

COMMENTARY

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Post-GAVI sustainability of the *Haemophilus influenzae* type b vaccine program: The potential role of economic evaluation

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ABSTRACT

Haemophilus influenzae type b (Hib) can cause severe invasive diseases which are, however, preventable by vaccination. To increase access to Hib vaccine, GAVI – the Vaccine Alliance – has provided financial support for 73 lower income countries worldwide. At the same time, GAVI has been implementing its co-financing policy, requiring recipient countries to pay a portion of vaccine costs and to increase this amount over time. Starting in 2016, 5 countries will stop receiving GAVI funding and procure the vaccine themselves. Although the graduating countries have access to the UNICEF/GAVI tendered vaccine price for 5 more years, the uncertainty in market vaccine price may hamper the post-GAVI program sustainability. A possible increase in vaccine price would cause a significant burden on governmental budgets, discouraging countries to continue the program. As a special tool, economic evaluation (EE) can assist decision makers by identifying the maximum affordable vaccine price for countries to pay. Given that only 6 GAVI-eligible countries have such analyses published, more EEs are necessary to strengthen countries' commitment during this transition period. The information will also be useful for manufacturers to determine their pricing policy.

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Haemophilus influenzae type b (Hib) is an important cause of morbidity and mortality in children younger than 5 y of age. Hib can cause meningitis, pneumonia and other less frequent diseases such as epiglottitis, osteomyelitis and septicaemia.^{1,2} Globally, it was estimated in 2000 that 8.13 million illnesses and 371 thousand deaths in children were due to Hib.³ The disease burden was higher in less developed countries in Africa and Southeast Asia. Although Hib can be transmitted from person to person through close contact, it is preventable by vaccination. However, despite an early introduction among high income countries in the 1990s, Hib vaccine was not available in lower income countries until many years later. It was estimated that by 2003 only 8% of the eligible population in the poorest countries had received Hib vaccine.⁴

Facing this significant challenge, a global public-private partnership effort led to the establishment of the Vaccine Alliance, or GAVI, in 2000. With seed money from the Bill and Melinda Gates Foundation, GAVI works closely with the WHO, UNICEF, World Bank, governments of developing and industrialized countries and the pharmaceutical industry to create equitable access to vaccines for children. By 2014, the cumulative contribution to GAVI from all sources was US\$10.7 billion.⁵ GAVI has been supporting 11 life-saving vaccines with an estimated 7 million future deaths prevented by 2015. For 2016–2020, it is expected to save 5 to 6 million more lives.⁵

Hib vaccine is one of the first vaccines that GAVI supported. It is distributed in the form of a combination vaccine protecting against 5 different diseases: diphtheria, tetanus, pertussis, hepatitis B and Hib (called pentavalent vaccine). With GAVI support, Hib vaccine was first introduced in Guyana in 2001 and finally reached all 73 GAVI-eligible countries in 2014, with South Sudan being the last one. Within the past 15 years, 237 million children have received Hib vaccine and the coverage rate for the recommended 3 doses has increased to 57% in low income countries worldwide.⁵ The introduction of Hib vaccine has led to a remarkable decrease in all invasive Hib diseases, especially Hib meningitis.^{6–9}

The pentavalent vaccine is also one of GAVI-supported vaccines subject to the GAVI co-financing policy. In order to enhance financial sustainability and encourage a country's ownership of vaccination programs, GAVI formally issued its co-financing policy in 2008 and, after 2 revisions, the third version was implemented in January 2016.⁵ By asking recipient countries to co-finance a portion of the vaccine cost and to gradually increase this amount as a function of the country's Gross National Income (GNI), GAVI hopes to prepare them for the future phase-out of GAVI support. In the 2016 co-financing policy, low income countries (GNI ≤ US\$1,045) continue to co-finance US\$0.20/dose without any annual increase.¹⁰ Phase 1 countries (US\$1,045 < GNI ≤ US\$1,580) start at an amount equal to the proportion of total co-financing

contribution out of total costs for all co-financed vaccines in the previous year. From year 2, they will have to increase the co-financing amount by 15% each year. For phase 2 countries (GNI > US\$1,580), the co-financing amount in the first year will be 15% higher than that of the last year in phase 1. Thereafter, this amount will increase linearly and reach 100% of the projected vaccine price after 5 y. At that point a country will enter a fully self-financing stage in which it will no longer receive GAVI support but will have access to the UNICEF/GAVI tendered vaccine price for 5 more years.¹⁰ In 2015, there were 19 countries entering phase 2 and in 2016, 2 more countries will join this group. Five other countries, including Bhutan, Honduras, Mongolia, Sri Lanka and Ukraine, will “graduate” from GAVI funding in 2016.

Indeed, GAVI co-financing policy is a one-of-a-kind initiative in global health care finance. There is no doubt that it has contributed substantially to the goal of program sustainability and self-financing, improving countries’ ownership of vaccination programs.¹¹ However, this policy is not without certain challenges that may hamper its success. One of the biggest challenges is the uncertainty of the Hib vaccine price in the post-GAVI period. Theoretically, countries remain eligible for the UNICEF/GAVI tendered vaccine price 5 y after they become financially independent; however, many countries are already faced with a significant financial burden even at the current price. For example, Vietnam, a phase 2 country, will incur a 6-fold increase in their vaccine budget when they self-finance the Hib vaccine if the price is unchanged.¹² The burden on the government’s budget will be larger if the vaccine price increases.

So, what causes uncertainty in the market Hib vaccine price? The pentavalent vaccine containing a whole-cell pertussis (wP) component was developed for use primarily in GAVI countries. Suppliers do not profit from sales of this wP-pentavalent vaccine in high and middle income countries where the acellular pertussis containing vaccine is used instead. They have entered the market for the wP-pentavalent vaccine because of the large demand in lower income countries generated by GAVI support. The estimated total annual global market of the wP-pentavalent vaccine is 3 hundred million doses.¹³ The lower price of Hib vaccine is made possible due to this market security and GAVI negotiation. However, as GAVI support begins to end, GAVI’s share of the global market will decrease substantially to about 50% during the 2016-2020 period, and possibly lower after that.¹³ Without GAVI funding, the demand for wP-pentavalent vaccine is unpredictable. Although graduating countries have committed to self-fund or self-procure the vaccine, the program’s sustainability is dependent on their ability to mobilize internal sources of funding. At present, these countries have not yet demonstrated a wish to discontinue the program after GAVI support ends. However, the fact that there have been defaulters – countries who failed to comply with the co-financing policy – raises concerns about their real financial capacity.¹¹

One of GAVI’s market shaping goals for the Hib vaccine is to achieve a low, but sustainable vaccine price for both countries and manufacturers.¹³ While manufacturers determine price based on the balance of demand and supply and other economic factors, how can countries determine what price they can reasonably afford to pay? Economic evaluation (EE)

is a special tool which can be used to facilitate decision making in this situation. A full EE compares the costs and outcomes of competing health care alternatives.¹⁴ Depending on how outcomes are measured, full EEs are categorized as either cost-effectiveness, cost-utility or cost-benefit analyses. Sources for cost, measures of health outcomes, and analytical methods distinguish EE types. Traditional research relies on randomized controlled trials to predict the health benefit and the economic investment of certain health care programs. By contrast, EE can be conducted using decision-analytic models which allow synthesis of different data sources and long-term measurement of costs and outcomes. In addition, EE offers various methods including threshold, deterministic and probabilistic sensitivity analyses to assess uncertainties in results.¹⁴ These methods estimate possible changes in study outcomes as a function of changes in the values of input variables, e.g. a fluctuation in the birth cohort or the increasing price of the vaccine.

When GAVI support is available, low income countries pay a co-financing amount which is much lower than the actual market vaccine price. This is analogous to a co-insurance rate for private insurance for medical care. From the countries’ perspective, the vaccine is definitely cost-effective and they can easily accept its introduction. Once countries become financially independent and responsible for vaccine procurement, the vaccine price will impact their willingness to continue the program. Policy makers can then rely on EE to determine the value of Hib vaccine compared to other health care options, and decide whether to continue the program. With a country-specific willingness-to-pay for an additional unit of outcome, sensitivity analyses can be used to estimate the maximum price above which Hib vaccine is no longer cost-effective. This is extremely important in lower income countries which have very limited resources and various competing priorities. Such information is also useful for manufacturers to determine their pricing policy. If they want to maintain a high demand, they would not increase vaccine price more than what most countries are willing to pay.

To date, most EEs of Hib vaccine programs have confirmed their cost-effectiveness.¹⁵ However, EEs of Hib vaccine have not been conducted widely in GAVI eligible countries. We conducted a PubMed literature search using key words “*Haemophilus influenzae*” and “cost effectiveness” or “cost benefit” or “economic” and “country name” for each of the 73 countries receiving GAVI support for Hib vaccine. There have been only 6 countries for which there are published analyses – India, Indonesia, Kenya, Somalia, Uzbekistan and Vietnam,^{12,16-22} and 2 studies conducted at the regional level.^{23,24} This search revealed a scarcity of such useful analyses in countries where they are needed the most.

In summary, GAVI has substantially improved health equity through providing support for new and underused vaccines, including Hib vaccine, to lower income countries. As countries gradually take financial responsibility for vaccine purchases in the years to come, different mechanisms are required to ensure their affordability and sustainability. In addition, scientific evidence is necessary to reinforce countries’ commitment during this transition. Specifically, EE can demonstrate whether a given health care program is worth the investment. Therefore, more country-specific economic evaluations of Hib vaccine

programs among GAVI recipients are needed. This will assist both vaccine manufacturers and country-level decision makers in determining an acceptable vaccine price threshold, which is a key to post-GAVI program sustainability.

Disclaimer

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