1. The rationale for conducting the meta-analysis.
2. The contribution that the meta-analysis makes to knowledge in light of previously published related reports, including other meta-analyses and systematic reviews.

Numerous studies (Kelley, Kaufusi, & Nerurkar, 2012; Reis et al., 2007; Seet et al.; Tay & Tan, 2006) and reviews (Chaturvedi et al. 2000; Huy et al. 2013; John, Lin, and Perng 2015; Page and Liles 2013; Yacoub et al. 2014) were conducted to propose potential severity biomarkers and timing of peak response. Nevertheless, one of the major hindrances of this effort is the inconsistency of results caused by heterogeneity among the studies. Level of biomarkers were found to be affected by factors such as timing of sample collection, processing of samples into plasma or serum, WHO classification method used to assign the disease’s severity, host’s immune status, and dengue serotypes (Srikiatkhachorn & Green, 2010). Therefore, this study aims to identify potential severity biomarkers and to study the factors causing inconsistency.

This study fills the gap in literature by performing meta-analysis on difference in levels of 53 biomarkers between healthy control, dengue fever and severe dengue infection in humans. Timing of sample collection in context of days of onset of fever was recorded with detailed subgroup analyses of (1) 1997 and 2009 WHO classifications, (2) plasma and serum samples, (3) patients’ antibody dependent enhancement status in context of dengue infection (primary and secondary infections) and (4) dengue serotypes were carried out. The outcome allows the identification of potential best severity biomarker and proposes the suitable timing to measure these severity markers.

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