENV transmission dynamics that will inform implementation of vector management strategies, interpretation of vaccine trial infection data as well as future deployment of vaccines when they become available.

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