



Cervical Cancer Prevention at PATH

Two decades of progress toward a world free of HPV-related cancers



PATH first began to focus on the problem of cervical cancer in 1991, supported by a small seed grant from the World Bank. Over the past 22 years our portfolio expanded tremendously, with the most rapid growth since 1998 and thanks in large part to grants from the Bill & Melinda Gates Foundation. Our four key areas of interest are summarized in the box below, and are described in depth later in this report.

ENCOURAGING PROGRESS IN CERVICAL CANCER PREVENTION

PATH has been at the forefront of efforts to build the evidence base for appropriate prevention interventions, share lessons related to successful strategies, and provide technical assistance to countries interested in making progress in cervical cancer prevention.

Today, with broad acceptance of new cervical cancer screening and treatment alternatives for adult women and expanding access to HPV vaccination among young adolescent girls—especially since the GAVI Alliance began offering the vaccine—for the first time in history it appears that elimination of cervical cancer is within reach. We have the tools; but we need to learn to use them effectively and we need sufficient political will to make it happen.

Human papillomavirus, or HPV, is the primary cause of cervical cancer. HPV is a common sexually transmitted infection (STI) that most women acquire at some point in their lives, although the majority of those infections clear up without treatment. However, within a decade following



School girls in Piura, Peru.

PATH cervical cancer prevention initiatives 2006–2013

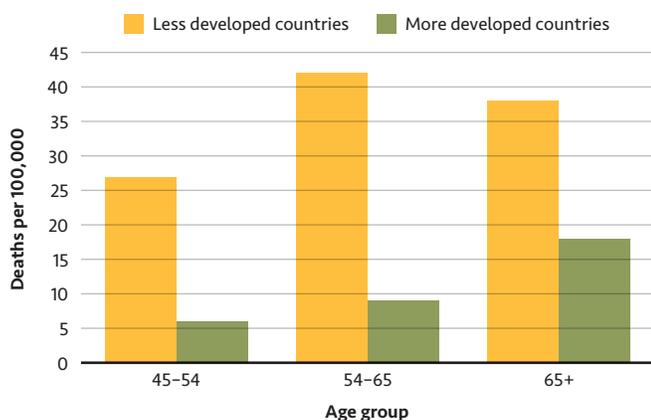
HPV vaccination—operations research exploring a variety of strategies for effectively delivering vaccine to girls in the developing world, plus analysis and computer modeling of supply and demand scenarios necessary to build a comprehensive evidence-base for national and global decision-making. PATH currently provides technical assistance with HPV vaccine program strategy and planning to low- and middle-income countries (page 3).

Innovative approaches to screening in low-resource settings—affordable solutions for situations where cytological (Pap smear) screening has not proven feasible, such as visual inspection with acetic acid (VIA) and molecular HPV tests designed especially for developing world conditions. PATH helped establish a regional training center for screening and treatment in Latin America and is now working to create one for Africa, and is helping low- and middle-income countries design and implement cost-effective screening programs (page 7).

Improved precancer treatment—following screening with VIA or HPV DNA tests, cryotherapy offers affordable, effective treatment for most women who have precancer, with few side effects. PATH is working to improve cryotherapy equipment and to explore appropriate alternative technologies (page 9).

Advocacy for comprehensive cervical cancer prevention—global partnerships and dissemination of science-based information for policymakers, program planners, clinicians, and the public (page 10). PATH’s RHO Cervical Cancer Library is a respected global resource and our work with partners in the Cervical Cancer Action coalition has raised awareness, mobilized political will, and fostered positive policy change worldwide.

FIGURE 1. Age-specific cervical cancer mortality rates



Many more women die of cervical cancer in the developing world than in wealthier countries. In the industrialized world, effective screening programs help to identify precancerous cervical lesions at a stage when they can easily be treated. But lack of screening programs in poorer countries means that the disease is not identified until it is too late, resulting in vastly greater mortality. Source: WHO/Globocan.

persistent infection, about ten percent of women develop precancerous lesions on the cervix. Without screening and treatment, about ten percent of those women will suffer advanced cervical cancer, often resulting in an early death. Cervical cancer usually kills women in their 40s, and 50s, while they still are highly productive, skilled members of their families and communities.

In wealthier settings Pap smears have helped detect and treat the precursors of cervical cancer, saving millions of lives. Despite its sub-optimal sensitivity for detecting precancerous lesions, routine Pap screening (cytology) continues to be a tool in those places where it can be used repeatedly. But low-resource countries do not have the resources to implement complex cytology-based programs, with the result that the vast majority of women do not have access to screening or treatment. Of the estimated 275,000 annual cervical cancer deaths worldwide, 88 percent occur in developing countries (see Figure 1). The loss of these adult women rends the fabric of their families, villages, and nations.

Fortunately new screening options now are available, in part due to PATH initiatives.

Furthermore, since 2006 two vaccines (Gardasil® and Cervarix®) have become available to prevent infection with HPV types 16 and 18, which account for 70 percent of cervical cancer cases worldwide. To some extent the vaccines also prevent infection by other, closely related HPV types. Both vaccines have been proven at least 90 percent effective in safely preventing infection when vaccination occurs prior to exposure to the virus (before onset of sexual activity).

Vaccinating young adolescent girls against HPV—while simultaneously improving cancer screening for older women—could reduce developing country cervical cancer deaths to the very low levels currently observed in many developed countries. Yet there are many challenges to ensuring that vaccines, screening, and treatment become available to those who need them most. Cervical cancer, while a serious problem, is not well-known or understood in many communities, making education and advocacy another top priority.

Following are descriptions of PATH’s contributions to the field, with a focus on activities in recent years.

For additional information about HPV and cervical cancer, consult the resource guide at the end of this report.

HPV VACCINATION: READY FOR ROLLOUT IN CHALLENGING ENVIRONMENTS

In 2006, shortly after new vaccines against HPV became available, PATH launched the *HPV Vaccines: Evidence for Impact* project. As mentioned previously, most cervical cancer deaths occur in developing countries. And while most of those countries have achieved good vaccine coverage for infants and very young children, HPV vaccine is intended for an older population—girls aged 9 and above. It is rare for developing world immunization programs to have robust systems for reaching young adolescents, so the question becomes “how and where can we best reach young adolescent girls with HPV vaccine?”

When the PATH studies began, no one knew whether communities would be open to the idea of vaccinating only girls, or whether they might react negatively when



A girl receives HPV vaccine in Ibanda, Uganda.

PATH/Robin Blietnik

they learned that HPV usually is transmitted through sexual contact. Understanding such social and cultural issues was crucial in order to effectively communicate with girls, their parents, and others in the community. It also was important to assess possible stresses on the health system and the vaccine infrastructure such as the cold chain.

The PATH project addressed these challenges by:

- **Generating an evidence base** with data for decision-making about public sector introduction of HPV vaccines. Formative and operations research was conducted in India, Peru, Uganda, Vietnam, and, to a lesser degree, in several other countries.
- **Using the data to inform and support global planning**, regional HPV vaccine strategies, advocacy, and introduction in interested countries.
- **Developing and disseminating strategic forecasts and decision-making tools** to inform and influence industry production capacity and pricing decisions, international agency financing initiatives, and country government introduction plans.

The PATH project was not a clinical trial of a new vaccine—the vaccines used in the project had already been licensed in each of the four countries (and in over 100 other countries). Instead, the project aimed to assess and document the best possible approaches to HPV vaccine delivery.

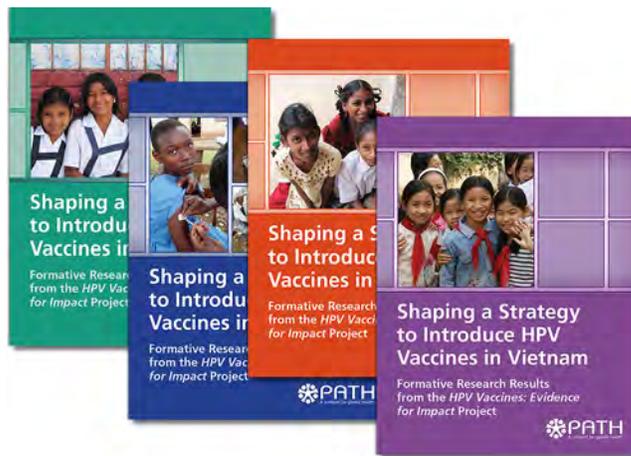
Shaping strategies for HPV vaccine introduction

PATH collaborated with many partners, including ministries of health and other government agencies, industry, and communities, to explore the most acceptable strategies for vaccinating young adolescent girls against HPV. The work was implemented in three phases:

- Formative research to explore the knowledge, attitudes, and beliefs of diverse audiences, and to better understand health system and policy factors.
- Operations research (demonstration projects), informed by formative research data, to evaluate various strategies for reaching girls with HPV vaccine.
- Rapid dissemination of lessons learned to serve as an evidence base for agencies or governments that wish to develop or scale up cervical cancer prevention programs.

Formative research

During the first two years of the project, PATH and our partners conducted formative research in each country to better understand the medical, policy, fiscal, and socio-cultural environments in which the demonstration projects would be implemented and to guide their design. PATH staff collaborated closely with local researchers, using a variety of qualitative and quantitative research methods. The teams met with national and regional



Formative research results for India, Peru, Uganda, and Vietnam are available in the RHO Cervical Cancer Library at www.rho.org.

stakeholders, policymakers, health care providers, parents, young adolescents, and other community members to understand which factors are most likely to result in a child receiving the HPV vaccine and which factors are most likely to foster institutional decisions that result in successful vaccine delivery. In addition to exploring target audience knowledge and attitudes about cervical cancer, the research teams also investigated clinic and school health programs, assessed equipment and training needs, and mapped the policy environment related to new vaccine introduction.

Summary of results: Overall, the research demonstrated low levels of knowledge and awareness regarding cervical cancer, HPV, and the HPV vaccine in all four countries. When given more information, however, most people responded positively about the HPV vaccine. Specific concerns about the vaccine and important health systems or policy obstacles were also identified in each country, and locally appropriate strategies were developed to address them (see box on page 5).

Demonstration projects

Drawing on the results of the formative research, PATH worked with national health officials and other local partners to design and evaluate effective vaccine delivery strategies, appropriate communication approaches, and targeted advocacy efforts. The demonstration projects assessed vaccine coverage achieved and program feasibility, acceptability, and cost.

For example, formative research participants in all four countries supported school-based delivery of the HPV vaccine, along with additional efforts to reach girls who do not attend school. Some respondents in Uganda and Vietnam expressed strong support for also assessing HPV vaccine delivery in the community or at health clinics.

Lessons from India, Peru, Uganda, and Vietnam

Cervical cancer, HPV, and vaccination: knowledge and perceptions

PATH's formative research found that awareness of cervical cancer varies both within and among the four countries studied. For example, in Uganda, very few people were able to define cervical cancer, although many recognized the condition's symptoms. In Vietnam, by contrast, 75 percent of parents in the study had heard of cervical cancer. Not many people had heard of HPV in any country, with the exception of some health workers in Uganda and Vietnam. In all four countries, once a general understanding was established, cervical cancer was perceived by most to be an important and very serious disease. As one teacher in India put it, "The mother is the heart of the family. If she got sick, the whole family would go into a depression."

Overall, participants in all four countries felt that vaccination is important for preventing illness and has significant health benefits. One father in the Gulu district of Uganda reported that, "These days our children do not suffer from certain diseases like measles...I think it is because they started

vaccinating children early in hospitals. That is the reason the disease is disappearing." In all four countries, when provided with objective information about the HPV vaccine by researchers, most participants responded positively. As one young adolescent girl in Peru stated, "We all have a right to receive that vaccine."

Participants in all countries did express concerns about side effects or possible long-term effects of the HPV vaccine. Concerns regarding fertility were expressed in Peru, Uganda, and Vietnam, due to the fact that the target group for this vaccine is young adolescent girls. However, it was widely noted in all countries that visible support from political and community leaders would go far in allaying people's doubts and fears. One participant in Vietnam explained, "The most important thing is to have support and leadership of people's committees and government agencies."

The formative research provided valuable guidance in designing the demonstration projects.

Key results from the PATH demonstration projects

- **HPV vaccine was highly acceptable to communities in all four countries.** Coverage rates tended to be above 80% and demand for the vaccine was high. The vast majority of girls received all three doses required (there was very little drop out between doses). It should be noted that this success followed careful work educating and mobilizing communities—we cannot assume that acceptability would have been similar in the absence of strong communications and training efforts.
- **School-based vaccination worked well.** That said, it is necessary to also create systems to reach girls who do not attend school or who were absent on vaccination days. Teachers tended to be enthusiastic proponents of vaccination, and efforts to educate them about cervical cancer prevention were good investments. When designing a school-based program, it is important to determine at what age greater numbers of girls tend to drop out of school and plan accordingly. It also is crucial to understand the school's annual schedule to ensure that all three doses can be administered during a single school year.
- **Clinic-based delivery also was successful.** In some countries, it may work best to offer vaccination at different venues for different situations, for example, using schools in urban settings (in which schools are near the clinics where vaccinators are based and therefore relatively inexpensive to visit) and using clinic-based services in rural areas in which clinics are far from schools.
- **Vaccine delivery costs tended to be similar across strategies.** However, costs tended to be higher in rural and more remote locations than in urban areas. Costs were lower when HPV vaccination was integrated with ongoing health outreach to girls (such as Uganda's Child Days Plus program).
- **When educating, focus on cancer prevention.** Most parents have a positive impression about vaccination and most are concerned about cancer, even if they do not understand it very well. For general audiences, it was important to emphasize that the purpose of HPV vaccination is to prevent cervical cancer, rather than to explain that it prevents infection with HPV, a virus most people have never heard about.
- **Look beyond parents and girls.** National-level stakeholders and the broader local community also should be engaged in educational activities. Ministry staff, community leaders, village elders, town council members, women's groups, youth organizations, and religious leaders are some of the groups that can inform parents about HPV vaccination of girls and screening for adult women.

Detailed study results have been disseminated in peer-reviewed journals and other publications.

In those two countries, a school-based vaccine delivery strategy was evaluated against a strategy using existing, non-school outreach systems. In Uganda, a semi-annual event called Child Days Plus delivers an integrated package of preventative services (e.g., catch-up immunizations, vitamin A supplementation, and deworming medicine) to older children through health centers, churches, community centers, and schools. The Uganda project measured the effectiveness of school-based delivery compared with delivery through Child Days Plus. And in Vietnam, where there is a strong clinic-based vaccination system already in place, the demonstration project compared delivery of the HPV vaccine through schools with delivery through commune health centers (see box on page 5).

Vietnam alternative dosing schedule study

While the main focus of the *HPV Vaccines: Evidence for Impact* project was operations research, not clinical studies, one important clinical question was addressed in Vietnam: do alternative dosing schedules for HPV vaccines—schedules that may mesh more effectively with country systems—offer the same levels of protection as the dosing schedules suggested by the manufacturers? Both 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 doses were offered quarterly, semi-annually, or annually. For example, the semi-annual Child Days Plus activities in Uganda create opportunities for providing the first and third vaccine doses only—special vaccination sessions had to be organized to provide the second dose. But if the



A vaccinator in Vietnam meets with school girls to explain HPV vaccine.

vaccine proves to be as effective when the doses are given six months apart—i.e., the second dose six months after the first and the third six months after that—it would be much easier for the girls and for the vaccinators, and may be less expensive for the government.

The Vietnam study, conducted using Gardasil vaccine, found that all three alternative schedules provided protection comparable to the standard schedule, as measured by the antibody levels approximately two years after the third dose was given. While a similar study would be needed with Cervarix to confirm the possibility of extended schedules with that product, the data from Vietnam raise the exciting prospect that countries could design delivery strategies based on semi-annual or annual contacts with girls.

Making the case for investment in HPV vaccination

Identifying and mobilizing resources for vaccine purchase and delivery is one of the most significant challenges to making the HPV vaccine widely available in the developing world. Therefore, another important element of the *HPV Vaccines: Evidence for Impact* project was to accelerate key supply, demand, and financing decisions related to HPV vaccines. As part of our country-level formative research, for example, PATH conducted baseline immunization financing assessments in each of the four countries. Also, as part of the demonstration projects, we explored affordability by estimating the program costs associated with introducing the HPV vaccine through different delivery strategies in each setting.

The GAVI Alliance, an immunization coalition of the world’s top global health agencies, governments, and private partners, offers subsidized vaccines to over 70 countries of the developing world. Many low-income countries will rely on support from the GAVI Alliance to



The *Cervical Cancer Prevention: Practical Experience* series summarizes lessons learned from the PATH demonstration projects. Available at www.rho.org.

FIGURE 2. Global progress using visual inspection with acetic acid (VIA) for cervical cancer screening



Use of VIA is expanding rapidly but countries need help to build screening and treatment infrastructure. Unfortunately there is no GAVI for screening. Source: Cervical Cancer Action.

procure HPV vaccine. Generally, GAVI makes decisions about whether to allocate funds to support introduction of certain vaccines based on an investment case that analyzes the value of the vaccine. In the first year of the project, PATH convened a meeting of representatives from the World Health Organization (WHO), GAVI, vaccine manufacturers, and the Bill & Melinda Gates Foundation, among others, to develop the components of an investment case demonstrating the value of introducing the HPV vaccine in GAVI-eligible countries.

In 2008 the GAVI Board made the decision to include HPV vaccine in their portfolio. The decision was based in part on data provided by PATH. And while the global recession

delayed GAVI implementation of the Board decision, in 2012 PATH worked closely with GAVI and WHO to design the GAVI application process and to help countries prepare successful GAVI applications. The first GAVI awards were approved in February 2013.

INNOVATIVE, COST-EFFECTIVE SOLUTIONS FOR SCREENING IN LOW-RESOURCE SETTINGS

As mentioned earlier, HPV vaccination and cervical cancer screening and treatment programs both are needed to reduce mortality, yet most developing countries lack the infrastructure and trained personnel needed to replicate the cytology-based, multi-visit approach used in wealthier countries to detect precancer (Pap smears followed by colposcopy and biopsy). In an effort to find alternative strategies suitable to low-resource settings, in 1999 PATH joined four other international agencies to form the Alliance for Cervical Cancer Prevention, or ACCP¹. Over the following nine years the ACCP partners conducted studies comparing a number of screening techniques, including cytology, visual inspection using acetic acid (also known as VIA; it is a low-cost and relatively easy-to-implement option), and a state-of-the-art HPV-DNA test. The tests were evaluated in over 20 low-resource settings around the world.

ACCP found that VIA compares well to cytology in terms of sensitivity for disease detection—in fact it generally has slightly higher sensitivity than Pap. VIA also requires fewer specialized personnel and less infrastructure, training, and equipment. Cervical cancer screening using VIA can be



275,000 women die of cervical cancer every year. Access to screening and treatment options appropriate for low-resource settings could save many lives.

1 The initial ACCP partners were EngenderHealth, International Agency for Research on Cancer (IARC), Jhpiego, Pan American Health Organization (PAHO), and PATH. ACCP papers and other materials can be found in the RHO Cervical Cancer Library (www.rho.org).

offered in remote, less equipped clinics, thereby reaching more women. Another important advantage is that VIA provides immediate results, making it possible to screen and either treat or refer women during the same visit.

Immediate treatment, where available, means that women do not have to make an extra visit to the health center, thus reducing the number of women who are lost to treatment because they cannot return for one reason or another. In the ACCP studies, and in subsequent PATH research, VIA was successfully paired with cryotherapy, a relatively simple, inexpensive, and safe method of freezing affected cervical tissue (see the next section). Cryotherapy can be done during the initial screening visit, or later at a convenient referral site. Studies have shown that cryotherapy can be effectively and safely performed by trained nurses or midwives, in addition to physicians and gynecologists—though, as with all screening approaches, attention to consistent quality standards is key.

As the body of evidence on the safety and impact of “screen and treat” approaches has accumulated over the past ten years, many countries have expressed interest in such strategies, and requests for assistance have exceeded the ability of technical agencies to respond. Countries like Thailand and the Philippines have implemented successful, large-scale, VIA-based programs, but more education and training are necessary if such programs are to expand regionally.

To help meet this need, in 2009 PATH and Jhpiego teamed with the Peruvian national cancer institute (INEN) to create a “training excellence center” for VIA and

cryotherapy. Training Excellence Centers, or TECs, can serve as a resources for governments and ministries of health ready to scale-up services. They not only provide structured competency-based training, but also support all aspects of a cervical cancer screening and treatment program to ensure quality and sustainability. TECs show tremendous promise for the development of quality cervical cancer prevention programming in the settings that need it the most. The first TEC was designed to serve both Peru and other countries in the region. The model proved successful as clinicians and trainers from Colombia, Bolivia, and Nicaragua received classroom training and field practice from INEN, and spin-off training centers have been inaugurated in two of the countries.

In 2013 PATH is working with the Uganda Cancer Institute to create a similar TEC for Africa.

New rapid, field-friendly, and more sensitive screening tests

“HPV testing” detects the presence of HPV DNA in a woman’s cervical or vaginal mucus. Global health experts recommend use of HPV DNA testing for primary cervical cancer screening, noting that it is much more sensitive than either cytology or VIA. Unfortunately, until recently HPV testing was too expensive and the equipment too unwieldy and fragile for most low-resource settings. PATH, working with a private company, was determined to change that.

In 2003 PATH launched the Screening Technologies to Advance Rapid Testing (START) project. The project



QIAGEN

The careHPV™ test produced by QIAGEN.

sought to develop two different HPV screening methods appropriate for use in the developing world. It was important that the tests be acceptable to women and their healthcare providers, relatively simple to use, accurate, affordable, and rapid, to allow for single-visit efficiencies.

By the time the project ended in 2008, START had developed a test based on the more complex Hybrid Capture II (HCII) HPV DNA test, produced by QIAGEN. Most HPV tests are not suitable for low-resource settings because of the requirement for sophisticated laboratory equipment, refrigeration, and other resources typically unavailable in areas with limited resources. But the new *careHPV*[®] test is compact (the full set of instruments fits on a desktop), its reagents do not require refrigeration, it detects 14 oncogenic HPV types, and results are available in less than three hours. Test results are easy to read and, unlike cytology and VIA, are not vulnerable to misinterpretation.

The second test developed under the START project—called the OncoE6[™] Cervical Test—does not look for HPV DNA, rather it detects the E6 protein associated with certain HPV types. E6 signals that cells have actually become precancerous (or cancerous). This is particularly useful because it directs clinical staff to treat women at highest risk of disease.

PATH recognizes that creation of new tests alone does not suffice. In developing countries, challenges exist to widespread adoption of new technologies. Before incorporating tests into national cervical cancer prevention strategies and plans, ministries of health need evidence that the tests are feasible and appropriate for their health system infrastructure and their geographic, cultural, and economic circumstances. In addition, private industry needs guidance navigating the complexities of product introduction in the public sector of developing countries, which are generally perceived as “high-risk and low-return” markets.

To address these challenges, in November 2007 PATH inaugurated a follow-up project to START, called START-UP. START-UP, ending in 2013, focused on conducting field assessments of *careHPV* in India, Nicaragua, and Uganda; examining the potential for using vaginal, rather than cervical, sampling for *careHPV* (thereby eliminating the need for a pelvic examination, which can be difficult to obtain in some settings, and creating possibilities for women to self-sample), and assessing the clinical performance of the OncoE6 test.

CareHPV and OncoE6 test results

The START-UP studies concluded that for both cervical or self-collected vaginal specimens *careHPV* (an objective test) had better clinical performance than the subjective tests it was compared against: VIA and Pap. While using *careHPV* with **cervical** samples offered the best

performance (sensitivity of 81.5%), using *careHPV* with **vaginal** samples can increase access to services because it does not require a pelvic examination. However it has lower sensitivity (usually 10% less than using a cervical sample).

VIA and Pap sensitivity were considerably lower—59.8% and 58.4% respectively.

The OncoE6 test results from China also are encouraging, showing 53.5% sensitivity even with the current version which includes only HPV types 16, 18, and 45.

While *careHPV* is currently being sold by QIAGEN, the OncoE6 test is not on the market at the time of writing this paper.

The promise of self-collected, vaginal samples

PATH is particularly excited about the strong *careHPV* test results using vaginal samples.

Due to resource constraints—a shortage of health staff capable of performing pelvic examinations and collecting cervical samples and lack of the speculums they need to perform the exams—vaginal self-sampling has important implications for future programming because it could dramatically increase access to screening for many women around the world. For example, field outreach teams could give self-sampling kits to women when visiting villages, and ask them to return the samples to the clinic later (or the team could pick them up at the end of the day’s session or in a return visit). Even in a clinical setting, women could be trained to sample correctly and be given a private place to do so, speeding sample collection. And if a woman did not feel comfortable collecting the sample herself, a nurse, nurse’s assistant, or female “health helper” could be trained to collect vaginal samples from the women without a pelvic evaluation, freeing up time of higher-level clinic staff and increasing screening rates.

It is easy to imagine teams of trained, lay village health assistants gathering hundreds of vaginal samples in a day, with clinic staff processing the samples overnight and returning the following day to seek out women who had tested positive. Such strategies could have a major impact on finally achieving national scale screening coverage in low-resource settings.

IMPROVED CRYOTHERAPY TREATMENT

Cryotherapy (freezing cervical tissue that is likely to develop into cancer) is an appropriate treatment method for low-resource settings. It is effective, has limited side effects, does not require electricity, is technically simpler and less expensive than other treatment options for precancerous lesions, and can be performed by local health workers.

PATH recognizes that it is important to develop programs offering comprehensive screening, diagnosis (where feasible), and treatment, not screening alone. In addition to identifying precancerous lesions, visual inspection with acetic acid (VIA)—discussed above—also allows clinicians to assess treatment options for patients with HPV infection, determining which are candidates for cryotherapy in the local clinic and which must be referred to higher level care for more specialized treatment, such as the loop electrosurgical excision procedure (LEEP). When screening using HPV testing becomes more common, VIA for treatment selection and cryotherapy for treatment still will be needed to manage women with positive HPV test results.

Members of PATH's cervical cancer team have contributed to the effective practice of cryotherapy by investigating crucial technical problems encountered by practitioners. In 2010, they published a study alerting providers that a common technique used to clear ice blockages of devices was resulting in temperatures that might not be sufficient to destroy precancerous tissue. Another study published by the team showed that some brands of cryotherapy devices did not reach temperatures low enough to ensure that precancerous tissue was destroyed. Subsequently, a manufacturer recalled its devices and worked to correct the problem. Another study—analyzing the effectiveness of different gases in cryotherapy devices—was done in collaboration with other teams in the US and Peru. PATH is also planning a study comparing new and underutilized devices for precancer treatment.

In 2011 the WHO published its guidelines for the use of cryotherapy. PATH authors contributed significantly to this important resource.

ADVOCACY FOR COMPREHENSIVE CERVICAL CANCER PREVENTION

As documented through PATH's formative research and other studies, accurate, in-depth knowledge about cervical cancer tends to be low worldwide. Education and advocacy initiatives implemented by PATH and our partners seek to raise awareness and help decision-makers, clinicians, and families make evidence-based decisions that will save lives.

Mobilizing communities globally

The issue of cervical cancer prevention has the potential to galvanize advocates from diverse fields, including cancer, reproductive health, adolescent health, and immunization, to name a few. PATH knows from experience that the impact of many advocates can be far greater than that of one individual organization working independently. We were therefore instrumental in the creation of a global advocacy coalition called Cervical Cancer Action or CCA (www.cervicalcanceraction.org) and PATH has



The CCA "Report Card" describes the state of current cervical cancer prevention worldwide. Available at www.cervicalcanceraction.org.

chaired the group since it was established. Other key CCA partners include the Pan American Health Organization (PAHO), the Union for International Cancer Control, Cancer Research UK, the American Cancer Society, the International Federation of Gynecology and Obstetrics or FIGO, the AIDS Vaccine Advocacy Coalition, Grounds for Health, and the International Planned Parenthood Federation (IPPF).

CCA quickly identified areas where we could drive the cervical cancer prevention agenda forward. For example, PATH and our CCA partners learned in late 2007 that WHO's Strategic Advisory Group of Experts (SAGE) on immunization had asked whether there was any evidence that developing world governments were interested in cervical cancer prevention. The GAVI Alliance Board, who were at that time considering whether they should adopt HPV vaccine, had a similar question. In response, PATH, in collaboration with UICC, produced CCA's "Evidence of Support for Improved Cervical Cancer Prevention in Developing Countries," a dossier compiling personal letters of support from ministries of health, nongovernmental organizations, and individuals in Africa, Asia, and Latin America. The dossier also includes editorials, op-eds, resolutions, and declarations calling for improved cancer control, along with the names of the 1,200 people who endorsed CCA's online Global Call to Stop Cervical Cancer. Hard copies of the dossier—which ran well over 200 pages—were hand-delivered to every SAGE and GAVI Board member. It seems that the dossier helped reassure both groups that there was strong interest in both HPV vaccine and cervical screening in Africa, Asia, and Latin America. In 2008 the GAVI Board voted to include HPV in its vaccine portfolio and in 2009 the SAGE issued strong recommendations for HPV vaccination. One can still peruse the dossier on the RHO Cervical Cancer website (www.rho.org/CCAdossier), where it has been posted for use by any interested advocacy group.

In addition to the dossier, CCA has organized global webinars, made presentations at the United Nations and other international venues, and produced a number of publications. The most popular of these is *Progress in Cervical Cancer Prevention: The CCA Report Card*. The report

assesses global readiness to fight cervical cancer using the latest approaches and technologies, especially in regions where the disease is a common killer. It also underscores the urgent need for the global community to prioritize cervical cancer prevention and control on global health and development agendas. The report includes maps showing adoption of VIA, HPV DNA screening, and HPV vaccination worldwide. Both the report and the maps are available on the Cervical Cancer Action website (www.cervicalcanceraction.org) in English, French, and Spanish.

Disseminating the evidence

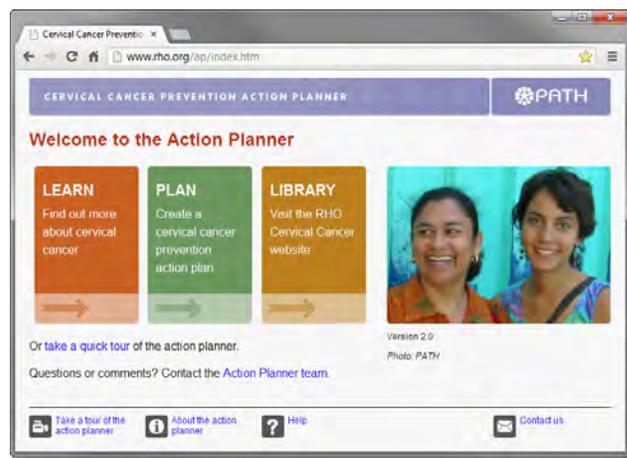
Given the clear need for better access to scientifically accurate information on cervical cancer, one of the first communication and advocacy tools PATH developed under the HPV vaccine project was the RHO Cervical Cancer website (www.rho.org), a comprehensive library of cervical cancer information. The website offers background papers, training materials, films, PowerPoint presentations, and a host of other documents and tools published by the world's leading HPV experts and organizations, including WHO, the US Centers for Disease Control and Prevention, US National Cancer Institute, UICC, PATH, and many others.

Sometimes news must be disseminated quickly, and waiting for users to visit a website is not adequate. PATH created *HPVflash* email updates to share timely, cervical cancer-related information around the globe. Recent alerts included an announcement about GAVI accepting applications for HPV vaccine, the licensing of *careHPV* in China, and invitations to the most recent CCA webinars. Readers can subscribe to *HPVflash* at: www.rho.org/subscribe.

Additionally, since the beginning of the project, PATH staff have contributed to or published more than 80 articles or reports documenting evidence on cervical cancer prevention. One paper designed for broad distribution is the HPV issue of PATH's flagship reproductive health resource, *Outlook*. It provides an easy-to-understand overview of the subject, and is available in English, French, and Spanish (see list of resources on page 12).



The *Outlook* issue on cervical cancer is a 12-page primer on prevention of the disease in low-resource settings. Available at www.rho.org.



PATH's Cervical Cancer Prevention Action Planner was designed especially for developing world program managers. Use the online tool at www.rho.org/ap.

ADVICE AND ASSISTANCE WITH CERVICAL CANCER PROGRAM PLANNING

PATH offers many resources to help when considering, or planning, HPV vaccination and cervical screening programs. Our Cervical Cancer Prevention Action Planner is an interactive, online tool that helps decision-makers think through the pros and cons of various options, and links them with helpful documents, tools, sample forms, and training and educational materials.

Agencies and governments are welcome to contact PATH directly to request technical assistance with program planning or evaluation (see PATH contact information on the back cover).

CONCLUSION

PATH is proud to have been involved in so many aspects of cervical cancer prevention, and for so many years. We are keen to share our knowledge about HPV vaccination and cervical screening strategies and systems with countries that are ready to reduce the burden of disease they suffer.

Political will for improved prevention is growing and the technical data are clear—it is possible to do something about cervical cancer in the developing world. We know how to train health workers to perform appropriate and effective procedures like VIA and to treat women using cryotherapy. And one day soon, when low-cost HPV-DNA tests become commonplace, the same trained staff can use the new tests as well. We know that a screen and treat approach can be incorporated into primary-care services and that it brings the services closer to where women reside, reduces the number of clinic visits required, and reduces barriers to screening and follow-up care. These lifesaving interventions are available and proven.

HPV vaccine also has an important role to play in a comprehensive cervical cancer control program. While screening is needed for women who may already have been infected with HPV, vaccines can protect young adolescent girls against infection in the first place. This comprehensive prevention strategy—screening plus vaccination—has the potential to save millions of lives over the next decades.

There is no need for any woman to die of cervical cancer in this day and age. And there is no excuse for countries, and the global health community, to fail to implement safe, effective vaccination and screening programs. The time for action is now.

PATH will continue working to ensure that every woman can realize her right to screening, and every girl her right to HPV vaccination.

KEY CERVICAL CANCER RESOURCES

RHO Cervical Cancer—an online collection of evidence-based information from the world’s leading institutions
www.rho.org

Outlook. Preventing Cervical Cancer: Unprecedented Opportunities for Improving Women’s Health
www.rho.org/ccresources.htm#outlook

Cervical Cancer Prevention: Practical Experience Series (PATH)
www.rho.org/HPV-practical-experience.htm

Evidence of Support for Improved Cervical Cancer Prevention in Developing Countries
www.rho.org/CCAdossier

PATH Cervical Cancer Programs
www.path.org/cervicalcancer

Cervical Cancer Action
www.cervicalcanceraction.org

Short BBC documentary on cervical cancer in Uganda (“Kill or Cure: The Real Lady Killer”)
www.rho.org/multimedia.htm

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PATH is an international nonprofit organization that transforms global health through innovation. We take an entrepreneurial approach to developing and delivering high-impact, low-cost solutions, from lifesaving vaccines and devices to collaborative programs with communities. Through our work in more than 70 countries, PATH and our partners empower people to achieve their full potential.

MAILING ADDRESS
 PO Box 900922
 Seattle, WA 98109 USA

STREET ADDRESS
 2201 Westlake Avenue
 Suite 200
 Seattle, WA 98121 USA

info@path.org
www.path.org