

# Clinical efficacy, safety, and immunogenicity of a live attenuated tetravalent dengue vaccine (CYD-TDV) in children: A systematic review with meta-analysis

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## Abstract

© 2017 Malisheni, Khaiboullina, Rizvanov, Takah, Murewanhema and Bates. Background: Dengue hemorrhagic fever is the leading cause of hospitalization and death in children living in Asia and Latin America. There is an urgent need for an effective and safe dengue vaccine to reduce morbidity and mortality in this high-risk population given the lack of dengue specific treatment at present. This review aims to determine the efficacy, safety, and immunogenicity of CYD-TDV vaccine in children. Methods: This is a systematic review including meta-analysis of randomized controlled clinical trial data from Embase, Medline, the Cochrane Library, Web of Science, and ClinicalTrials.gov. Studies that assessed CYD-TDV vaccine efficacy [(1 - RR)\*100], safety (RR), and immunogenicity (weighted mean difference) in children were included in this study. Random effects model was employed to analyze patient-level data extracted from primary studies. Results: The overall efficacy of CYD-TDV vaccine was 54% (40-64), while serotype-specific efficacy was 77% (66-85) for DENV4, 75% (65-82) for DENV3, 50% (36-61) for DENV1, and 34% (14-49) for DENV 2 . 15% (-174-74) vaccine efficacy was obtained for the unknown serotype. Meta-analysis of included studies with longer follow-up time (25 months) revealed that CYD-TDV vaccine significantly increased the risk of injection site reactions (RR = 1.1: 1.04-1.17; p-value = 0.001). Immunogenicity (expressed as geometric mean titers) in descending order was 439.7 (331.7-547.7), 323 (247 - 398.7), 144.1 (117.9-170.2), and 105 (88.7-122.8) for DENV3, DENV 2 , DENV1, and DENV4, respectively. Conclusion: CYD-TDV vaccine is effective and immunogenic in children overall. Reduced efficacy of CYD-TDV vaccine against DENV 2 notoriously known for causing severe dengue infection and dengue outbreaks cause for serious concern. Post hoc meta-analysis of long-term follow-up data ( $\geq 25$  months) from children previously vaccinated with CYD-TDV vaccine is needed to make a conclusion regarding CYD-TDV vaccine safety in children. However, CYD-TDV vaccine should be considered for use in regions where DENV 2 is not endemic as currently there is no specific treatment for dengue infection.

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## Keywords

CYD-TDV, Dengue hemorrhagic fever, Dengue shock syndrome, Dengue virus, Efficacy, Immunogenicity, Safety

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