



Progress in Cervical Cancer Prevention

The CCA Report Card 2015



Cervical Cancer
ACTION

A Global Coalition to STOP Cervical Cancer



ABOUT CERVICAL CANCER ACTION (CCA)

Cervical Cancer Action—a global coalition to stop cervical cancer—was created in 2007 to expedite the availability, affordability, and accessibility of new and improved cervical cancer prevention technologies for women and girls in developing countries.

We would gladly receive information and updates to complement the information provided in this report. Please email us at info@cervicalcanceraction.org with comments or suggestions.

FOR MORE INFORMATION

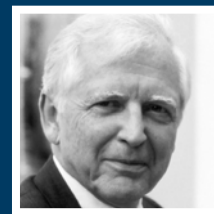
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HER EXCELLENCY MADAME ZUMA
FIRST LADY OF SOUTH AFRICA



PROFESSOR HARALD ZUR HAUSEN
2008 NOBEL LAUREATE
PHYSIOLOGY OR MEDICINE

FOREWORD

A New Era for Cervical Cancer Prevention

We live in an extraordinary time, one in which our human need to generate knowledge, implement creative solutions, and follow through on heartfelt commitments has resulted in a phenomenal opportunity to virtually eliminate one of the greatest causes of suffering and loss for families and communities around the world.

Low-cost, effective solutions are required for the prevention and treatment of cervical cancer in less developed countries where the disease is the primary cause of cancer-related deaths in women, and where cervical cancer death rates are much higher than in more developed countries. Such solutions should be underpinned by education and advocacy initiatives to raise awareness of the disease and its impact on women, their immediate families, and their countries.

Over the past decade, dedicated scientists, researchers, clinicians, frontline health workers, community leaders, and advocates have worked tirelessly to bring the scourge of cervical cancer to the world's attention and to develop and apply the necessary knowledge and technologies to prevent cervical cancer in developing countries. From Mumbai to Mexico City and from Kampala to Kathmandu, innovative programs have demonstrated how to successfully deliver effective cervical cancer prevention and treatment to the women and girls who need it most.

As this report highlights, countries are taking bold steps to improve cervical cancer screening and preventive

treatment for adult women and to successfully vaccinate girls against human papillomavirus (HPV), the virus that causes cervical cancer.

The international community has begun to take notice. Commitments by Gavi, the Vaccine Alliance, to offer HPV vaccines at subsidized rates to the poorest countries worldwide represent an exciting ramp-up of international leadership and support.

In order to save lives today, there must be an equal, if not greater, commitment to expanding other cervical cancer prevention initiatives. Without support for a comprehensive approach to preventing this disease—an approach that includes both cervical cancer screening/preventive treatment and HPV vaccination—countries with the highest burden of cervical cancer are likely to be the last to offer these lifesaving services at national scale.

With powerful solutions now within reach for all countries, we have an obligation to change the course of this disease. We strongly urge the international community to recognize the need, opportunity, and commitment documented in this report and to act swiftly to provide the leadership and resources necessary to encourage the expansion of programs to save the mothers of our nations and the families they nurture and preserve.

Introduction

Based on the laboratory work of Professor zur Hausen and his colleagues, along with critical epidemiological studies by Dr. Nubia Muñoz and her colleagues, research over the past 20 years has shown infection with certain cancer-causing types of human papillomavirus (HPV) to be the cause of cervical cancer. This slow growing and totally preventable cancer affects the most vulnerable women—those with little access to reproductive health care after their childbearing years and HIV-positive women of all ages (who are five times more likely to develop cervical cancer than women who do not have HIV).

Understanding the natural history of the disease has been fundamental to the development of safe and effective prevention modalities: locally appropriate **screening and preventive treatment^{*} technologies and HPV vaccines** (see Chapters 2 and 3). This confluence of knowledge, science, and possibility has triggered important changes in many high- and upper-middle-income countries and in an astounding number of low- and lower-middle-income countries, where, despite a lack of resources, governments and civil society leaders have rallied to take action.

During the past decade, we have seen a dramatic increase in the number of countries offering HPV vaccine to all young adolescent girls and those establishing screening and preventive treatment programs for adult women. There is

great momentum, but much remains to be done, especially in the lower-income countries where the burden of cervical cancer is highest.

Cervical Cancer Action (CCA) published our first Report Card—a snapshot of the international community’s collective efforts to improve cervical cancer prevention—in 2010. As this updated report goes to press, and as cervical cancer surpasses pregnancy-related complications (often called “maternal mortality”) as a leading cause of death among women in low-resource settings, our key call to action is to protect the global community’s investments and gains in women’s health and HIV by expanding our commitment to prevent cervical cancer. The comprehensive prevention approach endorsed by the World Health Organization (WHO), CCA, and many others—including both vaccination and screening/preventive treatment—will go far in solidifying gains for women at highest risk, while potentially strengthening existing health programs for both adult women and adolescents.

A comprehensive approach to cervical cancer prevention should include:

- Educating women, providers, and communities about cervical cancer—its cause and prevention;
- Preventing HPV infection, where possible, through vaccination of young adolescent girls;
- Ensuring women’s access to screening to detect precancerous changes and treat them appropriately before invasive cancer occurs;

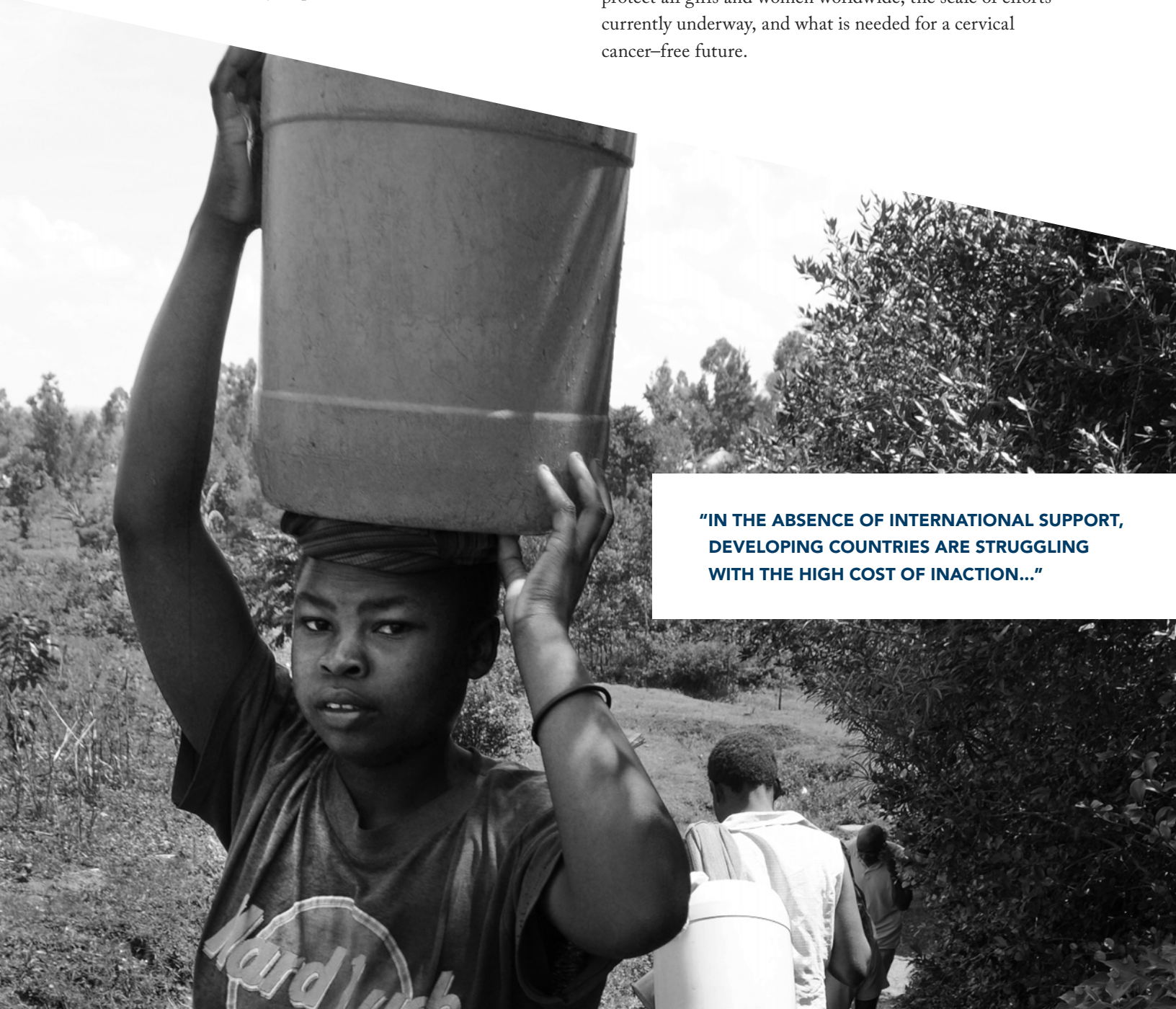
* “Preventive treatment” means treatment of cervical precancer (cervical lesions) as opposed to treatment of invasive cancer. Preventive treatment tends to be highly effective, while treatment of cancer is more expensive, more difficult, less available in low-resource settings, and generally less successful when the cancer has advanced.

- Encouraging the development of national plans to strengthen coordination and mobilize adequate human and financial resources to sustain prevention efforts; and
- Strengthening vital health information systems to monitor program impact.

This Report Card documents efforts taken by countries, communities, and their international partners to fight this disease, particularly in low- and lower-middle-income countries. These early steps have been hard won. In the

absence of adequate international support, countries are struggling with the high cost of inaction—hundreds of thousands of deaths each year—and the challenge of garnering the resources necessary to establish health programs that include vaccines for adolescents (HPV and other vaccines) and to protect gains in maternal health and HIV.

We hope this report will help the international community better understand the opportunity at hand to protect all girls and women worldwide, the scale of efforts currently underway, and what is needed for a cervical cancer-free future.



"IN THE ABSENCE OF INTERNATIONAL SUPPORT, DEVELOPING COUNTRIES ARE STRUGGLING WITH THE HIGH COST OF INACTION..."

Photo: PATH/Wendy Stone

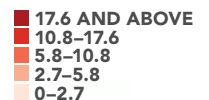
The Global Burden of Cervical Cancer

Global cervical cancer mortality highlights the inequities of our time—inequities in wealth, gender, and access to health services. Women worldwide are exposed to HPV as soon as they become sexually active, but it

is primarily women in the developing world who have little or no access to screening and preventive treatment, and who die from the consequences of infection.

1.1 CURRENT CERVICAL CANCER MORTALITY RATE

ESTIMATED AGE-STANDARDIZED MORTALITY RATE PER 100,000, CERVIX UTERI



SOURCE

- Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer; 2013. Available at: <http://globocan.iarc.fr>. Accessed September 21, 2015.



Photo: PATH/Nga Le

"BY 2030, CERVICAL CANCER IS EXPECTED TO KILL MORE THAN 443,000 WOMEN PER YEAR; 95 PERCENT OF THOSE DEATHS WILL OCCUR IN DEVELOPING COUNTRIES. THE LOSS OF THESE WOMEN—MOTHERS, DAUGHTERS, SISTERS, WIVES, PARTNERS, AND FRIENDS—IS ALMOST ENTIRELY PREVENTABLE. "

Key facts:

- Cervical cancer is the **number one cancer killer of women in most developing countries.**
- Each year, more than **528,000 women develop cervical cancer and about 266,000 women die from the disease.**¹ The vast majority of these preventable deaths occur in developing countries, or among disadvantaged populations in wealthy countries.
- Without significant investments in cervical cancer prevention now, WHO estimates there will be **443,000 deaths per year by 2030,**² an increase of 67 percent!

Over the past several decades, we have witnessed a steady drop in cervical cancer incidence and mortality in high-income countries. Effective screening and preventive treatment technologies have driven these reductions, allowing clinicians to detect and remove cervical anomalies before invasive cancer develops. In many countries, these efforts have been complemented by public education,

clinician training, improved cancer treatment, and strong health information systems designed to assess the impact of programs and policies. Between 1955 and 1992, cervical cancer mortality in the United States declined by nearly 70 percent, and incidence rates continue to drop by about 1.8 percent each year. Similarly, by 2012, European cervical cancer mortality rates were 81 percent lower than in 1980.³

Tragically, similar success has not yet been achieved in low- and lower-middle-income countries. After decades of attempting to implement the same strategies used in high-income countries—such as the Pap test for screening—lower-income countries have not seen the same reduction in disease. Instead, disease incidence is increasing, fanned by gains in life expectancy and population. WHO estimates that by 2030, the number of annual cervical cancer deaths will more than double the 200,000 anticipated deaths from pregnancy-related complications (maternal mortality).²

Screening and Early Treatment

Over the past decade, our knowledge, tools, and capacity to screen for and treat cervical precancer have changed dramatically. The Papanicolaou test, commonly called the Pap test or smear, for many years was the standard for cervical cancer screening worldwide. That test has been effectively employed in high-income settings despite its suboptimal performance in correctly identifying women with precancerous lesions. Test weaknesses have been mitigated by repeat testing and high rates of follow-up among women who need to return to a clinic for treatment.

In low- and lower-middle-income settings, however, the impact of Pap has been disappointing—the confluence of poor test performance, shortages of trained staff, limited recall systems, high cost, and challenges preventing many women from traveling repeatedly to clinics have crippled Pap-based screening systems for decades. Today, alternatives to the Pap test—visual inspection with acetic acid (VIA) and HPV testing—represent a breakthrough in our ability to deliver effective cervical cancer prevention in all resource settings.

HPV vaccination alone will not show an impact on cervical cancer incidence and mortality for years to come, so over the next few decades, screening and preventive treatment (treatment of precancer to prevent invasive cancer) will be the primary drivers of reduced suffering and death from the disease.

SPOTLIGHT

SELF-SAMPLING WITH HPV TESTS—A GAME-CHANGER?

In some settings, long waits at clinics, patient embarrassment at seeing male providers, and distaste for pelvic examinations can reduce adherence to screening regimens. Standard HPV DNA test scenarios rely on collection of cervical samples and require pelvic exams. But evidence suggests that vaginal samples, collected by women themselves (or with assistance from a female nurse or paramedic and without a pelvic examination) result in only a slight drop in test performance.⁴ This option has proven attractive to both women and providers.⁵

Simplifying specimen collection significantly speeds up the screening process, allows for collection outside of clinics, increases participation, and makes screening of entire populations feasible because hundreds of samples can be collected within a relatively short time. It reduces the level of effort by health staff because only women who test positive are asked to come to the clinic for further evaluation—likely with VIA—to determine whether they have precancer or cancer, and which treatment modality they need.

Vaginal self-sampling may prove an effective and efficient way forward, encouraging more women to get screened and reducing the burden of screening on already pressured health systems.

As shown in Figures 2.1 and 2.2, these new screening methods are becoming increasingly available in high-, middle-, and low-income countries. Pap testing is likely to be eclipsed because VIA and HPV tests feature much shorter turnaround times to identify and treat precancerous lesions, are much less expensive, and are less technically challenging. Both methods feature prominently in WHO guidelines for cervical cancer prevention because of their potential to significantly improve the reach and outcomes of cervical cancer screening programs.

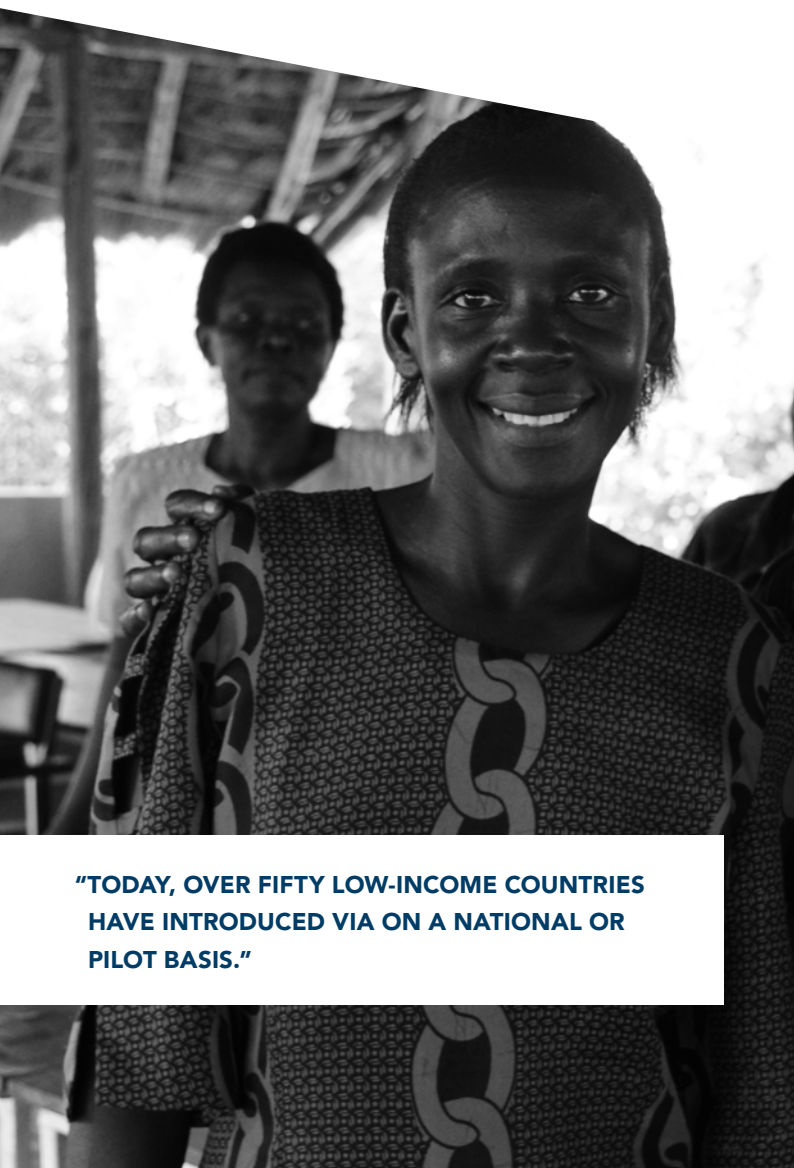
VIA AND THE SCREEN-AND-TREAT APPROACH

Studies in low-resource settings have shown that visually inspecting the cervix after applying a staining solution of acetic acid was at least as effective as Pap at identifying women with precancerous lesions (in some studies, it was shown to be more effective). This relatively simple approach can be performed by mid-level health personnel. Following VIA screening, cryotherapy can be offered for preventive treatment the same day, or very soon after screening, and without an additional diagnostic confirmation step. This “screen-and-treat” approach has been shown to be safe, effective, and appropriate in the most difficult to reach communities, especially as it significantly reduces the burden of repeat visits for women who live far from health services. Compressing cervical cancer prevention into as few visits as possible increases program impact by reducing the likelihood that women are lost to follow-up.

Today, many low-resource countries have introduced VIA on a national or pilot basis using governmental or nongovernmental providers, or both (Figure 2.1). Twenty-six countries have included VIA in their national norms and have introduced the method in areas previously lacking screening services, and another 35 countries have organized pilot programs to assess the approach. In most countries, first-time introduction of VIA has been complemented by crucial efforts to increase community awareness about cervical cancer and to improve follow-up and referral mechanisms for women in need of more advanced cancer care.

VIA offers a viable solution to communities where previously there were no feasible options, and it can help save lives now.

While most countries will eventually choose HPV DNA testing over VIA for primary screening (see next section), in such cases, VIA still will be useful to determine whether the patient has cancer or precancer and to guide decisions regarding treatment. A VIA program initiated now can easily integrate HPV DNA tests when they become broadly available, so investment in VIA pays off in both the short and long term.

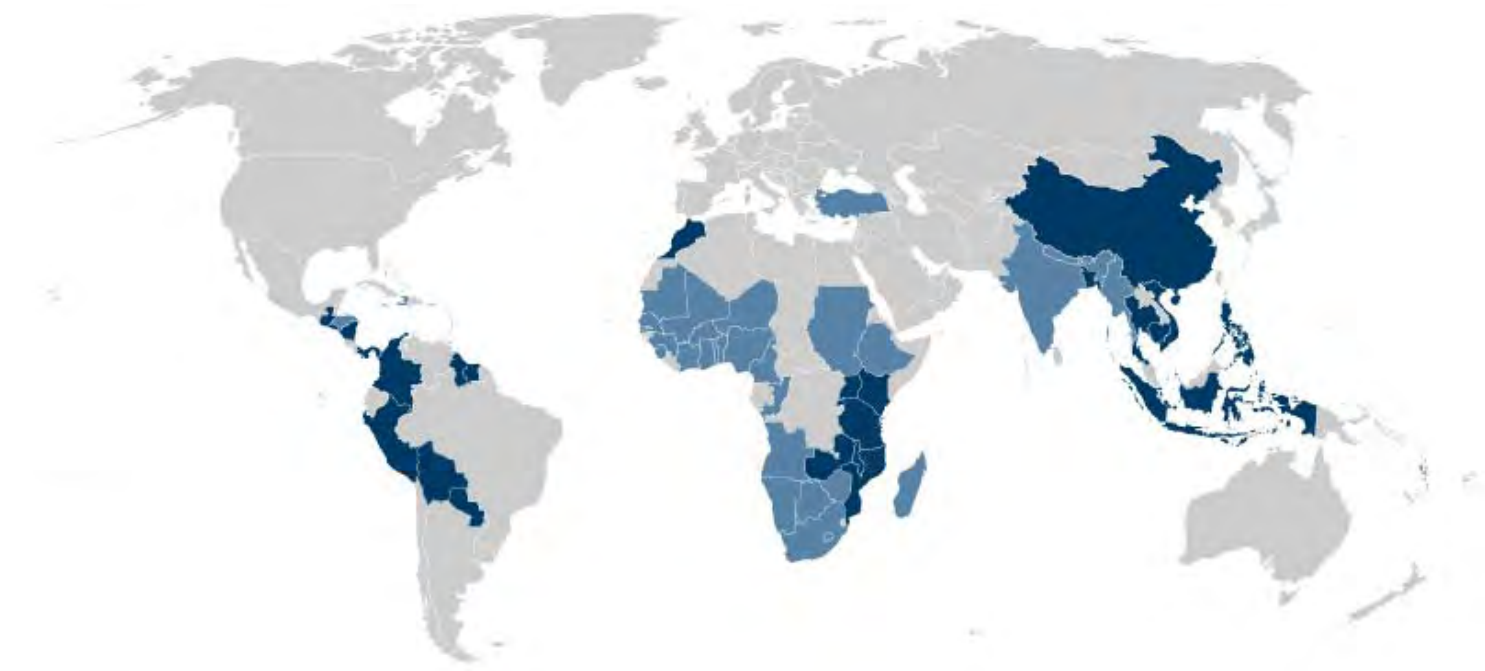


“TODAY, OVER FIFTY LOW-INCOME COUNTRIES HAVE INTRODUCED VIA ON A NATIONAL OR PILOT BASIS.”

Photo: PATH/Wendy Stone

2.1 INTRODUCTION OF VISUAL INSPECTION (VIA) FOR CERVICAL CANCER SCREENING

STATUS: AUGUST 2015



■ **NATIONAL PROGRAMS:** VISUAL INSPECTION IN THE NATIONAL SCREENING NORMS AND AVAILABLE ON A LIMITED OR UNIVERSAL BASIS THROUGH THE PUBLIC SECTOR

■ **PILOT PROGRAMS:** VISUAL INSPECTION AVAILABLE THROUGH PILOT OR DEMONSTRATION PROJECTS ORGANIZED BY THE MINISTRY OF HEALTH OR NGO PARTNERS

■ **NO VIA PROGRAM**


The information represented here has been collected through interviews with individuals and organizations involved with the countries represented and has not been verified with individual ministries of health. Any oversights or inaccuracies are unintentional.

NATIONAL PROGRAMS

Bangladesh	Mozambique
Bolivia	Nicaragua
Cambodia	Panama
China	Paraguay
Colombia	Peru
El Salvador	Philippines
Guatemala	Rwanda
Guyana	Suriname
Indonesia	Tanzania
Kenya	Thailand
Kiribati	Uganda
Malawi	Vietnam
Morocco	Zambia

PILOT PROGRAMS

Angola	Mali
Benin	Mauritania
Bhutan	Myanmar
Botswana	Namibia
Burkina Faso	Nepal
Cameroon	Niger
Côte d'Ivoire	Nigeria
Ethiopia	Republic of Congo
Gambia	Senegal
Ghana	Sierra Leone
Grenada	South Africa
Guinea	St. Lucia
Haiti	Sudan (North)
Honduras	Togo
India	Turkey
Lesotho	Vanuatu
Madagascar	Zimbabwe
Maldives	



“OVER THE NEXT DECADE, NEW AND EFFECTIVE SCREENING AND EARLY TREATMENT METHODS WILL BE THE PRIMARY DRIVERS OF REDUCED SUFFERING AND DEATH FROM CERVICAL CANCER.”

COUNTRY PROFILE

ARGENTINA SCALES UP SCREENING FOR THE LEAST DEVELOPED PARTS OF THE COUNTRY

Argentina is a high-income country, but in northwestern Jujuy Province, socioeconomic indicators are lower than average. Like so many low-resource areas, Jujuy also suffers high cervical cancer mortality.

Despite several campaigns to promote HPV DNA screening since 2012, coverage remained low among socially vulnerable women. Part of the problem was the need to collect cervical mucus samples for the test. That process requires a pelvic examination, which some women prefer to avoid due to geographic or social barriers.

To improve screening coverage and to protect many more women against cervical cancer, the Jujuy Demonstration Project worked closely with provincial health authorities to assess the feasibility of using vaginal samples instead—samples that women could self-collect with the assistance of a community health worker. Because no pelvic exam was needed, sample collection was relatively fast and simple.

The study team compared their results against traditional cervical sampling and found that screening uptake was four times higher among women who had the option of self-collection. Although detection rates were a bit lower for self-collection—1.15 percent for self-collected samples versus 1.29 percent for clinician-collected samples—due to the increased coverage, the number of lesions detected in the self-collection group was three times higher. The project team concluded that HPV self-collection offered by community health workers can increase screening uptake and detection of cancer precursors. Self-collection now has been adopted as a core strategy in both Jujuy and Tucumán Provinces, specifically for screening under-utilizers.

Photo: PATH/Mike Wang

HPV DNA TESTING

HPV DNA testing is a molecular approach to screening that detects the presence of cancer-causing types of HPV. This testing approach is most appropriate for women older than 30 years of age, when precancerous lesions are more prevalent. A cervical mucus sample is taken during a clinical exam (or by vaginal self-sampling) and then transported to a laboratory for processing. Some HPV DNA tests offer portable processing equipment, which fits easily on a clinic table.

For countries that can afford HPV DNA testing, this powerful screening method has proven to be significantly more capable of identifying positive cases than either Pap or VIA. This allows for earlier and more effective treatment, resulting in reductions in cervical cancer rates and mortality.⁶ It also introduces the opportunity to reduce the number of screenings needed in a woman's lifetime, since a negative test has been associated with a very low risk of developing subsequent cervical precancer for at least five years, and perhaps much longer.

The United States was the first country to introduce HPV DNA testing as a screening protocol, in conjunction with the Pap test. As indicated in Figure 2.2, by August 2015, six countries—including two in Latin America—had made the test broadly available (Argentina, Italy, Mexico, the Netherlands, Spain, and the United States). The US Food and Drug Administration approved HPV DNA testing as a primary, standalone screening test (without Pap) in 2015,

2.2 INTRODUCTION OF HPV DNA TESTING FOR CERVICAL CANCER SCREENING

STATUS: AUGUST 2015



- **NATIONAL PROGRAMS:** HPV DNA TESTING IN THE NATIONAL SCREENING NORMS AND AVAILABLE ON A LIMITED OR UNIVERSAL BASIS THROUGH THE PUBLIC SECTOR
- **PILOT PROGRAMS:** HPV DNA TESTING AVAILABLE THROUGH PILOT OR DEMONSTRATION PROJECTS ORGANIZED BY THE MINISTRY OF HEALTH OR NGO PARTNERS
- **NO HPV DNA TESTING PROGRAM**

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NATIONAL PROGRAMS

- | | |
|-----------|---------------|
| Argentina | Netherlands |
| Italy | Spain |
| Mexico | United States |

PILOT PROGRAMS

- | | |
|-------------|---------------------|
| China | Paraguay |
| Colombia | Peru |
| El Salvador | Republic of Georgia |
| Germany | Rwanda |
| India | Uganda |
| Nicaragua | |

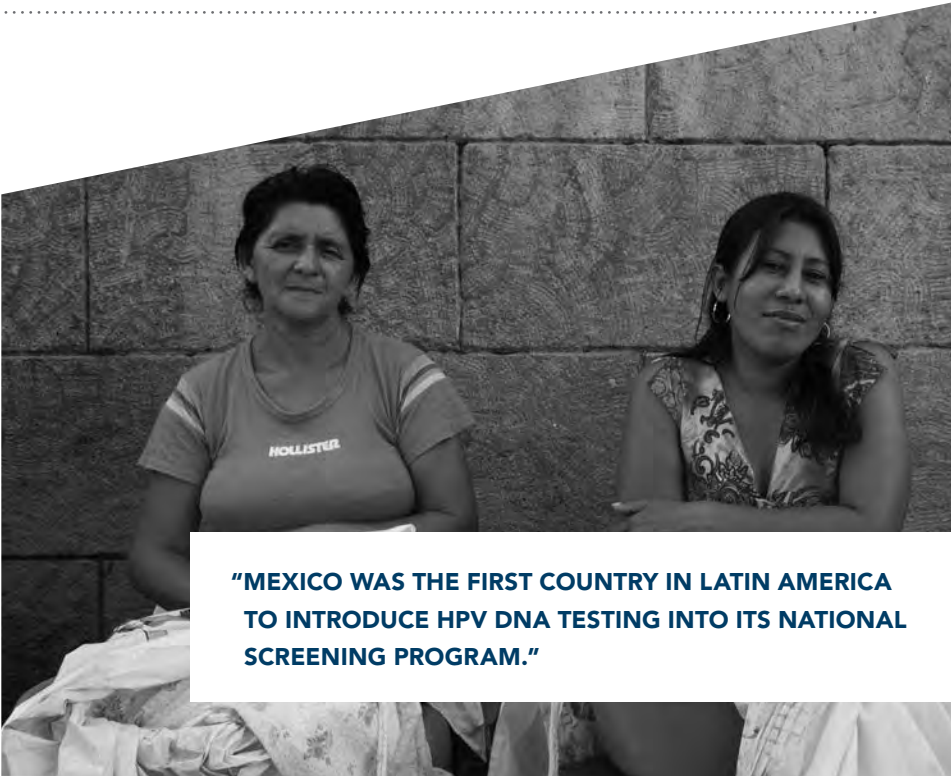


Photo: PATH/Mike Wang

SPOTLIGHT

DATA SUPPORT THE USE OF CRYOTHERAPY

Ensuring that women who test positive with VIA or HPV DNA have access to safe, effective, and affordable preventive treatment is crucial to saving lives and making an impact on cervical cancer. Lack of trained physicians and poor access to surgical facilities have been key barriers to treatment in low- and lower-middle-income countries. Cryotherapy, which uses a compressed gas to freeze and destroy abnormal cervical cells, is a proven non-surgical alternative. This outpatient procedure does not rely on electricity or sophisticated medical infrastructure and can be safely performed by trained, non-physician providers.

Research in Africa and Asia has shown that cryotherapy is a feasible and effective way to prevent and treat cervical precancer in low-resource settings, and can be combined with VIA—or HPV DNA testing followed by treatment selection using VIA—to screen and treat women.^{8,9} However, sometimes the gases needed for cryotherapy—carbon dioxide or nitrous oxide—are difficult to obtain or are expensive, especially in rural areas. Development of a cryotherapy tool that does not depend on supplies of gas could remove this barrier.



Photo: PATH/Doune Porter

and it is anticipated that additional countries will follow suit in the coming years.

In low- and lower-middle-income countries, the uptake of HPV DNA testing has been slower, though a number of these countries have assessed field use of the test in pilot programs. The cost of current HPV tests, along with the necessary infrastructural costs of improving treatment and reporting systems, has been daunting, even though investments in HPV DNA testing ultimately will translate into reduced suffering and financial savings.

The field of HPV testing is evolving rapidly and the range of options is increasing. As less costly HPV DNA tests (or other molecular tests) become available, it is likely that countries will rapidly adopt them because of the potential for achieving high coverage.

AVAILABILITY OF PREVENTIVE TREATMENT

Regardless of the screening method, no cervical cancer prevention program can be effective without offering preventive treatment for precancer and referral and higher-level treatment for invasive cancer. The simplest method of preventive treatment is cryotherapy—freezing abnormal tissue; it is appropriate for the majority of precancer cases. Using heat—a process called thermal or “cold” coagulation—to destroy the abnormal cells is another promising option for preventive treatment.⁷ However, in certain precancer situations, and for invasive cancer, neither cryotherapy nor thermal coagulation are effective and other treatment strategies are required.

Access to preventive treatment remains the Achilles’ heel of cervical cancer programs. Fortunately, some low- and lower-middle-income countries are finding ways to improve their preventive treatment systems. Over the past several years, governments and nongovernmental partners have sought to improve cryotherapy equipment, train providers in cryotherapy, and put sustainable systems in place.

The treatment of full-blown cancer remains tragically weak in the developing world. Few middle-income countries and even fewer low-income countries have the resources to treat women with cervical cancer or help manage the horrible pain of cancer sufferers. Preventive treatment of precancerous lesions—which typically has much higher cure rates than cancer treatment—should therefore become a national priority.

The challenge of establishing the infrastructure, training the providers, and securing the necessary equipment to provide services at scale continues to plague governments that are all too familiar with the ravages of cervical cancer. Increased global investment in screening and preventive treatment systems is urgently needed.

HPV Vaccination

Screening and preventive treatment are used to identify and treat precancer after HPV infection has already occurred; vaccination prevents infection in the first place. (For this reason, vaccination is called “primary prevention” and screening/treatment is called “secondary prevention.”) In order for HPV vaccine to be most effective, a girl should be vaccinated prior to HPV infection, which often occurs soon after sexual initiation.

Since 2006, HPV vaccine has become available in many countries either through government vaccination programs or through the private sector for individuals who can afford to pay. Effectively targeting the most common cancer-causing types of HPV, the vaccine has the potential to dramatically reduce the future burden of cervical cancer.

Because cervical cancer takes years to develop, reductions in vaccine-preventable cancer will not become apparent for decades to come. However, studies in Australia, England, the United States, and other countries have shown declines in the prevalence of HPV infection, in precancerous cervical lesions, and in genital warts (when a vaccine was used that also targets HPV types that cause warts).^{10,11} These early findings suggest that the vaccines will be effective in reducing the incidence of invasive cancer as well.

Post-introduction monitoring of vaccination has demonstrated that HPV vaccines have an excellent safety profile.¹²

WHO and other institutions recommend introduction of HPV vaccine as part of a national cervical cancer control strategy in countries where it is feasible and cost-effective, and where the vaccine can be delivered to adolescent girls effectively.

Australia, Canada, New Zealand, the United Kingdom, and the United States were among the first countries to introduce HPV vaccine in 2007 to 2008, and many other high-income countries quickly followed. In some countries, early vaccination efforts included catch-up campaigns to reach the maximum number of girls and young women who could possibly benefit.

Even though high-income countries typically have robust and effective screening and preventive treatment programs in place, and relatively low cervical cancer mortality, they still chose to establish HPV vaccine programs. By vaccinating girls (and sometimes boys as well), these countries hope to further reduce mortality and to minimize morbidity and costs related to treatment of precancer and cancer.

As of August 2015, 84 countries and territories had national public-sector HPV immunization programs and 38 had pilot programs. This represents a 60 percent increase since the last CCA Report Card was published in 2012. Many of these programs are in low- and lower-middle-income countries, in large part due to support for HPV vaccine by Gavi, the Vaccine Alliance (see box on page 15).

The greatest public health impact of HPV vaccination will be in countries where large portions of the population have limited or no access to screening, and where cancer treatment and palliative care continue to fall short of need.

In 2008, Mexico was one of the earliest middle-income countries to introduce a public-sector HPV immunization program on a pilot basis. Later the same year, Panama became the first middle-income country to provide universal access to HPV vaccine. The Pan American Health Organization's Revolving Fund gives participating governments in Latin America and the Caribbean access to HPV vaccine at significantly reduced prices.

When HPV vaccine first came on the market, three doses were thought to be necessary. The most significant factor in reducing the cost of HPV vaccination has been the finding that protection is robust after only two doses. In 2014, WHO recommended adoption of the two-dose regimen for girls younger than 15 years.¹³

After HPV vaccine became available, ministries of health, civil society, and international institutions focused on creating a foundation for HPV vaccine introduction in low- and lower-middle-income settings. For example, beginning in 2006, PATH, an international nongovernmental organization, established demonstration projects in India, Peru, Uganda, and Vietnam to assess the acceptability of HPV vaccination and compare vaccine delivery strategies. This early evaluation, and subsequent experience, helped dispel concerns that HPV vaccine might prove unacceptable to families or too difficult to deliver in lower-resource settings. In fact, the opposite seems to be true: there has been an extraordinary demand for vaccine among girls, parents, physicians, and ministries of health.¹⁴ With good planning, and strong communication and community mobilization efforts, vaccine coverage rates have been high—usually 80 percent or more. Furthermore, introduction of HPV vaccine increased public awareness about cervical cancer in general and increased demand for screening among adult women.

SPOTLIGHT

GAVI BRINGS HPV VACCINE TO LOW-INCOME COUNTRIES

Gavi, the Vaccine Alliance, subsidizes introduction of new vaccines in the lowest-resource countries. More than half of the global cervical cancer burden is in countries that are eligible for Gavi support, and the organization began offering HPV vaccine in 2013.

Gavi estimates that by 2020, more than 30 million girls in more than 40 countries will have been vaccinated against HPV with Gavi support.¹⁵

There are two ways that low-income countries may apply for HPV vaccine support through Gavi:

1. Countries that have demonstrated the ability to reach young adolescent girls with HPV or other multi-dose vaccines can apply for Gavi-supported national introduction.

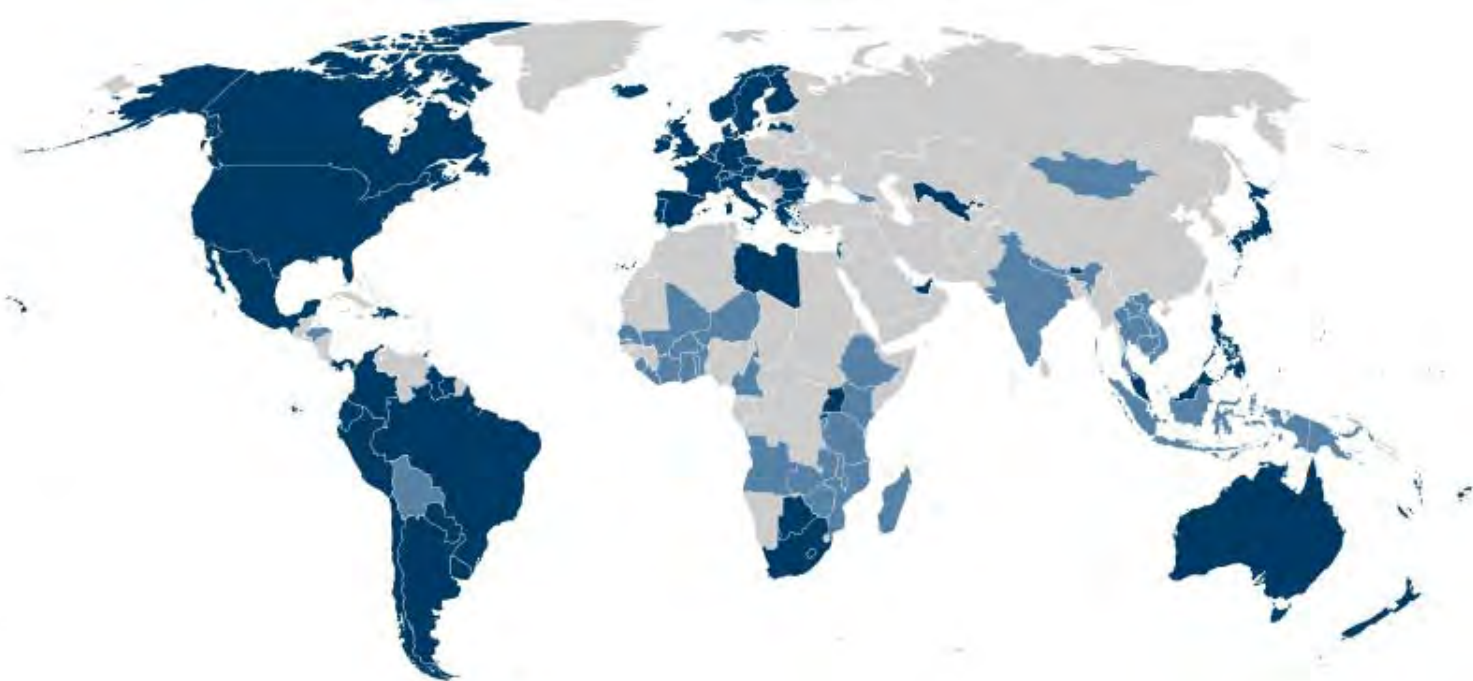
2. Countries that do not yet have enough experience reaching adolescent girls may apply for support to conduct smaller-scale demonstration projects. This provides the opportunity for countries to “learn by doing” and gain experience necessary for national rollout of vaccine.

Gavi has been extremely successful in negotiating low prices for HPV vaccine—currently they pay an average of US\$4.55 per dose. Low-income countries carrying out national introductions are required to pay only 20 cents per dose as co-payment.

Gavi's decision to tackle the burden of cervical cancer in countries with the most need will accelerate the reach of HPV vaccination and help protect future generations of women against a preventable cancer.

3.1 INTRODUCTION OF HPV VACCINE

STATUS: AUGUST 2015



- **NATIONAL PROGRAMS:** HPV VACCINE IN NATIONAL NORMS AND AVAILABLE ON A LIMITED OR UNIVERSAL BASIS THROUGH THE PUBLIC SECTOR
- **PILOT PROGRAMS:** HPV VACCINE AVAILABLE THROUGH PILOT OR DEMONSTRATION PROJECTS ORGANIZED BY THE MINISTRY OF HEALTH OR NGO PARTNERS
- **NO HPV VACCINE PROGRAM**

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NATIONAL PROGRAMS

American Samoa	Czech Republic	Luxembourg	San Marino
Andorra	Denmark	Macedonia	Seychelles
Argentina	Dominican Republic	Malaysia	Singapore
Aruba	Ecuador	Malta	Slovenia
Australia	Fiji	Marshall Islands	South Africa
Austria	Finland	Mexico	Spain
Bahamas	France	Micronesia	St. Eustatius
Barbados	French Polynesia	Monaco	Suriname
Belgium	Germany	Netherlands	Sweden
Belize	Greece	New Caledonia	Switzerland
Bermuda	Guam	New Zealand	Trinidad and Tobago
Bhutan	Guyana	Niue	Uganda
Botswana	Hungary	Northern Marianas	United Arab Emirates
Brazil	Iceland	Norway	United Kingdom
Brunei	Ireland	Palau	United States
Bulgaria	Israel	Panama	Uruguay
Canada	Italy	Paraguay	Uzbekistan
Cayman Islands	Japan	Peru	Vanuatu
Chile	Kiribati	Philippines	
Colombia	Latvia	Portugal	
Cook Islands	Lesotho	Romania	
Curacao	Libya	Rwanda	

PILOT PROGRAMS

Angola	Moldova
Benin	Mongolia
Bolivia	Mozambique
Burkina Faso	Nepal
Burundi	Niger
Cambodia	Papua New Guinea
Cameroon	Sao Tome
Cote d'Ivoire	Senegal
Ethiopia	Sierra Leone
Gambia	Solomon Islands
Georgia	Tanzania
Ghana	Thailand
Haiti	Togo
Honduras	Vietnam
India	Zambia
Indonesia	Zimbabwe
Kenya	
Lao PDR	
Liberia	
Madagascar	
Malawi	
Mali	

"LESSONS NOW EMERGING FROM THESE EARLY PROJECTS ARE ESTABLISHING A SOLID EVIDENCE BASE FOR THE WIDESPREAD INTRODUCTION OF HPV VACCINE, EVEN IN THE MOST CHALLENGING SETTINGS."



Photo: PATH/Amynah Janmohamed

COUNTRY PROFILE

FROM EVIDENCE TO IMPACT: HPV VACCINES AND UGANDA

Uganda was an early adopter of HPV vaccine, introducing it through a process of pre-introduction formative research in 2006, followed by careful, evidence-based planning of demonstration projects in two rural districts. The first vaccinations were offered to young adolescent girls in 2008; BBC World aired a film about the program two years later.** The project achieved coverage rates of 88 to 90 percent—considered remarkable given that the vaccine was not yet part of routine Ministry of Health services.

That success was indicative of the latent demand for protection against cervical cancer. While they may not have known the term “cervical cancer,” the Ministry found that many villagers were familiar with the symptoms and often had known someone who suffered from the disease. When they heard that there was a vaccine, they eagerly asked for their daughters to be protected.

In 2010, based on experience from the demonstration project, the Ministry published its five-year Strategic Plan for Cervical Cancer Prevention and Control in Uganda—one of the first comprehensive plans of its kind on the continent. Expanding vaccine reach was central to the plan. In March 2014, Uganda was approved for vaccine support from Gavi, with the 2015-2016 goal of vaccinating 1.1 million girls out of a total eligible population of 1.4 million.

Uganda’s thoughtful approach—taking time to develop evidence to guide program planning and to ensure adequate resources for sustainable delivery—is a sensible model for other countries to emulate.

** Two versions of the film can be streamed from www.rho.org/multimedia.htm.

A Comprehensive Cervical Cancer Response: Planning and Investment

Increasingly, leaders in developing countries are responding to the burden of cancer and other noncommunicable diseases (NCDs) on their communities. Building on the momentum of the UN High-Level Meeting on Prevention and Control of Non-communicable Diseases in September 2011, Member States of the World Health Assembly committed to a 25 percent reduction in premature deaths from NCDs by 2025. The Global Action Plan for the Prevention and Control of NCDs (2013–2020)—a roadmap for achieving the 2025 target—seeks to strengthen national efforts to address NCDs. Thoughtful planning, policy development and implementation are required to achieve this important global goal.

PLANNING

A national cervical cancer strategy, integrated into a national cancer control plan, is crucial for establishing a platform for national action and financial support. Working from a sensible plan, a wide group of stakeholders can become aware of the local burden of cervical cancer, set priorities for prevention and control based on proven strategies, and allocate sufficient funding to achieve targets. Program plans also provide a framework to assess the efficacy of current approaches and encourage fresh thinking about alternative uses of limited resources.

While developing cervical cancer strategies is an essential step, unless these plans are fully resourced, they cannot be

CHAMPION PROFILE

JACQUELINE FIGUEROA, MD, MPH
COORDINATOR OF CERVICAL CANCER
PREVENTION PROJECTS AND CANCER
REGISTRY AT THE MINISTRY OF HEALTH



An accomplished physician, registry advocate, and public health leader, Dr. Jacqueline Figueroa has dedicated her career to improving the effectiveness of cervical cancer prevention programs and local and national cancer registries in Honduras. In addition to working closely

with disadvantaged communities, Dr. Figueroa successfully established both the hospital registry of the Centro de Cáncer Emma Romero de Callejas in Tegucigalpa and—with passion and perseverance—the National Cancer Registry of Honduras, where she currently serves as director. The tremendous effort put forth by Dr. Figueroa helped to paint a more accurate picture of the scope of cervical cancer care in Honduras—one that will enable health authorities to plan effective interventions that make the best use of limited resources.

successfully implemented or effectively deliver change. A recent WHO assessment report highlights that as many as 81 percent of countries have cancer plans, policies, or strategies in place, but only 59 percent have an operational plan and only 48 percent have an operational plan with dedicated funding.¹⁶

Some countries, including Bolivia, Tanzania, and Uganda, have drafted targeted cervical cancer strategies to allow focused cervical cancer efforts to move forward even in the absence of a broader national cancer control plan. As more countries begin to establish or strengthen plans, it is crucial that they receive the necessary support to implement realistic and achievable strategies to reduce the burden of cervical cancer affordably, equitably, and quickly.

BETTER HEALTH INFORMATION AND CANCER REGISTRIES

The public sector's ability to implement effective cervical cancer strategies has been hampered by lack of awareness of disease burden in their countries. Cancer registries are crucial for understanding the burden of disease, but vary widely in their quality and scope. Although the greatest burden of cervical cancer is found in eastern Africa and South Asia, these regions have traditionally lacked the resources and information systems necessary to track cancers through population-based registries.

Similarly, few countries document the number of women screened for cervical precancer, and even fewer collect data on the number of women with abnormal screening results who receive treatment.

The availability of reliable cancer data—including cancer incidence, stage at diagnosis, and mortality—is vital for developing targeted and effective national cancer control plans and for evaluating the impact of national programs.

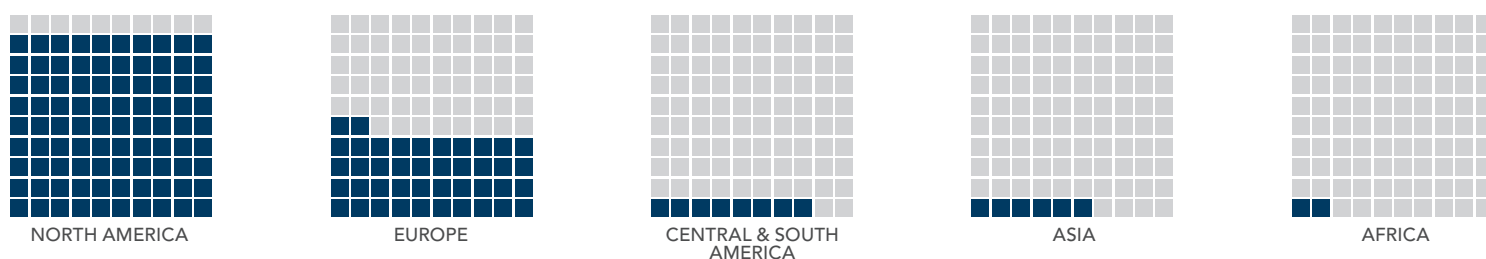
In the absence of systematic reporting, health planners and policymakers must rely on estimates of disease burden and on qualitative reports of cervical cancer prevention efforts. As women who die of cervical cancer are often marginalized, every effort must be made to identify a woman in need of care before cancer occurs, but we must also count those we have failed to protect.

FINANCING CERVICAL CANCER PREVENTION

A precipitous drop in HPV vaccine cost—due to dramatic price reductions and the adoption of a two-dose schedule (see Chapter 3)—along with Gavi subsidization for the poorest nations, puts HPV vaccine within reach of most countries. The fact that every functioning country has a long-established vaccination program means that HPV can be added to an existing system, though some of those programs may not yet have experience in vaccinating adolescents. As shown in Figure 3.1, 122 countries or territories are implementing some level of HPV vaccination.

Screening and preventive treatment programs are not as widespread. There is no organization like Gavi to provide funding for screening; low-resource countries must identify funding from their internal budgets or from international partners. Still, screening and treatment are good investments to make: WHO has declared that VIA screening, coupled with preventive treatment, is a “best

4.1 % OF POPULATION COVERED BY POPULATION-BASED CANCER REGISTRIES, BY REGION



SOURCE

- Forman D, Bray F, Brewster DH, et al., eds. *Cancer Incidence in Five Continents, Volume X*. Lyon, France: International Agency for Research on Cancer; 2014. Scientific Publication No. 164.

buy” in global health. As such, it is important that national screening programs not be abandoned to fund HPV vaccination programs. All adult women need access to screening and preventive treatment—even those who were vaccinated—because HPV vaccines do not protect against all cancer-causing HPV types. Even with high vaccination coverage, cervical cancer screening will remain a necessity for decades.

To date, donor support for screening and preventive treatment has been spotty, and few middle- or low-income countries provide screening services for all women. This situation must change.

NEW GLOBAL INVESTMENT TO PREVENT CERVICAL CANCER

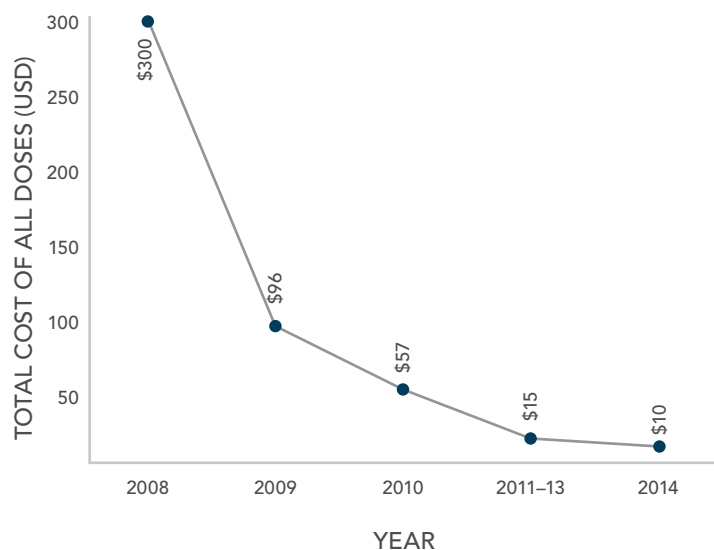
The growing recognition of the co-morbidity of cervical cancer and HIV has prompted attention and support from the US President’s Emergency Plan for AIDS Relief and potentially from the Global Fund to Fight AIDS, Tuberculosis and Malaria. The recent decision by the Board of the Global Fund to consider funding country requests that include the co-infections and co-morbidities associated with HIV and AIDS could open up a new, much needed avenue for funding. And we hope that CCA efforts to bring together a broad range of new cervical cancer investors will bear fruit.

One of the challenges of the past was uncertainty about the price tag for prevention. Now, using results from sophisticated models at Harvard University, we have a better sense of the costs. For example, the Harvard study found that investments totaling US\$3.6 billion are required over the next ten years to vaccinate all 10-year-old girls and provide screening and preventive treatment to women at highest risk for cervical cancer in low- and lower-middle-income countries. Much of this investment will come from country governments, but in many cases, donor investment will be needed to bring these services to scale.

WOMEN AT RISK, AT DIFFERENT TIMES IN THEIR LIVES

In recent years, impressive progress has been achieved in decreasing mortality from pregnancy-related complications (maternal mortality) in developing countries. This is the result of significant investment in evidence-based best practices and rigorous impact monitoring. This success in reducing maternal mortality is cause for great hope that with similar investments, these same mothers, having been saved during pregnancy, also will be protected 10 or 20 years later in life when they face the threat of cervical cancer.

4.2 HPV VACCINATION COST DROPPED FAST



The cost of full HPV vaccination was already dropping, and when WHO recommended using only two doses in 2014, the cost was cut by an additional 33 percent.

4.3 ILLUSTRATIVE COSTS OF SPECIFIC CERVICAL CANCER INTERVENTIONS[†]

HPV Vaccination	Cost (USD)	Impact
Vaccinate one million young adolescent girls in a country receiving HPV vaccine from Gavi (two-dose regimen, service delivery costs only, no GAVI co-pay included)	\$5m	n/a
Vaccinate all young adolescent girls in the five highest-burden low- and lower-middle-income countries (Gavi countries, two-dose regimen, vaccine + service delivery)	\$24m/year	66,000 deaths prevented
Purchase vaccine for one million young adolescent girls in a middle-income country (two-dose regimen, vaccine only)	\$27m	n/a
Vaccinate all young adolescent girls in the 21 highest-burden countries in Africa (two-dose regimen, vaccine + service delivery, 19 Gavi countries, 2 non-Gavi countries)	\$163m/year	156,000 deaths prevented
Screening and Preventive Treatment		
Purchase cryotherapy equipment to treat 100,000 women in a sub-Saharan African country	\$150,000	n/a
Screen and treat one million women aged 30–49 years in a sub-Saharan African country using VIA and cryotherapy	\$10.4m	4670 deaths prevented
Screen and treat one million women aged 30–49 years in India using HPV DNA testing and cryotherapy	\$11m	6040 deaths prevented
Screen and treat one million women aged 30–49 years in a sub-Saharan African country using HPV DNA testing and cryotherapy	\$17.7m	9630 deaths prevented
Screen and treat one million women aged 30–49 years in a Latin American country using HPV DNA testing and cryotherapy	\$31.2m	4100 deaths prevented
Screen and treat all women aged 30–49 years in the 21 highest-burden African countries using HPV DNA testing and cryotherapy in one year.	\$1.9b	1.2m deaths prevented

[†] The cost and impact estimates in this table were generated from sophisticated computer models run by Dr. Stephen Resch, Dr. Nicole G. Campos and their team at the Harvard University T.H. Chan School of Public Health, Center for Health Decision Science.

Conclusion

Over the past decade, the world has seen extraordinary advances in cervical cancer prevention. Until recently, the knowledge and tools needed to effectively tackle the disease in low-resource settings had not been developed or validated. Today, following extraordinary scientific breakthroughs, strategic field research, and tireless efforts by governments and their partners, a new reality is emerging. We now have the knowledge and tools to bring cervical cancer prevention to every country and to dramatically scale interventions that are proven to save women's lives.

Ramping up global commitment to cervical cancer prevention is critical to achieve current and emerging global health and development targets and the reduction of NCDs worldwide.

Cervical cancer prevention should be a core component of an integrated approach to protecting women, children, and adolescents throughout the life-course. We must support the integration of vaccination, screening, and preventive treatment into school health, women's health, and HIV/AIDS prevention and treatment programs.

It is time for international agencies, governments, and donors to step up their efforts to support national initiatives. Engagement in cervical cancer prevention could result in one of the most significant "easy wins" in global public health today. By working to improve and scale current prevention programs, we have the unique opportunity to strengthen health systems and expand equity and access for underserved women and adolescent girls.

"WE HAVE THE TOOLS AND KNOWLEDGE WE NEED. ENGAGEMENT IN CERVICAL CANCER PREVENTION COULD RESULT IN ONE OF THE MOST SIGNIFICANT 'EASY WINS' IN GLOBAL PUBLIC HEALTH TODAY."

SPOTLIGHT

AFRICA CALLS FOR PREVENTION

African health advocates and political leaders are leading the charge for increased access to HPV vaccination and cervical cancer screening and preventive treatment. Encouraged early on by a handful of dedicated women, including Princess Nikky Onyeri, a cancer advocate from Nigeria; the Honorable Sarah Nyombi, a former Ugandan parliamentarian; and a host of African First Ladies, cervical cancer prevention clearly is on the African agenda.

For several years, the Forum of African First Ladies Against Breast, Cervical and Prostate Cancer has called for improved national policies and expanded access to cervical cancer prevention services across the continent. In 2015, Kenyan First Lady Mrs. Margaret Gakuo Kenyatta graciously hosted the Ninth Stop Cervical, Breast and Prostate Cancer in Africa Conference. At the meeting, 20 African First Ladies signed the “Nairobi Cancer Declaration” and committed to raising awareness and resources to address Africa’s cervical cancer challenge.

There are many other examples. During her tenure as First Lady of Zambia (and continuing today), Dr. Christine Kaseba Sata—an obstetrician/gynecologist by training—provided critical support



First Lady Margaret Kenyatta of Republic of Kenya addresses the Ninth Stop Cervical, Breast and Prostate Cancer Conference in Africa.

Photo: American Cancer Society

to bring screening and HPV vaccine to her nation. And in Ethiopia, First Lady Mrs. Roman Tesfaye has played a key role in fostering a supportive environment for broad action to prevent cervical cancer, including recently scaling up screen-and-treat programs from 25 to 135 public facilities.

African advocacy for cervical cancer prevention has never been stronger!

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ADDITIONAL RESOURCES

- **RHO Cervical Cancer Library (PATH):** www.rho.org
- **Comprehensive Cervical Cancer Control: A Guide to Essential Practice—Second Edition (World Health Organization):** www.who.int/reproductivehealth/publications/cancers/cervical-cancer-guide/en/
- **Cervical Cancer Prevention: Practical Experience from PATH:** www.rho.org/HPV-practical-experience.htm
- **Human Papillomavirus Vaccine (Gavi, the Vaccine Alliance):**
www.gavialliance.org/support/nvs/human-papillomavirus-vaccine-support/
- **Cervical Cancer Initiative (Union for International Cancer Control):**
www.uicc.org/programmes/cervical-cancer-initiative-cci/issue
- **Guidance on Cervical Cancer (International Federation of Gynecology and Obstetrics):**
www.figo.org/sites/default/files/uploads/wg-publications/gynec-cancer/English_version.pdf

Cervical Cancer
ACTION

A Global Coalition to STOP Cervical Cancer