Making Cervical Cancer Vaccines Widely Available in Developing Countries: Cost and Financing Issues

Two new vaccines against the most dangerous strains of the human papillomavirus (HPV), the sexually transmitted virus that causes cervical cancer, have recently come onto the market. They have the potential to significantly reduce the global burden of this disease and alleviate suffering for millions of women and their families.

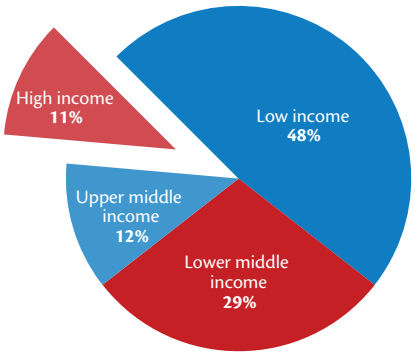
In order for these vaccines to be widely available to women and girls in resource-poor settings, issues of vaccine cost and financing need to be resolved. How will the vaccine be priced and how much will it cost to deliver it to the girls and young women who can benefit? How will they, or their governments, be able to afford the vaccine? Which institutions or funding mechanisms might be able to help?

To help answer these questions, the International AIDS Vaccine Initiative (IAVI) and PATH undertook a study of HPV vaccine costs and financing. This brief summarizes the main findings of the longer research paper.[1]

Background

The disease. In 2005, there were almost 260,000 deaths from cervical cancer and more than 500,000 new cases worldwide. The great majority of these new cases occurred in developing countries (Figure 1), where cervical cancer is the number one cause of cancer-related deaths among women. Women in developing countries are at greater risk of death from cervical cancer primarily because few have access to the screening and treatment services that have greatly reduced mortality in the industrialized world over the past four decades. About 75% of women in industrialized countries have been screened for cervical cancer in the previous five years, compared to less than 5% in developing countries.

Figure 1. Cervical cancer cases by country income category



The vaccines. GlaxoSmithKline's (GSK's) Cervarix® and Merck's Gardasil® are both nearly 100% effective in preventing cancer of the cervix due to the two HPV subtypes (16 and 18) responsible for about 70% of cervical cancer. Both vaccines currently require three doses. New HPV vaccines are under development that could require fewer doses and be cheaper, easier to deliver, or effective against more viral subtypes than the current vaccines, although none is expected to be available for a decade or so.

Delivering HPV vaccines will be challenging in developing countries, especially where health infrastructure is weak. Although most countries have established systems for vaccinating infants, few have much experience with immunization programs for adolescents. HPV vaccines will be offered first to preadolescent girls in most settings because the risk of exposure to the virus begins with sexual debut and it is not known if girls vaccinated in infancy would still be protected in adolescence and adulthood. (Data from clinical trials to date suggest that protection lasts at least five years.) Moreover, clinical trials have not been conducted in infants. Countries will have to reach girls with the required three doses through schools, clinics, mobile campaigns, or other novel strategies. Additional delivery challenges include insufficient cold chain and storage capacity at the national and local levels. Since awareness of cervical cancer is generally low, communities and key stakeholders will have to be mobilized in support of prevention strategies, including HPV vaccination. PATH, an international NGO, is organizing vaccine delivery demonstration projects in India, Peru, Uganda, and Viet Nam. This research will provide lessons to guide decision making and program planning.

How Much Will it Cost?

Merck has announced a private-sector price of US$ 120 per dose in the United States (U.S.) for Gardasil® and similar or higher prices in other industrialized countries. Even with a discount for the public sector, the HPV vaccine is the most expensive offered through the U.S. Centers for Disease Control and Prevention's Vaccines for Children Program. GSK's Cervarix® is also expensive and GSK has matched Merck's price in some countries. In the United Kingdom the private prescription price of both vaccines is £ 240 (US$ 490) for the three-dose

[1] International AIDS Vaccine Initiative & PATH (2007): *HPV Vaccine Adoption in Developing Countries: Cost and Financing Issues.* Available at http://www.iavi.org/HPVfinancing or at www.path.org/publications. This brief and the complementary report were made possible by a generous grant from the Hewlett Foundation, with additional assistance from the United States Agency for International Development (USAID).

series. Despite concerns over the affordability and cost-effectiveness of the vaccine at these prices, governments and insurers in at least 13 industrialized countries had decided to pay for it as of December 2007.

In developing countries, where the majority of those who would benefit from HPV vaccination reside, prices of above US$ 100 per dose would make the vaccine too expensive for virtually all governments to purchase and would put it out of reach of all but the wealthiest families. Both GSK and Merck have pledged to offer their vaccines to these countries at significantly reduced prices, but these prices have not yet been announced. In addition, common or "pooled" procurement on the basis of competitive bidding, conducted by the Pan American Health Organization (PAHO) Revolving Fund on behalf of its member countries and by UNICEF on behalf of a broader set of developing countries, has helped to reduce prices of other vaccines and could help to make HPV vaccines more affordable. In recent years the GAVI Alliance, a public-private partnership dedicated to strengthening and expanding immunization services in the poorest countries and an important source of external funding for vaccines (further discussed later in this brief), has worked closely with UNICEF to secure vaccines at affordable prices for low- and lower-middle-income countries.

But even at reduced prices, HPV vaccines will be significantly more expensive than the standard childhood vaccines, which cost pennies a dose, and may cost more than "underused" vaccines like *Haemophilus influenzae* type b (Hib) vaccine, which costs a few dollars per dose. And HPV will have to compete for scarce resources with new childhood vaccines against rotavirus diarrhea and pneumococcal disease, among others, thereby compounding the financing challenge.

Over the long run, prices can be expected to fall as vaccine demand grows, more suppliers enter the market, and patents expire. It will be critical, however, to shorten the time it takes for the HPV vaccine to drop in price so that it can reach large-scale production and widespread adoption. This can be achieved in part by building confidence in demand for the vaccine, which in turn requires ensuring that adequate funding will be available. Demand projections will help clarify the picture.

In addition to vaccine purchase cost, countries and donors will have to consider the cost of delivering HPV vaccines, which will include investments in cold-chain and storage capacity and costs associated with reaching adolescents who do not traditionally have much contact with the health system. An analysis of childhood immunization programs in 27 countries estimated that immunizing a child fully with the six vaccines included in the World Health Organization's (WHO) Expanded Programme on Immunization costs on average US$ 17. However, the lack of existing programs to immunize adolescents makes it difficult to estimate exactly how much HPV vaccine delivery would cost. PATH's pilot introduction projects, which have begun immunizing children through schools in Peru and will start in Uganda and Viet Nam in 2008, should yield valuable cost information by early 2009.

In the absence of firm data on vaccine price and delivery costs, we tried to identify scenarios under which HPV vaccine might be unaffordable to developing-country governments (Table 1). Our analysis shows that in Brazil, a middle-income country, a program that immunized 80% of 11-year-old girls at US$ 15 per girl would cost nearly US$ 20 million annually, or 0.05% of the national health budget. In poorer countries such as India and Kenya, vaccinating this proportion of 11-year-old girls at this price would require nearly 2% of what the government is already spending for healthcare.

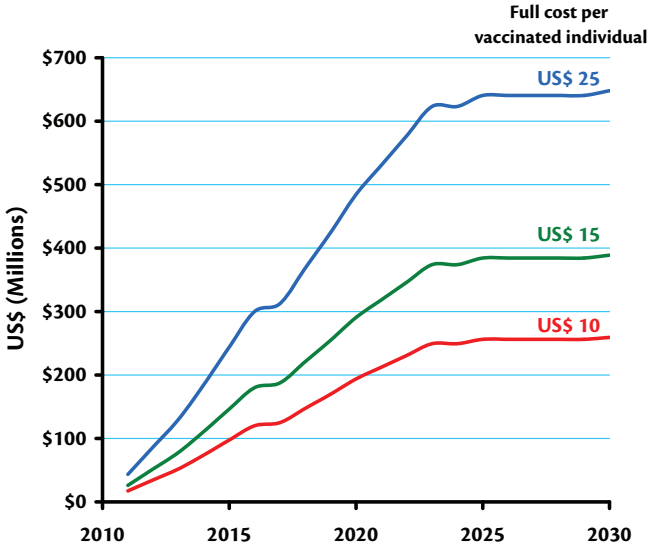
What would it cost to vaccinate this cohort of pre-adolescent girls in all low-income countries? Figure 2 suggests that, for the 72 countries eligible for GAVI funding, using the same average costs as in the previous table, total costs could eventually reach more than US$ 600 million a year. For comparison, GAVI projected spending between US$ 0.9-1.0 billion on all its programs in 2007.[2]

[2] CEO Report to GAVI Alliance Board Meeting. Annex 1. [Online] Available from http://www.gavialliance.org/resources/CEO_Report_Annexes.pdf. [Accessed on 2/29/08.]

Table 1. HPV Vaccination Cost Scenarios in Selected Countries

	If total cost per vaccinated girl were:		
	US$10	**US$15**	**US$25**
BRAZIL			
Total cost of reaching 80% of 11-year-old girls with HPV vaccine	13,043,200	19,564,800	32,608,000
HPV vaccination costs as share of public spending on health	0.03%	0.05%	0.09%
INDIA			
Total cost of reaching 80% of 11-year-old girls with HPV vaccine	83,553,600	125,330,400	208,884,000
HPV vaccination costs as share of public spending on health	1.26%	1.89%	3.16%
KENYA			
Total cost of reaching 80% of 11-year-old girls with HPV vaccine	3,352,000	5,028,000	8,380,000
HPV vaccination costs as share of public spending on health	1.09%	1.63%	2.72%

Figure 2. Full HPV Immunization Costs for GAVI Countries under Alternative Cost Assumptions



The graph assumes a six-year ramp-up to 80% coverage of a single-year cohort of adolescent girls and takes into account that some countries are likely to adopt the vaccine sooner than others. GAVI-eligible countries include all low-income countries and a few lower-middle-income countries.

Would HPV Vaccination Be Good "Value for Money"?

In deciding whether to adopt HPV vaccines, policy-makers faced with limited budgets will need to consider cost effectiveness as well as affordability. They will have to weigh the benefits of HPV vaccines against their costs and compare this benefit/cost ratio to those of other health interventions, including enhanced cervical cancer screening and treatment as well as other new vaccines. In developing countries, the primary benefit of HPV vaccination would be reduced cervical cancer mortality and morbidity, while in industrialized countries, where access to cervical cancer screening and treatment is widespread, much of the benefit would take the form of reductions in pre-cancer diagnosis and treatment costs.

Nine HPV vaccine cost-effectiveness studies have been published (as of the end of 2007); seven focused on industrialized countries and two on Brazil. All of these studies found that HPV vaccines can be cost-effective by conventional standards. In Brazil, however, cost effectiveness depends greatly on total vaccine cost; this in turn depends primarily on price, which is not yet known. In certain cost ranges, a combination of vaccination and cervical cancer screening is more cost-effective than either alone, demonstrating the continued importance of screening. There have been no studies to date focusing on low-income countries – such studies are urgently needed.

Who Will Pay?

Developing countries. Historically, immunizations have largely been paid for by governments, especially as vaccination has been viewed as a "public good" with widespread benefits that extend beyond the vaccinated individual. But in low-income countries, where government health budgets are as low as US$ 2-12 per person per year, donors already pay about two-thirds of childhood immunization costs. As Table 1 illustrates, low-income and many middle-income countries will find it difficult to finance the HPV vaccine without external assistance.

GAVI. The GAVI Alliance, founded in 2000, is now the largest source of external financing for vaccines for developing countries. GAVI has recently been strengthened by an important new financing mechanism, the International Finance Facility for Immunisation, which allows GAVI to frontload expenditure on vaccine purchase and delivery by borrowing from the capital markets on the basis of long-term pledges of support from donors.

Countries with a gross national income of less than US$ 1000 per capita in 2003 qualify to receive GAVI funding. Since about 54% of cervical cancer cases occur in GAVI-eligible countries, the GAVI Alliance could play a critical role in accelerating the adoption of the HPV vaccine. But GAVI must first agree to finance the purchase of HPV vaccines and eligible countries must apply for GAVI funding. In addition, countries will have to contribute up to US$ 0.30 per dose, depending on national income.

GAVI has used an investment case framework to decide whether to fund new vaccines. In the future, it appears that the HPV vaccine will be considered alongside other new vaccines about to enter the market or on the horizon. If GAVI approves HPV vaccines, it could become an important source of financing for many countries in Africa, Asia, and parts of Latin America.

In advance of a GAVI decision on funding for HPV vaccine purchase, countries can apply to GAVI for immunization system strengthening funds, which could be used to prepare the infrastructure for HPV vaccine delivery. Even with GAVI funding in hand, however, countries will need to consider whether they will be able to afford the HPV vaccine co-pay and whether they will be able to sustain HPV vaccine programs after GAVI funding ends. And both GAVI-eligible and other developing countries will need to weigh expenditure on HPV vaccines against spending on other new vaccines and other health priorities.

Other possible sources. Other financing mechanisms that could help support HPV immunization programs include:

- **Advance Market Commitments (AMCs)** – Through this mechanism, donors promise to subsidize purchase

by eligible developing countries of a new vaccine that meets specified technical standards. Developing countries contribute a co-pay. When the AMC funds run out, participating manufacturers are required to continue to provide the vaccine at an affordable price. A pilot AMC for pneumococcal vaccines was announced in 2007 and is expected to begin operating shortly. AMCs could eventually be extended to other vaccines, including second-generation HPV vaccines.

- **Bilateral aid** – Although most donor countries channel support for immunization through multilateral mechanisms like GAVI, bilateral aid remains a potential source of HPV vaccine financing. Japan is the largest bilateral donor for immunization.
- **PAHO Revolving Fund** – The Fund procures vaccines on behalf of participating countries through a competitive bidding process and facilitates delivery. All countries pay the same price for vaccines, based on an average of suppliers' prices. Although the Revolving Fund is not a source of external funding, it has played an important role in ensuring broad access to vaccines at affordable prices in Latin America and the Caribbean.
- **World Bank** – HPV vaccine programs could be supported through traditional lending mechanisms or through the Bank's innovative "buy downs," in which loans are converted to grants when the borrowing country successfully implements a program with large public goods effects or social benefits that may be undervalued by the government.
- **Donation programs** – Programs such as Merck's Gardasil® Access Program could also help to bring HPV vaccines to developing countries. While these donation programs are only a short-term solution, they could help build experience with HPV vaccine introduction and garner support from international donors and national governments.

What Needs to Be Done?

HPV vaccines have the potential to greatly reduce cervical cancer morbidity and mortality in developing countries, reducing suffering and saving lives, especially when the vaccines are used in conjunction with cervical cancer screening.

To realize the potential of HPV vaccines, however, several major cost and financing issues need to be addressed urgently. Our study suggests that developing country and donor officials, advocates for cervical cancer prevention, vaccine industry leaders, and representatives from concerned NGOs should work together over the next few years to ensure that:

- *prices* for HPV vaccines are set at levels that meet developing country needs and match their financial situation, thereby making HPV vaccination programs affordable and cost-effective;
- *the value* of HPV vaccines is demonstrated relative to competing health and development opportunities, so that finance ministries and donor officials are convinced that HPV vaccination is a priority;
- *demand* for the HPV vaccine materializes and domestic and external financing is secured, so that manufacturers are convinced to scale up production to meet the needs of developing countries; and
- *adequate and predictable external financial assistance* is available to low- and lower middle-income countries for vaccine purchase, at least until vaccine prices fall to affordable levels.

Once these elements are in place, the world, and especially developing countries, stand to benefit enormously from a new era of successful cervical cancer control.

Ensuring broad and rapid access to future AIDS vaccines in the developing world will require overcoming many of the same challenges that HPV vaccines now face – delivering a vaccine to young adolescents, communicating clearly about complex concepts like partial protection, preventing stigma, and ensuring affordability. Through its work with PATH and others on HPV vaccine introduction, IAVI can bring its experience to bear while learning valuable lessons for the future.

PATH has been active in cervical cancer prevention efforts since 1991 and for the past eight years has been collaborating closely with the other partners of the Alliance for Cervical Cancer Prevention. PATH's projects are facilitating development and introduction of effective and affordable HPV screening tests and piloting and documenting introduction of HPV vaccines in Africa, Asia, and Latin America.

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IAVI's mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world.

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PATH's mission is to improve the health of people around the world by advancing technologies, strengthening systems, and encouraging healthy behaviors.