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Cost-effectiveness analysis of dengue vaccination in the Philippines

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Background: From years 2001–2010, the Philippines ranked 4th among the ASEAN in annual average reported dengue episodes with 45,409 cases. The WHO aims to achieve 50% reduction in dengue mortality and 25% reduction in morbidity by 2020 through integrating vector control approaches with vaccine introduction. Dengue has yet to be prevented and 20 years of development has finally yielded a candidate vaccine that has reached Phase III efficacy clinical trials: Sanofi Pasteur's dengue vaccine, a recombinant, live, attenuated, tetravalent dengue vaccine (TDV).

Methods & Materials: This study aims to assess the cost-effectiveness of different dengue vaccination strategies in the Philippines from both a societal and a public payer's perspective. Coudeville and Garnett's (2012) dengue dynamic transmission model was populated using Philippine-specific dengue vector, epidemiology, and cost data from literature and records review which were validated through consultations with dengue experts from the field of family medicine, vaccine research, molecular biology, epidemiology, public health, entomology, and infectious diseases.

Results: Main results show that over a period of 5 years, conducting a school-based vaccination program targeting nine year-olds for routine vaccination decreases dengue cases and DALYs lost due to dengue relative to status quo by 24% and 26%, respectively. Expanding the vaccination to more children by adding age cohorts close to nine years such as 10 to 11, 10 to 13, 10 to 15, 10 to 17, and 10 to 20 translates to more DALYs averted and less dengue disease costs the government must shoulder.

Conclusion: Cost-effectiveness threshold prices following cost-effectiveness definition of less than or equal to 1x GDP per capita for the public payer and societal points of view are found to be 13 USD per dose and 24 USD per dose, respectively. This cost-effectiveness threshold set by the Philippines' Department of Health is more stringent than the WHO recommended cost-effectiveness thresholds.

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A poxvirus-based vaccine reduces virus excretion after MERS coronavirus infection in dromedary camels

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Background: The recently emerged Middle East syndrome coronavirus (MERS-CoV) can cause severe and fatal respiratory diseases in humans. Antibodies against MERS-CoV can be found in camels in the Middle East but also outside this region. The high prevalence of circulating MERS-CoV neutralizing antibodies in dromedary camels from different geographic regions may indicate wide circulation of MERS-CoV in camels. The ongoing MERS-CoV outbreak in the Middle East and the lack of treatment options or licensed vaccines is of great concern. Vaccination of camels could potentially prevent the spread of this virus.

Methods & Materials: We vaccinated 4 dromedary camels twice with a 4 week interval with 10⁸ PFU MVA-S via both nostrils and intramuscularly. Four control animals received non-recombinant MVA (n=2) or PBS (n=2). Three weeks post-boost, all animals were tested for presence specific antibody responses by MERS-CoV ELSA and virus neutralization assay (VNT). Next, all camels were challenged with a high dose of MERS-CoV and to study the pathological changes, two animals per groups were euthanized and necropsies were performed at day 4 and 14 pi. The antibody response, and pathology were analysed by MERS-CoV-S or MVA ELISAs, -VNTs, qRT-PCR, virus titration, immunohistochemistry (IHC) and *in situ* hybridization (ISH).

Results: All vaccinated animal developed detectable serum neutralizing MERS-CoV or MVA specific antibody titers 3 weeks post boost vaccination. No clinical signs were observed in MVA-S vaccinated animals but mild clinical sign and a runny nose were observed in control-vaccinated animals after virus challenge. Interestingly, significant reduction of infectious virus excreted and viral RNA transcripts in the vaccinated animals nose after MERS-CoV challenge was observed as compared with control animals, and these protection correlated with presence of neutralizing antibody to MERS-CoV. In addition, in the nose of MVA-S vaccinated animals at day 4 pi, a few MERS-CoV infected cells were detected by IHC and ISH as compared with control camels. Interestingly, sera from MVA-S vaccinated animals cross neutralized camelpox virus.



Conclusion: Our results demonstrate that vaccination of camels with MVA-S confers protection against MERS-CoV infection. In addition, induction of MVA specific antibody cross neutralize camelpox virus, suggesting that MVA-MERS-S can be used as a dual vaccine in dromedary camels.

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Integrated analysis of immunogenicity data from 11 dengue vaccine trials across 14 countries at risk for dengue



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Background: Dengue is a mosquito-borne viral infection with a very rapid global expansion during the last 50 years. This disease has become an important public health problem in Asia and Latin America with over half the world's population at risk¹. Sanofi Pasteur is developing a recombinant, live, attenuated, tetravalent dengue vaccine (CYD-TDV) for countries at-risk of dengue². The results from CYD-TDV trials are useful to observe the trends in immunogenicity (GMT) titres across various countries.

OBJECTIVES: To assess immunogenicity titres after 3 doses of CYD dengue vaccine in children, adolescents and adults up to 60 years by revisiting pre- and post-vaccination GMTs from Sanofi Pasteur CYD-TDV trials.

Methods & Materials: Dengue neutralizing antibody (Ab) levels were assessed by a plaque neutralization test with a 50% endpoint (PRNT50) for each serotype. In total, 25 clinical studies from Phase I to Phase III have been included in the clinical development plan. Of these 25 clinical studies, the integrated immunogenicity analysis presented here is based on results from 11 trials conducted in 8 Asian countries (Philippines, Indonesia, Malaysia, Vietnam, Thailand, Singapore, Australia, and India) and 6 Latin American countries (Brazil, Colombia, Honduras, Mexico, Peru, and Puerto Rico).

Results: Immune titres increased after 3 doses from baseline, and higher GMTs were observed with increasing age and endemicity in all countries considered at-risk of dengue. Further exploration in older adults in Australia³ vaccinated with 3 doses of CYD-TDV, revealed that both the 18-60 age group (N=655) and the 46-60 age group (N=241) had similar GMTs which were higher than baseline.

Conclusion: Integrated analysis from CYD-TDV trials in children, adolescents and adults up to 60 years of age showed a consistent finding of higher GMTs in the vaccinated arm versus control arm. Subjects who received 3 doses of CYD-TDV elicited a balanced immune response against all four serotypes.

References: WHO Dengue factsheet No. 117 (updated May 2015) Guy B and al., Vaccine, 2011 Toressi et al, Vaccine, 2015

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Preliminary immunoinformatics research for prediction the most immunogenic linear and conformational B-cell epitopes of 14-3-3 antigen in echinococcus granulosus



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Background: Cystic Echinococcosis (CE) is one of the most important zoonosis parasite diseases which caused by the larval stage of Echinococcus granulosus (Eg). The Eg14-3-3 protein is a vaccine candidate antigen which exists in different development stages of E. granulosus. The basement of vaccine design strategies is identification the most efficacious epitopes of the antigen. This study presents linear and conformational B cell epitopes of the Eg14-3-3 antigen via computational tools.

Methods & Materials: The protoscoleces (PSC) of E. granulosus was aspirated from infected lungs and livers of slaughtered sheep (Tabriz, Iran) and then DNA samples were extracted. The polymerase chain reaction (PCR) was performed using specific primers (forward: ATGTCTCTCTCAGTAAGCGCGA and reverse: ATCGGCTTTCGGCGGTTTCAG) and basing on the sequence in GenBank (Access No. AY942149). After sequencing the PCR products, our regional Eg14-3-3 sequence was utilized (the sequence of our local Eg14-3-3 shall be published soon). The linear B-cell epitopes were predicted by Bepipred Linear Epitope Prediction algorithm with threshold 0.35. The conformational B-cell epitopes were predicted using a sequence-based server named CBTOPE which uses the support vector machine (SVM) threshold -0.3, and also the three dimensional (3D) properties of the antigen such as, Relative Solvent Accessibility, Number of Transmembrane Domains and protein tertiary structure prediction. The structural details of Eg14-3-3 which are usable in the epitope-based vaccine design evaluated via SCRATCH Protein Predictor.

Results: The Best linear B-cell epitopes were selected based on their length (<9 amino acids) and score (highest), so that the high scales consist of ATEVAEGDMQIT, DTLPEESYK, EQKHDG-DAK and TGDERKQASDN. Based on CBTOPE algorithm five high