

## Cervical Cancer Vaccine Project

Human papillomavirus (HPV), a common infection that most women acquire at some point in their lives, causes cervical cancer and other health problems. New vaccines against the two HPV types that account for 70 percent of cervical cancer cases worldwide (types 16 and 18) soon will be available in many countries. In clinical trials, the vaccines have proven at least 95 percent effective in preventing persistent HPV infection and 100 percent effective in preventing type-specific cervical lesions.

**HPV vaccination could reduce developing-country cervical cancer deaths to the very low levels currently observed in many developed countries, especially when combined with simple, evidence-based screening and treatment approaches.**

The industrialized world has successfully reduced cervical cancer mortality significantly. But we have not seen the same progress in the developing world. Cervical cancer rates are highest there among the poor, in large part because effective screening and treatment programs often

are not available, and most women with cervical cancer only reach health centers when their disease is advanced—and incurable.

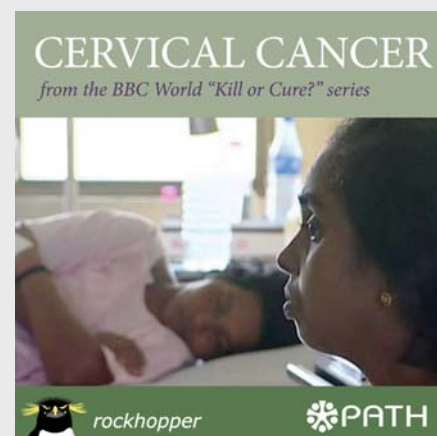
The deaths of these women between the ages of 30 and 60 leave a gap in the fabric of their families, villages, and communities. In many parts of Africa, their deaths magnify the tragedy of the HIV/AIDS epidemic, as these are the same women who often care for sick or orphaned children.

We now have tools to change this tragic situation. Vaccinating most young adolescent girls against HPV could sharply reduce cervical cancer rates during the next several decades.

### **Will the vaccine be available for the women who need it most?**

Since it is normally babies who receive routine vaccinations, not pre-teens, new delivery strategies will need to be put in place to reach those young people. Clear and accurate information must be made available to government decision-makers, health advisors, health care providers, community leaders, parents of pre-teens, and the youngsters themselves so that they have an understanding of cervical cancer and realistic expectations for the vaccine.

There are financial and supply challenges as well. Initially, the



*Women in the developing world are helping in the fight against cervical cancer, as seen in PATH's video filmed in Costa Rica and India.*

### **Cervical Cancer Facts**

- Cervical cancer affects an estimated 490,000 women worldwide each year and leads to more than 270,000 deaths.
- About 85 percent of women who die from cervical cancer reside in developing countries. Each year, 75,000 women die from the disease in India alone.
- If current trends continue, by the year 2050 there will be over one million new cases annually.
- Cervical cancer can be prevented if precancerous lesions are identified and treated early on.
- But most women in the developing world do not have access to screening and treatment programs, making routine vaccination an important disease control strategy.
- New vaccines are safe and effective in preventing HPV and type-specific cervical lesions.

new vaccines will be expensive and out of reach of many countries without significant donor assistance. Accurate vaccine demand estimates are needed nationally, regionally, and globally to ensure a sufficient supply of vaccines and to support price negotiations. Both vaccine manufacturers and international donors will have to be engaged in developing solutions to these challenges. It will take resources, commitment, and cooperation from many entities to realize the promise of this vaccine in the developing world.

### **Exciting global partnerships**

Fortunately, a significant number of partners have committed to working together to shorten the gap between HPV vaccine introduction in the industrialized world and the developing world. The World Health Organization (WHO), the Alliance for Cervical Cancer Prevention (ACCP), the International Agency for Research on Cancer (IARC), the Bill & Melinda Gates Foundation, Harvard University, and PATH are among the organizations seeking to help developing countries understand HPV disease burden and determine how best to introduce the new vaccine.

### **The PATH project**

In June 2006, PATH was awarded a major grant to strengthen the capacity of developing countries to prevent cervical cancer by:

- Generating and providing necessary evidence for decision-making about public sector introduction of HPV vaccines.
- Leveraging introduction activities in four countries to inform and support global advocacy efforts, regional HPV vaccine strategies, and introduction in other countries.
- Developing and disseminating strategic forecasts, investment cases, and decision-making tools to inform and influence industry production capacity and pricing decisions, international agency financing initiatives, and country government introduction plans.

PATH is working closely with ministries of health and civil society organizations to conduct clinical and operations research in India, Peru, Uganda, and Vietnam. The studies will look at a variety of vaccine introduction questions, including what sociocultural barriers may impede acceptance of the vaccine; how the vaccine can be most effectively delivered to adolescent girls; how an HPV vaccine can be integrated into (and strengthen) existing health programs; what the cost implications of an HPV vaccine program are (including the ultimate public-sector price); and what combination of program activities (including screening and treatment services) could

have the most impact on cervical cancer rates?

Results from the country work will be rapidly synthesized and broadly disseminated to inform HPV vaccine policy, program, and funding decisions made by other countries and by regional and global agencies. This advocacy and dissemination role will build on existing advocacy mechanisms and will be implemented in close collaboration with WHO and other global partners.

The project will also build on country and regional experience to develop a global demand estimate for the HPV vaccine to guide manufacturers' supply and pricing decisions. Furthermore, the project will provide demand estimates to the GAVI Alliance, UNICEF, the Group of Eight Advance Market Commitment financing teams, and other potential HPV vaccine decision-makers.

For more information about PATH's cervical cancer vaccine project, visit:

**[www.path.org/cervicalcancer](http://www.path.org/cervicalcancer)**

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# Update: Cervical Cancer Vaccine Project

## May 2007

### Plans for HPV vaccine demonstration projects moving forward

PATH currently is working in partnership with key government agencies, industry partners, research institutes, and other organizations in **India, Peru, Uganda, and Vietnam** to prepare for HPV vaccine demonstration projects. These partnerships will focus primarily on operations research to explore the most effective and acceptable strategies for vaccinating young people against HPV (see next page for examples of research questions we will investigate in the demonstration projects).

The data generated by the studies will help guide future HPV vaccination program planning. We expect most demonstration projects to begin in early 2008, preceded by a range of formative research activities.

### Formative research underway

The Peru and Uganda country projects soon will have formative research data to share nationally and with other countries in their regions. The focus of the research is to better understand the medical, policy, fiscal, and sociocultural environments in which the demonstration projects will be

implemented. Using a variety of qualitative and quantitative research methods, country teams interact closely with national stakeholders, in-country medical experts, health care providers, parents, and young adolescents. Key issues of interest (among many others) include:

- What do the various audiences know about cervical cancer? About HPV? Is it a priority for them?
- What sociocultural barriers may impede acceptance of HPV vaccine?
- What current policies may support or constrain health care for adolescents?
- In the opinions of the respondents, how can the vaccine be delivered most effectively to girls aged 10 to 14?
- How can HPV vaccine be integrated into (and strengthen) existing health programs, and what aspects of the current medical system may need to be altered in order to reach older children and young adolescents?

Formative research will begin soon in India and Vietnam. We anticipate publishing data from all four countries in 2008.

### Alternate dosing schedule study

While the main focus of the project is operations research, not clinical studies, one important clinical question will be addressed: do alternative dosing schedules for HPV vaccines—schedules that may mesh more effectively with country systems—offer the same levels of protection as the ideal dosing schedules suggested by the manufacturers?

Both of the HPV vaccines currently in the global market require three doses for full coverage. They also have similar vaccination schedules: the second dose is given either one or two months after the first dose, and the third dose is given six months after the first dose. However, it may be that more children could be reached more efficiently if the vaccines were offered quarterly, semi-annually, or annually.

The PATH project in Vietnam will measure immune responses generated by these alternate schedules to determine if there is any immunogenic disadvantage when using the vaccines in this way. The study will begin in September, 2007 and should generate results on all alternative schedules by 2009.

## Sample demonstration project research questions

The final design of demonstration projects will build upon in-country partnerships and the results of formative research, but we anticipate that they will include questions like those below.

The **primary outcome** for each study is full vaccine coverage among target-age girls.

**Secondary outcomes** include partially vaccinated subjects and resource use, cost, acceptability, and cost-effectiveness data.

### Best age for maximum acceptability?

- **Objective:** To select a target age that maximizes acceptability and operational feasibility in a community outreach vaccination strategy.



Photo: PATH

- **Method:** Develop strategies tailored to needs of younger (e.g., 10–12 years) vs. older (e.g., 14–15 years) adolescent girls. Cluster-randomize selected communities to the two strategies.

### Feasibility of adding HPV vaccine to semi-annual child health days?

- **Objective:** To compare a primary school-based strategy with a school and community outreach approach for reaching girls aged 11 or 12 through existing semi-annual child health days.
- **Method:** Cluster-randomized comparison of two approaches.



Photo: Molly Mier

### Cost-benefit of active follow-up for second and third doses?

- **Objective:** To compare a school-based vaccination strategy without active follow-up to one that includes follow-up.
- **Method:** Cluster-randomized comparison of two approaches.



Photo: Jacqueline Sherris

### Best strategy for reaching 14-year-old girls?

- **Objective:** To identify the most cost-effective strategy for reaching 14-year-old girls.
- **Method:** Compare (1) school-based strategy with (2) a facility-based strategy and (3) a combination strategy. Three-arm cluster-randomized approach.



Photo: Michael Berman

## Generating data on potential vaccine demand, supply, and financing options

Another important element of the project is to accelerate key supply, demand, and financing decisions related to HPV vaccine. PATH is collaborating with partners to develop an “investment case” for HPV vaccine and mapping HPV decision-making pathways in order to anticipate—and address—potential bottlenecks. We will also encourage and support ongoing dialogue between national governments, the GAVI Alliance, and industry relating to vaccine price and will provide them with up-to-date demonstration program data as they are generated.