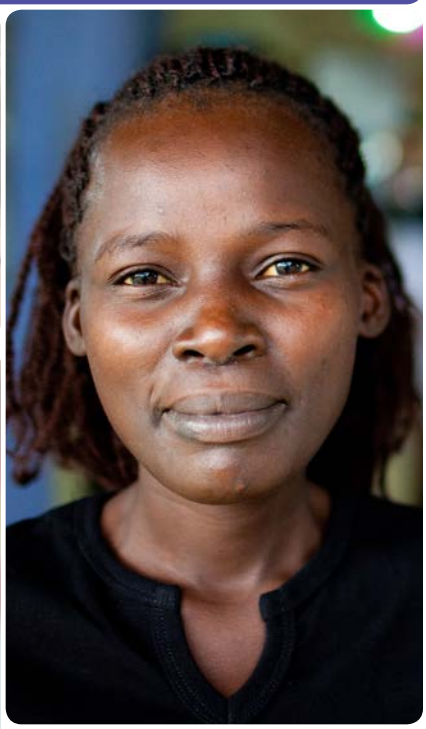
Cervical Cancer Prevention:
Practical Experience Series

Cervical cancer screening and treatment in low-resource settings

PRACTICAL EXPERIENCE FROM PATH | 2013



PATH

Dr. John Sellors (1946–2011)

This paper is dedicated to the memory of Dr. John Sellors. Many of the lessons and insights in these pages were generated on John's watch.

John was a passionate advocate for improved reproductive health. His career took him from work on sexually transmitted diseases as the director of the family practice unit at McMaster University in Hamilton, Canada, to directing PATH's START project, where he developed new alternatives for cervical precancer screening and treatment, especially for low- and middle-income countries.

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ABOUT PATH

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.

Headquartered in Seattle, Washington, PATH operates offices in 33 cities in 22 countries. PATH currently works in the areas of health technologies, maternal and child health, reproductive health, vaccines and immunization, and emerging and epidemic diseases.

For more information, please visit www.path.org.

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INTRODUCTION TO THE CERVICAL CANCER PREVENTION: PRACTICAL EXPERIENCE SERIES

About the PATH HPV vaccination demonstration projects

From 2006 to 2011, PATH conducted HPV vaccination demonstration projects in four low- to middle-income countries—India, Peru, Uganda, and Vietnam—to provide evidence for decision-making about public-sector introduction of human papillomavirus (HPV) vaccines. The *Cervical Cancer Prevention: Practical Experience Series* of five units summarizes lessons learned that can help guide future cervical cancer prevention program planning, especially in low-resource settings around the globe.

In conducting the vaccination demonstration projects, PATH worked closely with ministries of health, civil society organizations, and other key stakeholders to carry out formative and operations research in each country. The studies looked at a variety of vaccine introduction questions, including how sociocultural barriers may impede acceptance of the vaccine; how the vaccine can be most effectively delivered to adolescent girls; how HPV vaccination can be integrated into (and strengthen) existing health programs; and what the cost of implementing HPV vaccinations might imply for health programs.

Each Practical Experience unit focuses on an important aspect of cervical cancer prevention:

1. **Strategic Planning and Situation Assessment for Cervical Cancer Prevention.** The first unit helps decision-makers and program planners focus on key "big picture" questions about cervical cancer prioritization and on opportunities and challenges for improved cancer prevention in their countries.
2. **Conducting Formative Research for HPV Vaccination.** The second unit demonstrates that preliminary formative research is a necessary component of overall planning, discusses formative research issues specific to cervical cancer, and explains how research results may be used for strategic planning within the cervical cancer context.
3. **Implementing HPV Vaccination Programs.** The third unit offers resources on general immunization topics such as how to set up an immunization site or to give a safe injection. However, the main focus is on practical issues relevant to HPV vaccination, such as working in school settings and developing effective messaging about the vaccine.
4. **Evaluating HPV Vaccination Programs.** The fourth unit focuses on how program monitoring and evaluation can be accomplished within existing health infrastructures in an efficient manner.
5. **Cervical Cancer Screening and Treatment in Low-Resource Settings.** The fifth and final unit (this document) of this series examines the second component of a successful cervical cancer prevention program—screening and treatment of adult women for precancerous lesions.

For information about cervical precancer screening and treatment and related topics, visit the RHO Cervical Cancer Library (www.rho.org).

For more information about PATH's cervical cancer vaccine project, visit: www.path.org/projects/cervical_cancer_vaccine.php or contact info@path.org.

PATH resources for information on cervical cancer and HPV vaccination

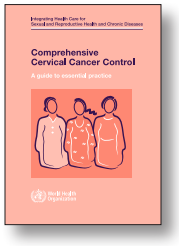
Information on cervical cancer

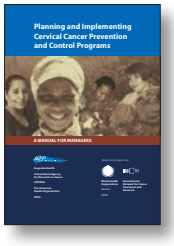
- The RHO Cervical Cancer Library is a comprehensive online source for detailed information about cervical cancer and how it can be prevented.
- *Outlook*: Progress in preventing cervical cancer: Updated evidence on vaccination and screening is a 12-page primer on all aspects of cervical cancer prevention, published in 2010.
- PATH's Cervical Cancer Prevention Action Planner provides a wealth of information and interactive exercises to assist with program planning.

Key resources on screening and treatment

- Comprehensive Cervical Cancer Control: A Guide to Essential Practice
  This WHO manual, also known as the "Pink Book," is an excellent source of information about cervical cancer and its prevention. The 2006 version is available from the WHO website and from the RHO website. An updated, expanded version will be published in 2013. Be sure to look for the new volume on the RHO and WHO websites.
- Planning and Implementing Cervical Cancer Prevention and Control Programs: A Manual for Managers
  Published in 2004, this detailed and practical manual by the ACCP focuses on VIA and cryotherapy programs in particular.
- Evidence-Based, Alternative Cervical Cancer Screening Approaches in Low-Resource Settings andRecent Evidence on Cervical Cancer Screening in Low-Resource Settings
  A 2009 article, along with a 2011 update, were authored by ACCP partners.

All resources are available online at www.rho.org/HPV-screening-treatment.htm.





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ABBREVIATIONS/ACRONYMS

ACCP	**Alliance for Cervical Cancer Prevention**
CICAMS	**Cancer Institute, Chinese Academy of Medical Sciences**
HPV	**Human papillomavirus**
LEEP	**Loop electrosurgical excision procedure**
NGO	**Nongovernmental organization**
PATH	**Program for Appropriate Technology in Health**
START	**Screening Technologies to Advance Rapid Testing for Cervical Cancer Prevention**
START-UP	**Screening Technologies to Advance Rapid Testing for Cervical Cancer Prevention—Utility and Program Planning**
UNFPA	**United Nations Population Program**
VIA	**Visual inspection with acetic acid**
VILI	**Visual inspection with Lugol's iodine**

Introduction

This unit presents basic information about cervical precancer screening and treatment, with a special focus on PATH experience with screening programs in low-and middle-income countries. In addition to providing useful guidance and sharing lessons learned, the unit also includes links to a diverse array of background documents, program management tools, and training and educational materials, all available for free online from PATH and other organizations.

Many of the lessons and resources included here were generated through four projects implemented by PATH and partners. For more information about these projects, visit the PATH website (www.path.org).

The Alliance for Cervical Cancer Prevention

In 1999, five international health organizations came together to create the Alliance for Cervical Cancer Prevention (ACCP). For the next eight years, the partners worked on a coordinated research agenda aimed at assessing a variety of approaches to cervical cancer screening and treatment (especially those that may be better suited to low-resource settings), improving service delivery systems, ensuring that community perspectives and needs are incorporated into program design, and increasing awareness of cervical cancer and effective prevention strategies. On the basis of their findings, in 2009 the ACCP partners summarized and shared key findings and recommendations for effective cervical cancer screening and treatment programs in a peer-reviewed paper in the journal *International Perspectives on Sexual and Reproductive Health*. Their findings are summarized on page 6.

START and START-UP

PATH's START project (Screening Technologies to Advance Rapid Testing for Cervical Cancer Prevention, 2003–2007) focused on developing two simple, rapid biochemical tests that would be less expensive than the current HPV DNA test, acceptable to women and health care providers, safe, accurate, reliable, and appropriate for use in low-resource settings. The *care*HPV™ Test, from QIAGEN, Inc., detects cancer-causing (oncogenic) human papillomavirus (HPV) DNA. The Arbor Vita OncoE6™ Cervical Test, from Arbor Vita, Inc., detects the E6 oncoprotein biomarker.

A follow-up project, called START-UP (Screening Technologies to Advance Rapid Testing for Cervical Cancer Prevention—Utility and Program Planning, 2007–2013) built on START activities, carrying out demonstration projects in three low-

* The five original ACCP partners were EngenderHealth, International Agency for Research on Cancer, Jhpiego, Pan American Health Organization, and PATH. In 2008, three new partners joined the Alliance: the International Union Against Cancer, Partners in Health, and Programme of Action for Cancer Therapy/International Atomic Energy Agency.

resource countries to generate evidence on field use of *care*HPV™ in real-world public health settings. The project also explored options for the use of vaginal HPV sampling by a trained provider or by the woman herself (self-sampling). START-UP also evaluated the clinical utility of the OncoE6™ test by conducting clinical research in China in collaboration with the Cancer Institute, Chinese Academy of Medical Sciences (CICAMS).

HPV Vaccines: Evidence for Impact

In 2006, PATH initiated the *HPV Vaccines: Evidence for Impact* project (2006–2012) to generate evidence to help policymakers and planners worldwide make informed decisions regarding regional and national HPV vaccine-introduction efforts. The main project activities were implemented in India, Peru, Uganda, and Vietnam.

All four countries also implemented limited precancer screening and treatment initiatives as part of the broader projects. The objective was to assess service implementation and to explore the barriers and facilitating factors to continuing and expanding screen-and-treat cervical cancer prevention programs using visual inspection with acetic acid (VIA) and cryotherapy.

The following document summarizes the accumulated learning and resources of these four initiatives, which PATH hopes will facilitate an expansion of cervical precancer screening and treatment services. We look forward to the day when cervical cancer mortality in the developing world reaches the low rates already found in wealthier countries. Improved screening and treatment programs are crucial to achieving that goal.

PATH/Miguel Alvarez

Understanding cervical cancer screening and treatment

HPV and cervical cancer

Cervical cancer is a preventable disease affecting an estimated 530,000 women each year and leading to nearly 275,000 deaths.[1] If current trends continue, by the year 2050 there will be more than one million new cases annually.

About 88 percent of women dying from cervical cancer reside in developing countries.[1] The lack of effective screening and treatment programs in these countries is the main cause of this health inequity.

Research conducted over the past 30 years established that HPV is the primary cause of cervical cancer. HPV infection is very common; the majority of men and women become infected within a few years after becoming sexually active. The HPV types that cause most cervical cancer cases—about 70 percent worldwide—are types 16 and 18.[2]

Infection rates for women tend to be high during their teens and 20s. Most women spontaneously clear infections within a year or two, but in about 10 percent of infected women the infection persists, causing precancerous lesions to develop. If not detected through screening programs (and then treated), precancer develops into invasive cancer in about 10 percent of women with lesions (about 1 percent of all infected women).[3]

Fortunately, cervical cancer does not develop quickly. The progression from infection to precancer takes 10 to 20 years, and from precancer to cancer another 10 or 20 years. Therefore there are many opportunities to stop the disease before it becomes fatal.

Currently there are two ways to prevent cervical cancer: HPV vaccination to prevent infection, and cervical screening to detect disease early, when it is easier to cure.

HPV vaccines provide protection against the two HPV types that cause most cervical cancer, but not against all cancer-causing HPV types. Because the vaccines do not protect against all types, girls vaccinated now will need to be screened as adults to prevent disease caused by other HPV types. Screening also is crucial to protect the many women living in the world today who have already been infected, and for whom vaccination offers little benefit.

Most experts agree that countries should consider comprehensive cervical cancer prevention, offering programs for screening and treatment of adult women for

precancer and cancer, as well as HPV vaccination of young adolescent girls. A good example of a comprehensive strategy for prevention is the Strategic Plan for Cervical Cancer Prevention and Control in Uganda.

A recent issue of PATH's publication *Outlook*, Progress in Preventing Cervical Cancer: Updated Evidence on Vaccination and Screening, provides an overview of cervical cancer and current prevention options, including both vaccination and screening.

Screening for cervical precancer and cervical cancer

If not detected and treated early, cervical cancer kills. Over the past 50 years, widespread use of cytology (the Pap smear) to test for early signs of disease has resulted in a dramatic decline in cervical cancer deaths in wealthier countries. But the situation is different in the developing world, where there is a shortage of efficient, high-quality screening programs. Even in well-resourced countries with high-quality screening programs, inequities exist among different population groups.

Cervical Cancer Screening Methods

- Cytology (Pap smear)
- VIA (visual inspection with acetic acid) or VILI (with Lugol's iodine)
- HPV DNA testing

Ideally, all women over the age of 30 should be routinely screened for precancerous lesions of the cervix, but in reality only a small percentage of women are.[4]

Although cytology-based screening programs using Pap smears have been effective in the United States and other developed countries, most developing countries lack the infrastructure and trained personnel needed for that sort of technician-dependent, multi-visit testing approach. Therefore, in situations where health care resources are scarce, resources should be directed toward cost-effective strategies that are more affordable and for which quality can be assured. For this reason, PATH cervical cancer prevention programs generally have not focused on Pap, and we have not included a section on Pap in this paper.

Studies have shown that the most efficient and effective strategy for secondary prevention of cervical cancer in low-resource settings is to screen using either HPV DNA testing or VIA (visual inspection with acetic acid), then to treat precancerous lesions using cryotherapy (freezing affected tissue on the cervix), as appropriate, and to refer women needing more complex care.[4]

VIA is a low-cost procedure that can be done in any clinic. VIA has been shown to be about as effective, or more effective, than Pap testing in identifying cervical cancer precursors, but Pap requires much more sophisticated equipment, training, and logistics systems. Lessons learned about VIA begin on page 12.

HPV DNA testing—a high-tech solution—is more sensitive than either VIA or Pap, but current tests are expensive and require a laboratory. Fortunately, easier-to-use and less expensive HPV DNA tests soon will become available, and may

revolutionize cervical cancer screening around the globe. See page 14 for lessons learned about HPV DNA testing.

Subsequent to screening using an HPV DNA test, VIA is still useful for treatment selection to identify those patients for whom cryotherapy is not appropriate.

While HPV DNA tests perform best (they have the highest sensitivity) when cervical samples are used, those samples can be collected only during a pelvic examination. Unfortunately, providers trained to perform pelvic examinations often are in short supply in the developing world, as is the equipment needed for the exam (specula and gloves, for example).

However, data recently generated by PATH's START-UP project suggest that HPV DNA collected from the vagina yields test results more sensitive than VIA or Pap smear, but slightly less sensitive than cervical specimens, and without the need for a pelvic exam. The sampling may be done by a provider; additionally, several studies have shown that women can be taught to use a soft brush to swab the vaginal wall near the cervix and to gather the mucus sample themselves.

It should be noted that in developing countries, cervical cancer screening once, twice, or three times in a lifetime could have a significant impact on the lifetime risk of cervical cancer, compared with no screening.

Computer models using data related to five low- and middle-resource countries projected that screening women once in their lifetime, at the age of 35 years, with a one-visit or two-visit screening strategy involving VIA or DNA testing for HPV in cervical cell samples, reduced the lifetime risk of cancer by approximately 25 to 36 percent. Relative cancer risk declined by about 70 percent after two screenings (at 35 and 40 years of age).[5]

Treatment of cervical precancer

Cryotherapy has been shown to be a safe, effective treatment for the majority of cases of cervical precancer.

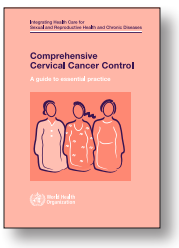
Main Precancer Treatment Methods in Low-Resource Settings

- Cryotherapy (freezing)
- Loop electrosurgical excision procedure (LEEP)
- Cold knife conization

Cryotherapy, when conducted by a competent provider, results in cure rates of 75 to 85 percent. It requires some special equipment, but it is simpler than other methods for treating precancerous lesions.

For cases where cryotherapy is not appropriate, other treatment methods may be available at higher-level facilities, such as loop electrosurgical excision procedure (LEEP) or cold knife conization.

The WHO manual Comprehensive Cervical Cancer Control: A guide to essential practice is an excellent resource on both screening and treatment, but be sure to look for the new version on the WHO website (to be published in 2013).



The RHO Cervical Cancer Library has an extensive selection of free documents, tools, presentations, videos, and other resources related to cervical cancer screening and treatment.

ACCP Key Findings on Screening and Treatment (2009)*

1. Simply providing new screening and treatment technologies and approaches is not sufficient to ensure uptake and program success.
2. In low-resource settings, the optimal age-group for cervical cancer screening to achieve the greatest public health impact is 30–39-year-olds.
3. Although cytology-based screening programs using Pap smears have been shown to be effective in the United States and other developed countries, sustaining high-quality cytology- based programs is difficult in low-resource settings. Therefore, in settings where health care resources are scarce, they should be directed toward cost-effective strategies that are more affordable and for which quality can be assured.
4. The most efficient and effective strategy for detecting and treating cervical cancer precursors in low-resource settings is to screen using either VIA or HPV DNA testing and then to treat using cryotherapy (freezing). This strategy is optimally achieved in a single visit and can be carried out by competent physicians and non-physicians, including nurses and midwives.
5. The use of HPV DNA testing followed by cryotherapy results in a greater reduction in the incidence of cervical cancer precursors than the use of other screen-and-treat approaches.
6. When conducted by competent providers, cryotherapy is a safe way of treating precancerous cervical lesions and results in cure rates of at least 85%.
7. Unless cervical cancer is suspected, the routine use of an intermediate diagnostic step (such as colposcopy) between screening and treatment is generally not efficient and may result in reduced programmatic success and increased cost.
8. Women, their partners, communities, and civic organizations must be engaged in planning and implementing services, in partnership with the health sector.
9. For maximum impact, programs require effective training, supervision, and continuous quality improvement mechanisms.
10. Additional work is needed to develop rapid, user-friendly, low-cost molecular tests and to improve cryotherapy equipment.

* The key findings above were published in this form by ACCP in 2009. The following year the authors published an expanded, peer-reviewed paper that summarized the evidence and rationale for the findings.[4]

Lessons related to precancer screening and treatment in general

Over the years, PATH and the ACCP have conducted formative research and evaluated programs in Africa, Asia, and Latin America, with the aim of better understanding the types of barriers women face in accessing cervical cancer screening and treatment services and the challenges that health program managers must overcome to provide sustainable, reliable, high-quality services.

David Jacobs

Interestingly, while researchers noted differences in different countries, overall the findings are remarkably similar, even when coming from diverse societies. For example, it is common for women all over the world to report that they generally would prefer that a female conduct their pelvic examination, or to point out that long distances to travel and long wait times at clinics make it more difficult for them to be screened.

Some key reasons women gave for seeking screening services included:

- They were concerned about cancer: they feared death or feared that their children would be left without a mother.
- They worried about discomfort or pain they were experiencing.
- They were referred for screening by a health care provider or other knowledgeable figure.
- A screening project or campaign was promoted in their community or they were exposed to effective community outreach.

Factors that improve access and attractiveness of screening and treatment services, as reported by clients and providers, included:

- Services (screening and treatment) were convenient and low cost, and did not take too much time.
- Staff was trusted and was friendly; they explained procedures clearly.
- Test results were available rapidly (same day or within a few days).
- They had strong family support for the procedure, especially spousal support.
- They also felt community support. Their communities supported screening and women who sought screening were not stigmatized.

Respondents also reported factors that hinder access to screening and treatment services:

- The clinic was far from their homes, transportation was difficult, it took too much time to go to the clinic, there were long wait times for services, and/or associated costs were too high.
- There was lack of capacity to serve all women who came for screening and some were turned away.
- The clinics lacked space and equipment for VIA or cryotherapy, or they did not have specula, vinegar, or gas.
- Services were not offered at times or on days when women were free to come.
- Staffing issues: providers were stretched thin by demand for services, they faced a heavy workload and felt burned out, and there was high staff turnover and loss of trained VIA providers.
- Because most clinics offering screening did not also have follow-up and treatment available in the clinic, and women had to be referred for treatment to another facility, many women dropped out of the process before receiving treatment. The longer the delay between the screening test and treatment, the greater the drop-out rate.
- For women receiving Pap services there was a long delay getting results.
- Sometimes employers did not give permission for the women to miss work and attend the clinic.
- Sometimes cryotherapy equipment broke down and there were no replacement parts.
- In some countries only doctors were allowed to perform cryotherapy, not nurses or other trained staff, and access to the doctors was limited.

Lack of information and cultural barriers also play a role in preventing women from being screened:

- Often in communities, and even among providers, there are low levels of knowledge about screening in general and specifically about the availability/timing of screening and treatment services. However, this situation is changing.
- Women may not go for screening because they do not perceive themselves to be at risk or do not perceive that there is any benefit. There is the misconception that "cancer is incurable, so what is the point of screening?" Many only seek care when they experience symptoms.
- One of the most common fears mentioned was that they would be diagnosed with cancer. They feared needing treatment (often assumed to be surgery), feared "losing a part of the womb," and worried about subsequent infertility or inability to perform sexually.
- Many women had heard rumors about screening that caused them to be afraid. Sometimes they confused screening (which, while it can be

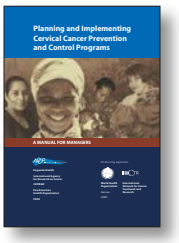
uncomfortable, generally is not painful) with surgical treatment of advanced cancer—like a hysterectomy—or with a biopsy. For these reasons, many women said that fear of pain during screening was an important barrier.

- Many reported that women dislike a speculum exam. Some also had concerns that the procedure might be difficult or might cause, or accelerate, cancer spread.
- Women were concerned about stigmatization associated with having cancer. Some worried about what people would say if they knew she had gone for screening.
- Sometimes husbands or family elders objected and would not give permission to go to the clinic. In some cases the subject of the exam was so embarrassing that the woman did not want to discuss it with her husband.
- Many women prefer to present to a female provider and feel shy or embarrassed exposing their genital region to a male doctor when they are not in pain or giving birth. Men often did not want their wives "viewed" by a male provider.
- In some places families do not have faith in the quality of public health clinics—some were concerned for example about whether the specula had been properly sterilized and whether "dirty" equipment could spread infection or cause cancer.

See pg. 21 for links to sample educational materials for health workers and communities.

Lessons related to successful screening program strategies

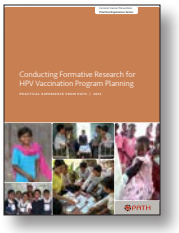
Key lessons relating to program strategy are summarized below. Detailed guidance for developing screening and treatment programs can be found in ACCP's Planning and Implementing Cervical Cancer Prevention and Control Programs: A Manual for Managers.



- **Audience research**: An overarching lesson is that data from formative research—including client and provider needs assessments and health facility assessments—are extremely valuable when designing cervical cancer screening and treatment programs and educational materials.

  While formative research can be organized in a rigorous and formal manner when human and financial resources allow, even rapid and simple studies can yield findings that are useful and can ensure that women, their families, and community organizations are consulted about the kinds of services that

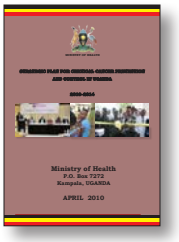
are most accessible and attractive to them so that program managers may actively address anything that impedes maximum use of services.



PATH's Conducting Formative Research for HPV Vaccination Program Planning provides guidance in selecting appropriate audience research methods and strategies for any type of cervical cancer prevention programming.

- **National program guidelines**: It also is clear that national cervical cancer prevention guidelines, which have been endorsed and promoted by local medical professional organizations and especially OBGYNs, provide valuable technical and political support for program planners.

  Such guidelines can help designers to match screening modalities with specific situations most appropriately. For example, they may endorse cytology (Pap) in areas where the infrastructure supports it (perhaps the capital city) and promote VIA or HPV testing in other areas. The Strategic Plan for Cervical Cancer Prevention and Control in Uganda is a good example.



  Guidelines may also support "task shifting"—training nurses and other non-physicians to screen clients (using VIA or HPV-DNA testing) and in some cases to treat them as well (using cryotherapy). It will be difficult to develop the human resources needed for large-scale screening efforts if clinical services can only be performed by physicians.

- **Improving treatment follow-up**: A weakness in many screening programs has been the link between screening and treatment, and especially ensuring access to treatment in a timely manner. Data clearly show that the longer the gap between the screening test, obtaining the test result, and obtaining treatment services, the more a program suffers from "loss to treatment"—women who screened positive but never returned for treatment, and who one day may find themselves suffering from invasive cervical cancer.

David Jacobs

Treatment of screen-positive women is best achieved in a single visit. But if treatment is not possible during the same clinic visit, it should be arranged as soon as possible, and as conveniently as possible for the women, so as to reduce loss to treatment.

Offering treatment services at or near the health facility where women were screened has been shown to improve access to treatment, but not all clinics can afford cryotherapy equipment, or have the volume of patients needed to justify such an expense. Furthermore, not all precancer cases are treatable with cryotherapy and some women will require treatment with LEEP, cold knife conization, or other procedures only available at higher-level facilities.

When screening results are not immediately available (e.g., with Pap or HPV DNA), it is crucial to develop an effective system to follow up with women, provide their test results and, most importantly, to offer treatment to screen-positive women. Effective recall systems can be difficult in situations where people do not commonly have telephones. And even when it is possible to call, sometimes the cost of a phone call was a barrier, as PATH found in Uganda. Each program or clinic will need to design a follow-up system best suited to local conditions.

- **Increasing convenience for women**: Standard clinic hours may not be convenient for women who work in the fields or in a factory or an office. For example PATH has observed that in some countries women have more time available in the afternoon, but clinics offer screening only in the morning. Access to screening may be enhanced by offering women's health services at times when women are more likely to be able to attend—on holidays or times when women may routinely come to town (such as on market days).
- **Equipment and supplies**: Repairing broken cryotherapy equipment and maintaining sufficient supplies of vinegar (for VIA) and carbon dioxide (CO_2) or nitrous oxide (N_2O) gas for cryotherapy also has been a challenge. In order for cryotherapy to be sustainable, it is advisable to develop local capability for repairing or replacing the equipment. And while it would seem that something as inexpensive and common as vinegar should be easy to procure, if it is not included on standard Ministry of Health resupply forms—or in the clinic's budget—managers report having to go to the market to purchase vinegar using their own money.
- **Monitoring**: Plans for quality-control monitoring should be considered from the beginning of the program development process. Monitoring helps identify areas that require additional support or supervision (e.g., higher or lower than expected positivity rates and low same-month treatment rates). However, routine monitoring of screening and treatment can be difficult to implement if overall health information systems are weak.
- **Messaging**: When promoting screening services, emphasize that:
  - A positive screening result does not usually signify cancer; it most often signifies a precancerous (early) condition.
  - When cervical cancer is treated early (precancer stage), treatment tends to be fast, painless, and effective, often without any cutting.

- Screening and early treatment can prevent the "loss of the womb." Surgery is more likely when cancer is allowed to advance.
- Cervical cancer does not result in obvious symptoms until the cancer has advanced. At that point it is difficult to treat. It is important to be screened even if you feel healthy.
- Women who come for screening and the age of those women should be consistent with recommendations in your country.
- If your formative research shows that families are concerned about the safety of screening, when offering pelvic examinations, reassure women that the instruments have been sterilized and that there is no reason to worry about "catching" cancer during screening or that existing cancer would spread more rapidly after screening (some people believe that).

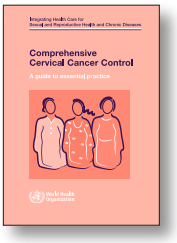
Lessons specific to VIA

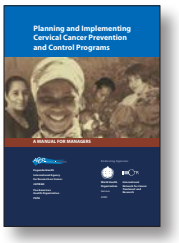
PATH and other ACCP partners have worked with VIA programs in the developing world for many years. The evidence in support of VIA as a primary screening method and for treatment selection is strong, and VIA is featured prominently in cervical cancer screening guidance from the World Health Organization, the International Federation of Gynecology and Obstetrics, the United Nations Population Programme, the ACCP, the Cervical Cancer Action coalition, PATH, and many other organizations.

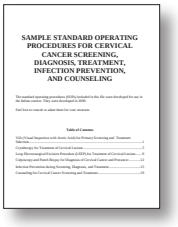
The findings below come from years of experience with the method, and most recently, from audience research conducted in Africa, Asia, and Latin America by PATH and local partners.

The WHO "Pink Book" and ACCP's Planning and Implementing Cervical Cancer Prevention and Control Programs: A Manual for Managers both are excellent, detailed resources on VIA programming.

A set of sample standard operating procedures for cervical cancer screening, diagnosis, treatment, infection prevention, and counseling used in India includes information on VIA.







Client- and provider-perceived benefits of VIA

- VIA is more sensitive than cytology (though less sensitive than HPV DNA testing).
- Results of VIA are available immediately.
- VIA also provides immediate guidance in treatment selection (e.g., whether the lesions are treatable with cryotherapy, or whether there is a suspicion of invasive cancer).

- VIA screening by an experienced professional requires only 10 to 15 minutes.
- VIA is relatively inexpensive to provide, but some equipment (exam table, speculum) and supplies are needed (especially vinegar for VIA and CO_2 or N_2O gas for cryotherapy).
- Because results are immediate, in some situations women can be screened and treated (with cryotherapy) during a single visit. But even if cryotherapy is not available at the screening site, with VIA the screen-positive woman can be counseled and referred to treatment during her screening visit. This may result in reduced loss to treatment and likely will be more convenient and less expensive for the women.
- Nurses and other non-physicians have been successfully trained to perform VIA (and cryotherapy) and training takes only one to two weeks.
- Investing in VIA now makes sense for many countries because they can begin preventing cancer immediately and will also be preparing themselves to introduce new screening tests when they become affordable. In such cases, VIA may be replaced by HPV DNA testing as a primary screening tool, but VIA still will be useful for treatment selection.

Client- and provider-perceived drawbacks of VIA

- Sensitivity is lower than HPV DNA testing.
- VIA requires a pelvic exam (unlike vaginal sampling with HPV DNA).
- VIA requires training and continuing supervision (but much less than Pap).
- VIA assessments are more subjective than HPV DNA and results can vary from one provider to another and even from one day to another.
- Because the evidence supporting VIA is relatively new, some health professionals may not be aware of the data and may not accept VIA; they may think of it as "second-class medicine."

Strategies appropriate for VIA

- Introduce VIA and associated treatment methods as broadly as possible in regions where there are no existing screening programs, where they are weak, or where current coverage with Pap is low.
- Introduce cryotherapy as broadly as possible. However, due to costs it may be necessary to designate one treatment center offering cryotherapy to serve a cluster of screening centers. Higher-level facilities offering LEEP or other treatment options also will be necessary to treat cases not appropriate for cryotherapy.
- Invest in high-quality training in both VIA and treatment, including ongoing quality control and supportive supervision (see section on training below).
- In order to meet the demand for screening services, create regional and national training centers focused on teaching VIA and cryotherapy clinical skills and program management.

Messaging specific for VIA

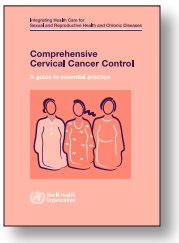
- Women no longer have to wait a long time for exam results (unlike for Pap). You will have your result immediately.
- VIA uses the same vinegar we cook with (don't use the term "acetic acid" as "acid" can be frightening to women).

Lessons specific to HPV DNA testing

HPV DNA testing has been available in wealthier countries for years. PATH worked with two medical equipment companies (Digene, which later was bought by QIAGEN) to adapt technology from a laboratory-based, rather expensive HPV DNA test called Hybrid Capture II™ and to create a more "field-friendly" test , now called *care*HPV™. The lessons below relate primarily to *care*HPV™, though some also are relevant to other molecular tests.

HPV DNA testing has been endorsed as a primary screening method by the World Health Organization, the International Federation of Gynecology and Obstetrics, the United Nations Population Program (UNFPA), the ACCP, the Cervical Cancer Action coalition, PATH, and many other organizations.

The findings below come from a decade of experience with the method, and most recently, from audience research conducted in Africa, Asia, and Latin America by PATH and local partners.



The WHO "Pink Book" is an excellent, detailed resource on HPV DNA programming.

Client- and provider-perceived benefits of HPV DNA testing

- HPV DNA testing is much more sensitive than VIA or Pap.
- *Care*HPV™ provides good results with either cervical or vaginal specimens (though sensitivity when using cervical samples is slightly higher).
- In cases where it would be culturally appropriate, clients can be taught to collect a vaginal sample themselves, in a private space at the clinic or at home.
- HPV DNA and other molecular tests are more objective than VIA or Pap.
- *Care*HPV™ results are available much more rapidly than Pap results.

Client- and provider-perceived drawbacks of HPV DNA testing

- At the time of writing this paper, no molecular tests are commercially available at the low prices needed for broad introduction. However, *care*HPV™ is slated for commercial distribution in 2013.

- Because the *care*HPV™ Test detects HPV infection rather than lesions, and infection can resolve spontaneously, use of HPV DNA testing may lead to some unnecessary treatment.
- Even if the cost of the tests plummets, because the test format is optimized for multiple samples to be run at the same time (90 samples in the case of *care*HPV™), HPV DNA testing could still be expensive for low-volume screening. On the other hand, waiting to gather enough samples for the test run to be cost-effective may delay delivery of results.
- Because the test requires two to three hours to produce results, and because samples likely will be batched for testing to save money, HPV DNA is less amenable than VIA to same-day screen and treat strategies.
- Because the evidence supporting HPV DNA testing is relatively new, health professionals in lower-resource settings may not be aware of the data and may not readily accept it. They may perceive HPV DNA testing as inappropriate or too high-tech for their setting.

Strategies appropriate for HPV DNA testing

- Develop a VIA-based screening platform now, then introduce HPV DNA or other molecular tests when they become affordable (and use VIA for treatment selection).

Messaging specific for HPV DNA testing

- The new test (*care*HPV™) works much better than the old test (Pap).
- It only takes a few minutes to take the sample, and the process is not painful.
- Results will be available later in the day, or the next few days (or whenever appropriate given your program).
- You can choose to have the test sample taken by a provider or you can do it yourself, in private (if the program offers self-sampling).

Lessons specific to vaginal sampling using *care*HPV™

There are advantages to offering pelvic examinations beyond cervical cancer screening and treatment. However, in most countries the capacity to conduct pelvic exams is low as is the capacity to treat conditions that pelvic exams might reveal. Furthermore, many women do not like pelvic exams because they are uncomfortable and may be embarrassing, so the exams can represent a barrier to achieving high screening coverage.

PATH/Jose Jeronimo

PATH studies in India, Nicaragua, and Uganda have shown that vaginal sampling, including self-sampling, is an attractive option for many women. Providers may initially be skeptical of self-sampling in particular, but in PATH's experience they quickly begin to see its potential for reducing the burden of pelvic examinations and expanding screening coverage.

Client- and provider-perceived benefits of vaginal sampling and self-sampling

- Vaginal sampling is rapid and convenient, both for women and for providers.
- Vaginal sampling avoids the discomfort associated with pelvic exams.
- Many women report that self-sampling was less embarrassing than exposing themselves during a pelvic exam. However, some patients reported that they did not like touching their genital area.
- The sensitivity of vaginal samples is acceptable, though it is slightly lower than for cervical samples. It is higher than for Pap or VIA.
- In general patients felt that self-sampling was easy to do once it had been explained to them clearly. Most said it was not painful.

Client- and provider-perceived drawbacks of self-sampling

- Some women had concerns about not sampling correctly. They were afraid that the sample might become contaminated or otherwise unsuitable. They worried that they "could not see down there" and they felt that a trained provider could collect a sample more reliably.

- Some—a minority—said that self-sampling was painful or uncomfortable or they were concerned about hurting themselves. Some worried about pushing the sample collection brush in too far, or they thought that the brush might be stiff or coarse. (In reality it is very soft.)
- Obese women may have trouble reaching their genital regions and may need the provider to obtain a sample (either cervical or vaginal).

Strategies appropriate for vaginal sampling and self-sampling.

- Consider offering vaginal sampling by nurses or other staff, or if the woman prefers, guide her to collect the sample herself.
- Vaginal sampling, without the need for a pelvic examination, has the potential to dramatically increase access to screening for many women around the world. For example, in campaign-style situations, 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 collect them at the end of the outreach visit or pick them up in a return visit). Even in a clinical setting, women could be trained to sample correctly and given a private place to do so, speeding sample collection.
- 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 a vaginal sample from the woman, freeing up higher-level clinic staff's time and increasing screening rates. Such strategies could have a major impact on screening coverage in low-resource settings.
- Some women may assume that the sample collection brush is coarse or stiff like a toothbrush or hairbrush. To reduce concerns about hurting themselves during self-sampling, when talking to women, show them the demonstration brush and how soft it is. Let them feel the brush on their arms.

Messaging specific for vaginal sampling and self-sampling

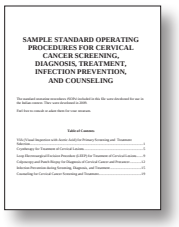
- A vaginal sample is nearly as good as a cervical sample.
- Speculum exams are not necessary for collecting vaginal samples.
- It is very easy to take a vaginal self-sample; many women in many countries have done it with no problem.
- Don't worry about doing it incorrectly or contaminating the brush; just follow the simple directions, step by step.
- Self-sampling can be done in private, even in your home if you wish.
- The brush used for sampling is very soft, like a feather (not like a hair brush) and it is very small. (Consider showing women the brush when explaining the procedure.)
- Insert the brush until you feel resistance. This should be 5 to 8 centimeters (2 to 3 inches), or half the length of the brush.

Lessons specific to treating cervical lesions with cryotherapy

There are a number of cervical precancer treatment options appropriate for lower-resource settings. PATH recently conducted a search for and evaluation of treatment technologies and scored them for how they met a set of criteria important in low-resource areas. The treatments include excision methods such as the loop electrical excision procedure (LEEP) and laser conization; ablation methods such as cryotherapy and cold coagulation; and pharmaceutical methods such as inhibitors of cell proliferation and anti-viral agents. The criteria selected as important for use in low-resource areas were verified by experts in the field, and included high efficacy and safety, usability for low-level providers, appropriateness for remote settings, and low cost. This document is titled treatment technologies for precancerous cervical lesions in low-resource settings.

This section focuses only on cryotherapy, highlighting how 1) cryotherapy is appropriate for the majority of precancer cases, 2) it also is appropriate for use in some field settings, and 3) PATH and the ACCP have worked with cryotherapy programs for many years.

Cryotherapy equipment runs on either CO_2 or N_2O gas. The gas usually is stored in large canisters.



A set of sample standard operating procedures for cervical cancer screening, diagnosis, treatment, infection prevention, and counseling used in India includes information on cryotherapy.

Client- and provider-perceived benefits of cryotherapy

- Cryotherapy is a highly effective intervention in many situations, with good cure rates.
- Nurses and other staff can be trained to perform cryotherapy safely.
- Cryotherapy does not require mains electricity (though the provider must have a lamp or torch to be able to visualize the cervix).
- The initial equipment costs for cryotherapy may be high, but the equipment is long-lasting and the only consumable supply is gas.

Client- and provider-perceived drawbacks of cryotherapy.

- In some places CO_2 or N_2O gas may be difficult and/or expensive to procure on a routine basis.
- Cryotherapy equipment may be difficult to set up or repair locally.
- The quality of gas varies and lower-quality gas can cause problems with the equipment.

- Sometimes it can be difficult to maintain effective freezing temperatures at the cryotherapy probe tip.
- Women experience a watery discharge for about four weeks after treatment while they are healing. During that time, they need to avoid sexual intercourse, or use a condom during sex to avoid infection.

Strategies appropriate for treatment using cryotherapy

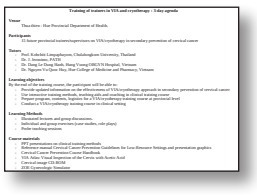
- Due to cost of equipment and difficulty of maintaining gas supplies in widespread locations, it may not be feasible or cost-effective to to implement cryotherapy services everywhere that screening could be offered. Therefore, some programs now are creating hubs of cryotherapy services that treat women referred by associated health posts and clinics which offer VIA or HPV DNA screening.
- Higher level facilities, in hospitals, for instance, can offer more complex, physician-dependent treatment such as LEEP.
- Programs also may choose to organize periodic outreach of mobile cryotherapy services when sufficient cases have accumulated at a facility or in a community.

Lessons specific to training

It is not only community members who lack information about cervical cancer. PATH has also discovered relatively low levels of up-to-date knowledge among health professionals (and especially among field-level health workers). Awareness-raising among a broad range of health workers, along with skills training in screening and treatment for clinical staff, is necessary to ensure high-quality, acceptable, and accessible cervical cancer prevention services.

Target audiences for training: Obvious target audiences for training include the clinicians who will provide screening and treatment services and the health educators who inform communities about the services. But women and their families often view any health staff as experts and ask them questions, so short orientation sessions can also be organized for clinic and hospital managers, supervisors, midwives, teachers, and others whose support is needed administratively, or who have access to and credibility with community members.

Existing training materials: Fortunately there are a number of existing course materials and outlines, including a web-based training tool, which training teams can consult or adapt as they develop their own materials. Sample agendas of clinical training and trainings of trainers used in the PATH projects can be found at www.rho.org/HPV-screening-treatment.htm.



Course methods and timing: The ACCP partners and PATH have learned that trainees respond well to courses that hold trainees accountable for achieving clinical competencies and that include interactive training methodologies and the opportunity to practice new skills with actual patients—under the supervision of an experienced clinician (an obstetrician/gynecologist may be ideal).

Generally about five days of classroom and clinical practice are necessary to train nurses and physicians to perform VIA and cryotherapy. If the providers are not already skilled in pelvic examination technique, more time may be required. A significant portion of that time should be dedicated to supervised practice.

Training strategy: As a general strategy for training large numbers of health workers across the country (either for awareness-raising and/or clinical skills-building), a cascade training system—with highly experienced, national master trainers at the top who train and supervise teams of lower-level trainers—likely makes the most sense. To the extent possible, it is best to reduce the number of "layers" of trainers since the further removed on-the-ground trainers are from direct contact with the master trainers, the greater the potential for loss of quality in the training program.

Maintaining a set of master trainers helps provide a sensible structure and helps ensure that the quality of information on screening and treatment is sustained at a high level. Having a reliable core group of master trainers also allows for retraining, both for staff who need a refresher and for new staff entering the program.

If outreach materials have been carefully designed and tested with community members, they can become excellent resources to use when training outreach providers.

Quality assurance during and after the course: Because VIA is a subjective test, regular assessment of clinician skills helps ensure quality.

Supportive supervision is an important element for maintaining quality after the training course is over, guiding corrections as necessary and providing continued learning among health staff. Supportive supervision means that supervisors regularly interact with field staff and are aware of their roles and how they are fulfilling those roles, and that the emphasis of supervision is on supporting staff to do a better job, not on blaming or punishing them.

Any work plans developed as part of a supervision visit should clearly specify what actions are needed and should identify a responsible person at the health facility level to follow up on implementation of solutions.

Supportive supervision training presentations and other documents on supportive supervision can be found at www.rho.org/HPV-screening-treatment.htm.

In some cases it may be possible to enlist the help of experienced providers in reviewing VIA cases through digital imaging and email, as has been tried in Zambia. However, unless reviewers are available whenever women are screened, such a system could introduce delays and negate the benefit of presenting immediate results to the patient. Most likely distance reviews would be beneficial in only certain situations, for example if there is a question about treatment selection.

Lessons specific to communication and community mobilization

Overall, PATH has found that more communication about cervical cancer with more audiences is better than less communication, but of course resources usually dictate how broadly programs can reach out to various communities.

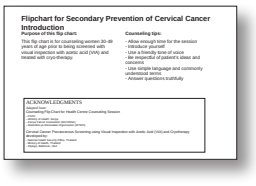
First and foremost, it is crucial to ensure that all women presenting for screening (or being recruited for it) understand the purpose and the procedure, what a positive or negative result means ("positive does not mean you have cancer"), and what might happen if there is a positive (or "abnormal") result.

In PATH programs, sensitization workshops with key community stakeholders and other health providers early in the service introduction process—well in advance of actual service delivery—helped promote buy-in and reduced the spread of negative rumors and other misinformation.

Women and their families appreciate receiving information about screening services through both direct communication with knowledgeable experts (e.g., trained health workers and teachers) and from mass media (such as radio or TV).

Integrating information about cervical cancer and new screening methods into existing health education sessions in schools or in women's groups has proven successful in a number of countries.

Health promoters appreciate having materials that synthesize key messages to share with community members.


Flipchart for Secondary Prevention of Cervical Cancer

Introduction

Counseling tips:

ACKNOWLEDGMENTS

Sample flipcharts, including a flipchart for secondary prevention of cervical cancer, leaflets on VIA and other documents for communities can be found at www.rho.org/HPV-screening-treatment.htm.

PATH/Lesley Reed

Strategies appropriate for communication and community mobilization

- Base communication strategies and messaging on evidence generated through formative audience research.
- Consider using multiple communication channels, including interpersonal strategies and mass media.
- Educate not only women, but also their husbands and other influential family members because women's health decisions may not be made by the woman alone.
- Ensure that strategies reach women in the target age range for cervical screening.
- Invest in broad community education and mobilization where possible; this could pay off in terms of higher screening coverage, so it is important to move beyond the clinic and the family and implement effective community outreach programs. For example, you may wish to organize reproductive health talks during women's group meetings, or mobilize village health teams and local teachers to talk about cervical cancer with the community.
- Encourage women who have been screened to become local advocates. Ask them to talk about screening with friends and neighbors and to tell stories about people they have known who suffered from cervical cancer. Cancer survivors (and precancer survivors) and family members who have lost loved ones to cervical cancer often are the most passionate and energized community activists!

Conclusion

Screening women for cervical cancer and precancer, and treating those who test positive, has dramatically reduced cervical cancer mortality in wealthier countries over the past 50 years. However, the method used for screening—cytology, also known as the Pap smear—is too complex and expensive to be sustainable in most low-resource settings. Due to the lack of screening and treatment programs, about 88 percent of cervical cancer deaths now occur in the developing world.

Fortunately, new screening alternatives have been shown to be even more sensitive than Pap, and are less expensive and provide results more rapidly. VIA and HPV DNA testing could for the first time make national, large-scale screening feasible in much of Africa, Asia, and Latin America.

A wealth of free guidance documents can help program managers develop appropriate screening program strategies—the best of them are linked from this document. More can be found on the RHO Cervical Cancer website (www.rho.org).

PATH is enthusiastic about the promise of the new screening and treatment methods and is committed to providing technical assistance to countries as they design and roll out new programs. If you would like to consult with PATH, contact us at info@path.org.

References

All resources referenced in this paper can be accessed online at www.rho.org/HPV-screening-treatment.htm.

1 Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. *Globocan 2008 V1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]*. International Agency for Research on Cancer 2010;Available at: URL: http://globocan.iarc.fr/.

2 World Health Organization. *Comprehensive cervical cancer control: A Guide to Essential Practice*. Geneva: World Health Organization; 2006.

3 PATH. *Progress in Preventing Cervical Cancer: Updated Evidence on Vaccination and Screening*. 2010 May. Report No.: 27.

4 Sherris J, Wittet S, Kleine A, Sellors J, Luciani S, Sankaranarayanan R, et al. Evidence-based, alternative cervical cancer screening approaches in low-resource settings. *International Perspectives on Sexual and Reproductive Health*. 2009 September;35(3):147-54.

5 Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar A, Levin C, Mahé C, et al. Cost-effectiveness of cervical-cancer screening in five developing countries. *New England Journal of Medicine*. 2005 November 17;353(20):2158-68.

www.path.org