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DENGVAXIA: AGE AS SURROGATE FOR SEROSTATUS IN VACCINE INDUCED RISK

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Developed by Sanofi Pasteur, a tetravalent dengue vaccine, Dengvaxia, was recently recommended by the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) on Immunization, based partially on modeling results, to be used in countries with high dengue endemicity as evidenced by seroprevalence in the targeted age group of more than 50% (preferably 70%) [1].

Analyses of clinical trial data demonstrate that individuals who were seronegative (never infected with a dengue virus prior to vaccination) when vaccinated routinely develop non-protective dengue antibodies [2,3]. Surprisingly, despite high rates of overt disease among vaccinated seronegative persons, mathematical models of populations with a seroprevalence of 70% have estimated an overall reduction of dengue hospitalizations on the order of $10-30\%$ over a period of 30 years, with 80% vaccine coverage of 9 year-olds [1,4]. More recently, modelers from Sanofi Pasteur have predicted that Dengvaxia, if given to 90% of 9-year-old children living in dengue endemic settings, can reduce disease burden significantly, ranging from 21% to 29% over 20 years [5]. It should be noted that accurate predictions in complex systems such as described in [4,5] can be only made for short periods of time. A 20-30-year prediction horizon puts in doubt the beneficial results of vaccine administration [6].

In this talk I will present an age structured model that was developed based on the WHO-SAGE recommendation to vaccinate persons age 9-45 years in dengue endemic countries. The model was used to explore the clinical burden of two vaccination strategies: 1) Vaccinate individuals, ages 9-45 years, seropositives and seronegatives, and 2) vaccinate individuals, ages 9-5 years, who are dengue immune only [7]. A sensitivity analysis of the proposed model will be discussed.

Our mathematical model finds that significant reduction of hospitalizations can be only achieved

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when vaccine is directed exclusively to seropositive individuals [7]. When using a more recent data set by age and serostatus from the combined CYD14, CYD15, CYD57 trials, as reported in Table 1 in Martinez-Vega et al. [8], we confirm statistically the vaccine induced risk in seronegative individuals [9].

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