

**Project Title:** Rapid Seroincidence and Syndromic Surveillance for Dengue and Norovirus in Latin America

**Background and Rationale:**

Dengue virus (DENV) and Norovirus (NoV) are two of the most significant pathogens in the developing world, with 100 million cases of dengue fever and 2 million cases of norovirus acute gastroenteritis (AGE) every year.<sup>1-3</sup> With treatment limited to supportive measures only, vaccines offer the most important intervention for reducing disease. Despite the potential benefits of vaccines, several important gaps remain in assessing their efficacy and effectiveness. To address these gaps, we propose a study to validate two surveillance strategies and characterize local epidemiology for both DENV and NoV.

Dengue and norovirus vaccine studies need accurate epidemiologic data in order to measure vaccine efficacy. These studies also need to be undertaken in areas with high rates of DENV and NoV infection and disease, which will allow a smaller sampling population to detect a similar reduction in disease. Surveillance will be critical in identifying these study sites. The most commonly used surveillance methods have significant limitations. Prospective cohort studies with regular serologic testing are the most accurate, but also require significant resources. Sentinel surveillance, where enrolled participants present to a health facility for symptomatic disease, are less costly, but miss the majority of infections, which are mild or asymptomatic. New surveillance strategies are needed that are both accurate and cost-effective.

Currently, there are limited data on incidence rates of asymptomatic DENV and NoV infection, especially in Latin America. Limited prospective cohort studies have found high rates of asymptomatic infection,<sup>4-7</sup> and data from cluster surveillance during outbreaks were similar. (CDC-Dengue Branch)<sup>8-11</sup> While less relevant from a clinical standpoint, asymptomatic DENV and NoV infections have significant implications for vaccine efficacy and effectiveness, including herd protection, and will be an important secondary outcome in Phase 3 trials.

**To address these gaps**, we propose the development of 2 surveillance platforms that may allow accurate estimates of infection *and* disease without significant infrastructure are household cluster surveys and participatory syndromic surveillance. The Centers for Disease Control and Prevention (CDC) has used satellite mapping and household cluster surveys to measure DENV incidence in outbreak settings. This strategy was successfully utilized in several recent outbreaks,<sup>8,13,14</sup> leading to a rapid assessment of DENV seroincidence in various communities, including both recent and current infections. For NoV, household surveillance has recently been utilized among a prospective cohort of infants in Peru,<sup>6</sup> but rapid household cluster surveys have not been reported.

Participatory syndromic surveillance (PSS) is a novel surveillance method that uses modern communication technology (text messaging, email) to identify syndromic illnesses in a community, such as acute febrile illness (AFI) or acute gastroenteritis (AGE). PSS is a major component of AGE and NoV surveillance in developed countries,<sup>15-17</sup> including both outbreak<sup>18</sup> and routine<sup>19-21</sup> surveillance. PSS systems have not been widely utilized in low resource settings where infrastructure is limited.

Household cluster surveys and PSS could be used to rapidly assess DENV and NoV incidence in areas lacking surveillance infrastructure and to obtain valuable baseline data on the Phase 3 dengue and norovirus vaccine study site populations.