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Cost-Effectiveness Analysis of Pneumococcal Vaccination with the Pneumococcal Polysaccharide NTHi Protein D Conjugate Vaccine in the Philippines

Xu-Hao Zhang, PhD[1,], Maria Carmen Nievera, MD[2], Josefina Carlos, MD[3], Marilla Lucero, MD, PhD[4], Gyneth Bibera, MD[2], Maria Isabel Atienza, MD[5], Oleksandr Topachevskyi, PGDip[6], Cecilia Gretchen Navarro-Locsin, MD[5]*

[1]*GlaxoSmithKline Vaccines, Singapore;* [2]*GlaxoSmithKline Vaccines, Makati City, Philippines;* [3]*University of the East Ramon Magsaysay Memorial Medical Centre, Quezon City, Philippines;* [4]*Research Institute for Tropical Medicine, Muntinlupa City, Philippines;* [5]*St. Luke's Medical Centre, Quezon City, Philippines;* [6]*GlaxoSmithKline Vaccines, Wavre, Belgium*

ABSTRACT

Objectives: To compare the cost-effectiveness of a universal mass vaccination (UMV) program with a 2 + 1 schedule of a 10-valent pneumococcal polysaccharide nontypeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV) against two strategies: 1) a no-vaccination strategy and 2) a pneumococcal 13-valent conjugate vaccine (PCV13) 2 + 1 strategy in the Philippines. **Methods:** A published Markov cohort model was adapted to simulate the epidemiological and economic burden of pneumococcal diseases (meningitis, bacteremia, pneumonia, and acute otitis media) within a projected birth cohort in 2012 of 1,812,137 newborns over lifetime. Analyses were conducted at an annual discount rate of 5% from the perspective of the Philippine government. The current evaluation was updated with the best available local/regional clinical epidemiological data and published efficacy evidence. **Results:** Compared with the no-vaccination strategy, the PHiD-CV 2 + 1 UMV program was projected to prevent 3,343 deaths due to invasive pneumococcal diseases and pneumonia and 326,862 cases of pneumococcal diseases, resulting in an incremental cost-effectiveness ratio of 50,913 pesos/quality-adjusted life-year gained, which was considered to be highly cost-effective according to the threshold recommended by the World Health Organization. In comparison with the PCV13 2 + 1 strategy, the PHiD-CV 2 + 1 strategy was estimated to have a substantial reduction in acute otitis media (127,680 cases) and therefore a cost saving of potential 92.5 million pesos assuming price parity between PHiD-CV and PCV13 (US $1 = 42.13 pesos in 2012). **Conclusions:** The PHiD-CV 2 + 1 UMV program is projected to be cost-effective, compared with no vaccination, and would provide substantial savings with higher quality-adjusted life-year gains as compared with the PCV13 2 + 1 strategy in the context of the Philippines.

Keywords: cost-effectiveness, PCV13, PHiD-CV, Philippines, vaccination.

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Background

The World Health Organization (WHO) estimated that 1.6 million people die every year from invasive pneumococcal diseases (IPDs), and an estimated 0.7 to 1 million of these are children younger than 5 years [1]. A study conducted in the Philippines showed that the peak incidence of IPDs is in children younger than 4 years. The same study estimated that one third of the children younger than 5 years with IPD would die [2].

Acute otitis media (AOM) is also a significant, although largely underestimated, public health burden among Filipino children. There is a paucity of good surveillance data regarding the extent of the burden of otitis media (OM) and/or AOM in Filipino children. A local study indicated that up to 25% of the children with pneumonia had concomitant OM [3]. In a recent national survey, the overall prevalence of clinically diagnosed AOM in children aged 0 to 12 years in the Philippines was estimated at 9.57%, with the 0 to 2 years age group having the most prevalent cases of AOM in the sample [4]. This prevalence rate is considered as high on the basis of the WHO classification for the prevalence of OM [5].

At present, two types of pneumococcal conjugate vaccines are available for use in children in the Philippines market. These are Synflorix™ (GlaxoSmithKline, Rixensart, Belgium), a pneumococcal polysaccharide and nontypeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV) and Prevnar 13™ (Wyeth LLC, Madison, NJ, now part of Pfizer, Inc.), a pneumococcal 13-valent conjugate vaccine (PCV13). Both vaccines are licensed locally as a 2 + 1

Conflicts of interest: X. Zhang, M.C. Nievera, and O. Topachevskyi are employees of the GlaxoSmithKline group of companies. C.G. Navarro-Locsin has served as a speaker, an advisory board member, and a primary investigator for GlaxoSmithKline. G. Bibera is currently an employee of GlaxoSmithKline, but at the time of the study conduct and manuscript development, she was an employee of the Santa Ana Hospital. All the other authors declare that they have no competing interests.

* *Address correspondence to:* Xu-Hao Zhang, GlaxoSmithKline Vaccines, 150 Beach Road, #22-00, Singapore 189720.

E-mail: sharon.x.zhang@gsk.com.

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scheme in the Philippines for the active immunization of infants and children aged 6 weeks to 5 years against disease caused by *Streptococcus pneumoniae* (including meningitis, sepsis, bacteremia, pneumonia, and AOM) [6,7]. In addition, PHiD-CV is also licensed for use against OM caused by nontypeable *Haemophilus influenzae* (NTHi) and licensed for use in preterm infants [6].

Health economics has been increasingly incorporated into the comprehensive health technology assessment for formulary and vaccine policy decision making over the past decade. Published results from other countries might not be directly transferable because of the sensitivity of key local data inputs such as epidemiology, local treatment patterns, or prices [8].

The purpose of this study was to evaluate the epidemiological and economic consequences of pneumococcal conjugate vaccine(s) for a universal mass vaccination (UMV) program in addition to the current standard of care for pneumococcal diseases in the Philippines in 2012, using an adapted Markov cohort model. The two analyses presented in this article compared the cost-effectiveness of a UMV program with PHiD-CV 2 + 1 versus no vaccination, and that of PHiD-CV 2 + 1 versus PCV13, in the Philippines. The same model has been adapted for analyses in a number of different countries such as Norway and Sweden [9,10].

Methods

Markov Cohort Model

A published Markov cohort model was adapted to simulate the epidemiological burden of pneumococcal and NTHi-related diseases, including IPDs, community-acquired pneumonia (CAP), and AOM, within a projected registered live birth cohort of 1,812,137 newborns in the Philippines in 2012 [11,12]. Cohort-based analyses represent one of the most common forms of health economic modeling and are particularly useful for determining the direct effect of medical interventions [13].

In the Markov cohort model, the individuals of the birth cohort move between the Markov states, as shown in Figure. 1, according to estimated transition probabilities derived from the published incidence rates, over a projection of lifetime horizon. The model has a number of mutually exclusive disease-related outcomes, including meningitis, bacteremia, CAP, AOM, no pneumococcal infection, and death. Costs and quality-adjusted life-year (QALY) specific to each health state were estimated and summarized over the cohort's lifetime to calculate total accumulated costs and QALYs. The incremental cost and QALY gained of the two different strategies were computed as an incremental cost-effectiveness ratio (ICER) for each set of comparison (PHiD-CV vs. no vaccination; PHiD-CV vs. PCV13). The WHO-recommended thresholds for ICER were adopted in the study: 1) cost-saving: if the strategy costs less and provides higher QALYs; 2) cost-effective: the ICER is below three times the gross domestic product (GDP) per capita of the country; 3) highly cost-effective: the ICER is below one time the GDP per capita of the country; and 4) not cost-effective: the ICER is more than three times the GDP per capita of the country (GDP per capita of the Philippines in 2011 = 103,366 pesos) [14]. It was assumed in the base-case scenario that 100% of the birth cohort would be vaccinated according to the 2 + 1 schedule (dose 1 at 6 weeks, dose 2 at 14 weeks, and dose 3 at 13 months). Finally, it was assumed that there was no herd effect for the UMV program of both vaccines in the base-case scenario.

Epidemiological Data

The birth cohort size of 2012 used in the analysis was 1,812,137, which was projected from the 2010 Field Health Service Information System report using a 1.9% population growth annually (National Statistics Office, Average population growth rate

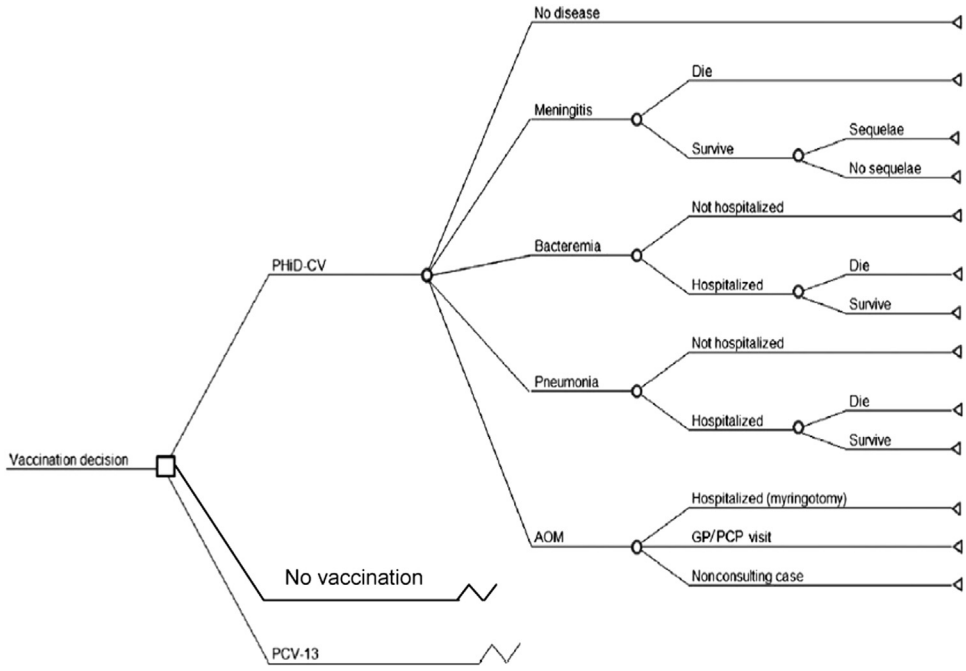

Fig. 1 – Markov cohort model design. The cohort model is Markov-based with three exclusive health states: no disease, sequelae, and death. The transition from "no disease" to "sequelae" or "death" is calculated on the basis of this decision tree. In the model, only meningitis can lead to long-term sequelae; meningitis and bacteremia include NTHi meningitis and NTHi bacteremia, respectively; and nonconsulting AOM are accounted for in the quality-of-life impact calculation. AOM, acute otitis media; GP, general practitioner; NTHi, nontypeable *Haemophilus influenzae*; PCP, primary care physician; PCV13, pneumococcal 13-valent conjugate vaccine; PHiD-CV, pneumococcal polysaccharide nontypeable *Haemophilus influenzae* protein D conjugate vaccine.

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