

Supplementary Methods S4

The laboratory dengue diagnosis was performed as previously described [15]. Briefly, a dengue-confirmed case was diagnosed by NS1 antigen detection using a capture ELISA assay [27] and/or SD BIOLINE Dengue NS1 antigen rapid test (Abbott Diagnostics, Lake Forest, IL, USA) according to the manufacturer's instructions and/or by RT-qPCR on the plasma sample obtained at admission [28]. Acute samples from the original dataset were also tested by qRT-PCR for the Chikungunya virus (CHIKV), which was circulating at that time in Cambodia [29]. Serological tests were performed on sera collected during the acute and convalescent phases of the infection for detection of antibodies against dengue virus (DENV), Japanese encephalitis virus (JEV), and Chikungunya virus (CHIKV), using an in-house IgM capture ELISA (MAC-ELISA) [30]. An IgM seroconversion against DENV, with no JEV cross-reactivity in paired acute and convalescent sera was considered as a dengue-confirmed case. Detection of dengue IgM antibodies with no JEV cross-reactivity in both serum samples, suggested a presumptive diagnosis of recent dengue infection. Moreover, detection of dengue IgM antibodies with JEV cross-reactivity in both serum samples, suggested a presumptive diagnosis of recent flavivirus infection. Within the epidemiological context of the dengue season, we considered this serological pattern presumptive of recent dengue infection as well.

Classification as SD or non-SD patient for acute or recent dengue cases was performed according to the WHO 2009 criteria using clinical, biological and ultrasound data recorded at admission, defervescence, and discharge [2] as previously described [15]. Briefly, we adapted the WHO 2009 classification by using ultrasound, which gave us the opportunity to semi-quantify the degree of fluid accumulation, providing a more accurate clinical diagnosis in

discriminating between DWWS and severe dengue (SD): (i) a minimal amount of liquid was considered as mild plasma leakage, i.e., a warning sign (DWWS); (ii) moderate or abundant amounts of liquid were considered as severe dengue, possibly leading to aggravation with respiratory distress (SD). This classification was applied after the final assessment using all available biological and clinical information [15].