Providing Vaccines Against Human Papillomavirus To Adolescent Girls In The Americas: Battling Cervical Cancer, Improving Overall Health

**ABSTRACT** Vaccines against the human papillomavirus (HPV)—the primary cause of cervical cancer—target adolescent girls, many of whom have limited contact with health services. Countries in the Americas are beginning to use HPV vaccines to increase the impact of cervical cancer programs and as an entry point to broader health services for girls. This strategy opens new opportunities to improve lifelong health habits; encourage regular cervical cancer screening and treatment, when necessary; and offer associated services such as reproductive health and nutrition guidance. Some of the early experiences with this strategy illustrate challenges and opportunities that may arise with other new vaccines.

Extremely cost-effective, vaccines are among the “best buys” in public health. Unprecedented disease control has been achieved through immunization programs, including the eradication of smallpox and polio, and the elimination of measles and rubella, in the Americas. New vaccines are making it possible to prevent other diseases, such as cervical cancer, through immunization.

As the second-leading cause of cancer deaths among women globally, cervical cancer is a major public health problem that disproportionately affects poorer women and women in developing countries. With vaccines against the human papillomavirus (HPV), the primary cause of cervical cancer, now available, an extraordinary opportunity exists to create synergies with existing cervical cancer prevention and control interventions. If successful, this approach would drastically reduce morbidity and mortality rates from this highly preventable disease and save the lives of thousands of women worldwide each year.

An estimated 15 percent of all women in the Americas are infected with HPV. These infections occur most commonly during late adolescence and early adulthood, and the estimated prevalence of infection in women under age twenty-five is 25 percent. The majority of these infections usually disappear without treatment, as part of the body’s natural immune response, within two years. But approximately 10 percent of them persist for several years and can later develop into precancerous cervical lesions that, if left untreated, can progress to cervical cancer.

There are more than a hundred types of HPV, but eight types (HPV 16, 18, 31, 33, 35, 45, 52, and 58) are most commonly found in cervical cancer cases. And two of these types (HPV 16 and 18) account for 70 percent of the cases. These two are the HPV types contained in the currently available HPV vaccines.

To be effective, the vaccines must be given before exposure to the virus, and they do not protect against all high-risk types of HPV. Thus, they will not replace the need to screen women for cervical cancer. But because the primary target of these vaccines is young adolescent girls who have not yet become sexually active, administering the vaccines can improve health services for a population that has traditionally lacked interaction with health care. HPV vaccines therefore both form an integral component of cervical cancer prevention and control.
cancer programs—complementing existing screening strategies—and can serve as an entry point for adolescent girls into broader health care.

In some countries the introduction of HPV vaccines has prompted a convergence of science, sexual health, and politics in sharp public debates about the evidence for and acceptability of vaccines that prevent infection from a sexually transmitted virus. The high cost of the vaccines has also received a great deal of attention. In this article we review what has been accomplished by using HPV vaccines as a component of a multifaceted health intervention, and we consider the challenges ahead.

**Study Data And Methods**

We reviewed recent literature on HPV vaccines, as well as policy recommendations and experiences with the vaccines’ introduction in the Americas.

We extracted data on HPV prevalence and cervical cancer from databases of the World Health Organization, including those of the International Agency for Research on Cancer. In addition, in May 2010 we used a standardized questionnaire to survey the managers of national cervical cancer programs in selected Latin American countries to collect information about vaccination and screening programs. Some of that information is summarized in Exhibit 1.

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**Cervical Cancer In The Americas**

Some of the highest rates of cervical cancer occur in the Americas, where the overall incidence rate is almost double the worldwide average. The region also has some of the greatest disparities in cervical cancer mortality rates between developed and less developed areas (Exhibit 2). For example, cervical cancer mortality rates are roughly seven times higher in Central America and the Caribbean than they are in the United States and Canada.

Each year, approximately 86,000 women in...
the Americas are newly diagnosed with cervical cancer, and 38,000 women die from the disease. In the United States, the average age of women diagnosed with cervical cancer is forty-eight, and the average age of women who die from the disease is fifty-seven. With demographic changes, such as the projected increase in population size and aging of the population, the number of new cervical cancer cases is projected to increase by 75 percent by 2025 in Latin America and the Caribbean. Screening with the Papanicolaou test—commonly known as the “Pap smear”—has historically been the main public health intervention to prevent cervical cancer. Well-organized screening and treatment programs have led to dramatic reductions in rates of the disease. In the United States, for example, cervical cancer incidence has fallen by 75 percent since the 1960s as a result of screening and treatment.

However, countries in Latin America and the Caribbean, which have had screening programs in place since the 1970s, continue to have high rates of cervical cancer (Exhibit 2). This is mainly because it takes a good deal of economic, material, and human resources within a well-organized and accessible health care system to establish screening programs with high rates of cervical cancer screening, high-quality testing, and complete follow-up diagnosis and treatment.

### The Effectiveness Of HPV Vaccines

When given to adolescent girls before they become sexually active, HPV vaccines have been proven to be safe and almost completely effective in preventing infection and precancerous lesions from HPV types 16 and 18. In addition, the vaccines have shown to provide some protection against HPV types 31, 33, and 45—although these types are not contained in the vaccines—which are responsible for 7 percent, 4 percent, and 5 percent of cervical cancer cases, respectively. The vaccines have not been demonstrated to have any therapeutic efficacy against already established HPV infections.

The cost-effectiveness of HPV vaccines, especially when used together with screening programs, has also been demonstrated. For example, in scenarios modeling low- and middle-income countries where the burden of cervical cancer is high and resources for investing in new interventions are scarce, HPV vaccination would be cost-effective compared to no intervention if the vaccine cost less than $10–$25 per vaccinated girl. The current price of the vaccine varies greatly, ranging from $16.95 to more than $100 per dose. Thus, the cost-effectiveness of the intervention varies by country and depends on the price at which the vaccination program purchases the HPV vaccines, among other factors.

Because the vaccines are relatively new—introduced just four years ago—the impact of vaccination on cervical cancer rates will not be known for many years to come. Therefore, researchers have used models to predict the magnitude of the impact. Although these models involve many assumptions, the results consistently estimate that vaccination alone, compared to the status quo, could lead to a 40 percent reduction in cervical cancer mortality over the lifetime of the vaccinated population. And when vaccination is coupled with at least three screening tests over the woman’s lifetime, the risk of cervical cancer could be reduced by 60 percent.
Policy Recommendations For HPV Vaccines
Based on the scientific evidence, the World Health Organization has recommended that HPV vaccines be incorporated into national immunization programs where cervical cancer prevention and control is a national priority and HPV vaccination is cost-effective, feasible, and sustainable. Although the top-priority target age group varies by country (Exhibit 1), the World Health Organization recommends that girls ages 9–13 be a priority and that vaccinations be delivered in such places as schools and community health clinics.

In addition, the Pan American Health Organization (PAHO) also recommends that HPV vaccines be included in national vaccination programs in the Americas wherever the use of such vaccines would be feasible and sustainable, and not at the expense of investments in screening programs or other new vaccines. In addition, in 2008 the PAHO Directing Council, comprising ministers of health of American countries, voted unanimously to urge all countries in the region to create a new way to pay for new or underused vaccines, including HPV vaccines, within their national budgets.

The Introduction Of HPV Vaccines
Since 2006, six American countries have incorporated HPV vaccines in their national public health programs: Canada, Mexico, the United States, Panama, Argentina, and Peru (Exhibit 1). Demonstration or pilot projects to evaluate feasibility are under way in four additional countries: Bermuda, Bolivia, the Cayman Islands, and Haiti. Results expected in 2011 from these demonstration projects are likely to result in the introduction of HPV vaccination into the public health programs of additional countries within the next three years.

Public Reactions To The Vaccines
Generally, there has been good public acceptance of HPV vaccines in the Americas, including parental consent for vaccination. Nonetheless, in 2006–07, when HPV vaccines were introduced in the United States, sociopolitical issues made them controversial, particularly when the discussion centered on whether to make the vaccines mandatory for young girls attending public school. The public debates focused on the lack of longer-term safety data and the concern of some Americans that vaccination might lead to increased sexual activity among teens or undermine messages in favor of abstinence.

Since 2007 there has been much less public debate and controversy over the HPV vaccines in the Americas overall. Parents and young adults have viewed vaccination positively, and the issue of HPV as a sexually transmitted infection does not seem to reduce the vaccines’ acceptability. This is reflected in the rates of HPV vaccination for the first dose, which is as high as 90 percent in some countries (Exhibit 1). But it remains a challenge to provide the required three doses over six months. Even in the United States, the vaccination rate for three doses is only 27 percent (Exhibit 1).

An Opportunity To Improve Girls’ Overall Health
Adolescents, particularly girls, are an audience that preventive health services often find difficult to reach. Many attitudes and health behaviors are formed during adolescence. By increasing girls’ contacts with the health system, HPV vaccines can improve their overall health throughout their lives. In addition, unmarried girls and women in some areas face political and social barriers to access to reproductive health services. HPV vaccination provides an excellent opportunity to offer girls a package of health services and complementary interventions, including check-ups; vision screening; and the provision of information on reproductive and sexual health, physical activity, and nutrition.

But because most vaccines are delivered during early childhood, new delivery strategies and approaches are required to reach adolescent girls. A combination of strategies based on vaccination at schools or at health clinics and outreach campaigns at the community level are all being employed. Which way of reaching adolescent girls is the most cost-effective will depend on a country’s available resources and infrastructure.

In the United States, for example, HPV vaccines are primarily delivered through pediatric and family practice clinics, while in Latin America a school-based strategy is more common. Recent school-based vaccination campaigns targeting Latin American adolescents for measles and rubella have been very successful. The number of annual rubella cases has dropped 98 percent in the region since the introduction of school-based vaccinations. Parents have expressed a preference for school-based delivery of HPV vaccines because of the challenges in getting their children to health centers.

A notable change has been the major reduction in the price of HPV vaccines since they were first introduced to the market, making them more affordable for national governments. In 2011 the price of the vaccines is $16.95 per dose if purchased through PAHO’s Revolving Fund for Vaccine Procurement, a bulk vaccine purchasing program for countries in Latin America and the Caribbean. This price is much less than the pri-
Future Challenges

Although some countries have already implemented HPV vaccination programs, the full extent of their operational challenges and benefits is not yet known. To fully achieve their potential for reducing cervical cancer, these evolving initiatives will need strong and sustained political commitment, public confidence in the vaccines, an affordable supply of vaccines, sustainable financing, and continuous high vaccination rates—all linked to broader and related public health interventions. Concerted efforts to integrate HPV vaccines into adolescent health programs are also important. To reach adolescents, the directors of HPV vaccination programs will need to overcome established barriers, including young people’s low frequency of health visits, low awareness of or misconceptions about HPV, and underestimation of their risk of cervical cancer.

In addition, there remain clinical questions that will require more study, years of follow-up with participants from clinical trials, and more monitoring and systematization of experiences within each country. Two of these questions are how long the vaccines will protect against infection, and whether a booster will be needed. Clinical trials have so far shown at least seven years of protection, but this may not be long enough to protect against later HPV infections and precancerous lesions in middle-aged women.

HPV vaccination will probably change the strategies used for cervical cancer screening. Vaccination of adolescents will reduce the incidence of precancerous lesions and invasive cancer cases, and as a result fewer lifetime screening visits are likely to be required. The resulting savings of resources could be used to improve the vaccination rate and the quality of a country’s screening program. For example, HPV DNA testing is now available as a screening tool. Although it is more expensive than a Pap smear, it is also more sensitive and can therefore improve the quality of screening programs while also measuring the prevalence of HPV and monitoring the impact of HPV vaccines.

Given the challenges posed by the three-dose schedule of HPV vaccines, studies are now evaluating the use of fewer doses. Preliminary results show that two doses still provide protection, but more evidence is needed before any new policy recommendations can be made. New vaccines that may offer protection against other HPV types are also being tested. These new vaccines may add tools to the package of interventions for cervical cancer prevention.

But the pressing issue now is for countries that have not yet introduced HPV vaccination to decide whether to do so at this point. They need to examine their disease burden, the vaccines’ cost-effectiveness and affordability, and whether introducing the vaccines into their national programs is the best use of their resources. When a country does introduce HPV vaccination, it should use the new program as an opportunity to improve cervical cancer screening strategies; reach more women with high-quality testing and treatment; provide adolescents girls with preventive health care and health information, including information about nutrition and sexual and reproductive health; and strengthen health systems to ensure that prevention is linked to cancer treatment and that cancer surveillance and monitoring are in place.

Conclusion

HPV vaccines are safe and effective, and in a growing number of settings they are proving themselves to be an integral part of cervical cancer control. Increased international leadership, political commitment, and investments in health infrastructure and vaccines are critical if HPV vaccination is to reach those who need it most. National health budgets need to provide funding for new vaccines and new screening strategies, without reducing the financing of other essential programs. To improve their capacity for sustained implementation of organized, comprehensive, and integrated cervical cancer prevention and control programs, national ministries of health may need to work with civic organizations such as national cancer societies and the international community.

In September 2011 the United Nations will hold a high-level meeting on noncommunicable diseases—a group that includes cervical and other types of cancer—to increase the political commitments of member countries in this area. The hope is that this level of global commitment can spur the international community to collaborate in efforts to increase available resources and to raise awareness among policy makers and health professionals around the world about the need to intensify cervical cancer prevention and expand HPV vaccination.

Available public health tools can prevent cervical cancer. The challenge now is to ensure that policies, funds, and health system capacity are in place to effectively deliver the necessary education, vaccination, screening, and treatment services in an integrated and sustainable manner.
Fighting Critical Diseases

NOTES


29 Peres J. For cancers caused by HPV, two vaccines were just the beginning. J Natl Cancer Inst. 2011;103(3):360–2.

In this issue of *Health Affairs*, Silvana Luciani and coauthors review efforts in the Americas to deploy the vaccine for the sexually transmitted infection caused by human papillomavirus (HPV).

Luciani is optimistic that rapid uptake of the vaccine and new screening techniques will begin lowering the burden of cervical cancer in the Americas. She hopes that readers of the *Health Affairs* article “will have a greater appreciation for the complexity of the cervical cancer problem, the inequities it represents, and the potential—with HPV vaccines and new screening strategies—to accelerate reductions in mortality.”

Luciani is a public health professional from Canada who has led national and international health programs on cancer, tobacco, and nutrition. Since 2000 she has directed the program in cancer prevention and control activities at the Pan American Health Organization (PAHO), and she is leading the organization’s Americas Regional Strategy for Cervical Cancer. Luciani received her master’s degree in health science from the University of Toronto.

Elisa Prieto-Lara is a public health physician who has specialized in family medicine, preventive medicine, and public health in Spain. She is currently serving as a project support specialist in chronic diseases at PAHO and providing technical assistance to countries in Latin America and the Caribbean on cervical cancer programs.

Prieto-Lara has conducted research on a range of topics in community medicine, including immunization. She earned her medical degree from Málaga Medical School, in Spain, and her master of public health degree from the Andalusia School of Public Health, also in Spain.

Andrea Vicari is an epidemiologist, Andrea Vicari started his professional experience at the local and national levels in Switzerland, his country of origin. After completing graduate studies, he was an Epidemic Intelligence Service officer with the US Centers for Disease Control and Prevention. Since 2004, when Vicari joined PAHO, he has served as an adviser in immunizations. He first coordinated the measles elimination initiative and later served in the PAHO/World Health Organization country office in Colombia, where he was immunization adviser and also coordinated technical cooperation in maternal and child health and infectious disease prevention and control.

Vicari earned a doctor of veterinary medicine from the University of Bern and a doctorate in epidemiology from North Carolina State University.