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Cost-effectiveness of pneumococcal conjugate vaccination in Croatia

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ABSTRACT

Objective: Pneumococcus is a known cause of meningitis, pneumonia, sepsis, and acute otitis media in children and adults globally. Two new vaccines for children have the potential to prevent illness, disability, and death, but these vaccines are expensive. The Croatian Ministry of Health has considered introducing the vaccine in the past, but requires economic evidence to ensure that the limited funds available for health care will be used in the most effective way.

Methodology: Croatia appointed a multidisciplinary team of experts to evaluate the cost-effectiveness of introducing pneumococcal conjugate vaccination (PCV) into the national routine child immunization program. Both 10-valent and 13-valent PCV (PCV10 and PCV13) were compared to a scenario assuming no vaccination. The TRIVAC decision-support model was used to estimate cost-effectiveness over the period 2014–2033. We used national evidence on demographics, pneumococcal disease incidence and mortality, the age distribution of disease in children, health service utilization, vaccine coverage, vaccine timeliness, and serotype coverage. Vaccine effectiveness was based on evidence from the scientific literature. Detailed health care costs were not available from the Croatian Institute for Health Insurance at the time of the analysis so assumptions and World Health Organization (WHO) estimates for Croatia were used. We assumed a three-dose primary vaccination schedule, and an initial price of US$ 30 per dose for PCV10 and US$ 35 per dose for PCV13. We ran univariate sensitivity analyses and multivariate scenario analyses.

Results: Either vaccine is estimated to prevent approximately 100 hospital admissions and one death each year in children younger than five in Croatia. Compared to no vaccine, the discounted cost-effectiveness of either vaccine is estimated to be around US$ 69,000–77,000 per disability-adjusted life-years (DALYs) averted over the period 2014–2033 (from the government or societal perspective). Only two alternative scenarios were borderline cost-effective (US$ per DALY averted less than 3 × GDP per capita of approximately US$ 40,000). The first was a scenario based primarily on the WHO 2008 pneumococcal disease burden estimates for Croatia. The second was a scenario that assumed a fairly dramatic drop in the price of the vaccine over the period. Both vaccines would need to be priced at approximately US$ 20 per dose or less to be considered cost-effective under base-case assumptions. PCV10 would be more cost-effective than PCV13 with base-case assumptions, but this is sensitive to the price of each vaccine.

Conclusion: Based on estimated health and economic benefits in children alone, PCV is unlikely to be cost-effective in Croatia. Both vaccines would need to be priced at less than US$ 20 per dose to be considered cost-effective for children. Further analyses should be conducted to estimate the health and economic burden of pneumococcal disease in older age groups, and to assess the influence on cost-effectiveness results when short-term and long-term indirect effects are included for older individuals. While there are important uncertainties around the price and effectiveness of both vaccines, our analysis suggests there is insufficient evidence to warrant a significant difference in the price of the two vaccines.

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1. Introduction

Vaccines used in the childhood immunization program in Croatia have been sequentially added since 1948, when BCG and diphtheria vaccines were introduced.

The program is mandatory and free of charge for children. Since 2010, vaccination against pneumococcal disease has been financed by the Croatian Institute for Health Insurance (CIHI) for some risk groups, e.g. bone marrow transplant. Three vaccines are used: 10- and 13-valent pneumococcal conjugate vaccines (PCV10 and PCV13), and a polysaccharide pneumococcal vaccine. Recommendations for the immunization program are based on criteria such as epidemiological data, availability of vaccines, vaccine characteristics, vaccine safety, and on other criteria such as public acceptance and affordability.

In the process of discussions at the national level about introducing new vaccines, the Croatian health system was offered assistance from the World Health Organization (WHO) and other ProVac International Working Group (IWG) partners to help evaluate the potential cost-effectiveness of adding PCV to the national immunization program. Two PCVs are licensed in Croatia, the 10-valent (PCV10) and the 13-valent (PCV13).

The National Immunization Technical Advisory Group (NITAG) recommended introducing PCV into the immunization program in 2011, but the decision has been postponed because the Ministry of Health (MoH) was not sure that the introduction of pneumococcal vaccine should be prioritized. The MoH requires economic evidence to ensure that the limited funds available for health care programs will be used in the most effective way. The results of this cost-effective analysis (CEA) will be used by the MoH to help make a more informed decision about whether introducing PCV would represent an appropriate allocation of funds. Another important study objective was to define the vaccine price required for PCV introduction to be cost-effective so that it can be used in negotiations with manufacturers and to help make an informed decision about choosing one of the two available PCVs. Because Croatia is a high-income country, it is not eligible to procure vaccines through UNICEF or any other mechanism, so it is particularly important to consider economic and financial evidence as well as clinical data when making a decision.

2. Methods

2.1. Model overview

The CEA was carried out using the TRIVAC vaccine impact and cost-effectiveness model, version 2.0. This is a static cohort model, developed in Microsoft Excel® by modelers from the London School of Hygiene and Tropical Medicine (LSHTM) for the Pan American Health Organization' ProVac Initiative [1]. The model includes the following parameters: demography, disease burden, health services utilization and costs, vaccination coverage, vaccine efficacy, and vaccination costs. Four syndromes were included: all-cause acute otitis media (AOM), pneumococcal pneumonia, pneumococcal meningitis, and pneumococcal non-pneumonia non-meningitis (NPNM). In this analysis, NPNM was used to refer to pneumococcal bacteremia/sepsis. The outcomes of the model include: number of pneumococcal disease cases averted due to the vaccine, deaths averted, costs of introducing PCV and costs prevented in health services if the vaccine was introduced as a result of cases of disease averted. The model also provides information on life-years saved and disability-adjusted life years (DALYs) averted through the lifetime of targeted cohorts. Numbers of deaths and life expectancy were used to calculate years of life lost (YLL) and numbers of cases, mean duration of illness and disability weights were used to calculate years of life with disability (YLD). Finally, the model provides a cost-effectiveness ratio which gives the cost in United States dollars (US$) per DALY averted.

For each alternative, CEA compares the relationship between health costs and benefits. This type of analysis does not explicitly take a sectoral perspective where the costs and effectiveness of all possible interventions are compared in order to select the mix that maximizes health for a given set of resource constraints. The estimated cost-effectiveness of a single proposed new intervention is compared either with the cost-effectiveness of a set of existing interventions reported in the literature or with a fixed-price cut-off point representing the assumed social willingness to pay for an additional unit of health [2]. The cost-effectiveness was determined by calculating the incremental net cost of the vaccination program (estimated as the total cost of the vaccination program less the costs saved from disease prevention) and dividing by the number of DALYs that would be averted by the vaccination program.

2.2. Analytic framework

This CEA compared the introduction of the PCV into the immunization program versus no introduction. The model was run twice, once for PCV10 and once for PCV13.

2014 was considered as the year of vaccine introduction and the model was used to estimate costs and effects for 20 successive birth cohorts of children vaccinated between 2014 and 2033. The primary outcome measure is the cost-effectiveness ratio (US$ per DALY averted), which is based on the total costs and benefits aggregated over the 20 cohorts. Both the governmental and societal cost perspectives were considered, with the latter also including household costs. Only the public health care system was considered; the private sector was not taken into account because all children in Croatia have access to health care with all costs covered through social security. Evaluated providers are social security clinics (for outpatient visits) and social security hospitals (mainly for inpatient admissions). For both vaccines, a schedule of three primary series doses (at 2, 4, and 6 months) and no booster dose was chosen. Procurement of administering syringes was not considered because PCV is presented as a prefilled syringe. Based on WHO recommendations, a discount rate of 3% was applied for both future health outcomes and future costs [2].

2.3. Demographic data

The demographic data required are number of live births per year, infant mortality rate, mortality in children under age 5, life expectancy at birth, and proportion of infant death before 1 month. These are used to estimate life-years at risk for each birth cohort between birth and age 5. For all inputs, national data were provided by the National Bureau of Statistics (Population Census 2001 and 2011) and by the Croatian National Institute for Public Health [3,4]. Demographic projections were estimated by scaling the United Nations population division projections to the Croatian data [5].

2.4. Disease burden data

(Table 1) Based on the number of reported inpatient- and outpatient-managed pneumonia cases, the annual number of all-cause pneumonia cases of children younger than 5 was estimated to be approximately 6000 [4]. The fraction of all-cause pneumonia due to pneumococcal is a contentious and uncertain parameter, and in Croatia, 95% of pneumonia cases reported through the mandatory notification system do not have a confirmed etiology. For the base case, and in accordance with previous WHO methods [7], we assumed that 8% of pneumonia cases were due to pneumococcal. This assumption was based on the percent of clinical