



## Reducing cervical cancer inequities worldwide

### WHY CERVICAL CANCER?

For over two decades, PATH has championed technical, systems, and policy innovations to reduce cervical cancer deaths among the world's poorest women. We have developed and tested new approaches for screening women for precancerous lesions caused by the human papillomavirus, or HPV. We also have used groundbreaking strategies that engage communities in supporting screening and necessary follow-up for at-risk women. We have carried out wide-ranging assessments of how HPV vaccine can be introduced in settings where disease rates are highest. And throughout, we have partnered with stakeholders at all levels to build the evidence, experience, and policy support necessary to establish programs that measurably reduce morbidity and mortality rates.

PATH's work in cervical cancer is driven by our commitment to addressing the stark inequity in cervical cancer burden between developed and developing country women, and by the reality that cervical cancer is an almost wholly preventable disease. In 1990, for example, incidence rates varied from a low of about 9 per 100,000 in North America to highs of over 40 per 100,000 in some sub-Saharan and Latin American and Caribbean countries.

We have excellent tools in hand and some exciting new ones on the horizon.

Still today, death rates echo these high incidence rates with 230,000 deaths in less-developed countries each year compared to 35,000 deaths in more-developed countries [GLOBOCAN 2012], and the numbers continue to rise (see Figure 1 on page 2).

In the early days of our work, the human face of these statistics was regularly emphasized by frustrated physicians in low-resource settings who asked PATH for help addressing the needs of women presenting at their clinics with advanced, incurable cancers. These health workers were all too familiar with the grim reality of women suffering and dying alone due to the symptoms and stigma of the most common cancer killer of women in their countries. They told stories of how children, families, and communities were impacted by the death of a woman in her middle years, when she often was a mainstay of food production, education, and health for her family and village (see box on page 3). They knew that the disease could be conquered and that in western countries, cervical cancer was an increasingly rare condition.

When PATH made a decision to invest in a program addressing cervical cancer inequities 25 years ago, we set a course for bringing our strongest skills and experience

to the challenge. In the coming years, we will build on the rich history of our work and the recognized expertise of our team to increase access to lifesaving tools and programs. We will identify and support innovations, programs, and policies that have the strongest potential to produce measurable decreases in morbidity and mortality, and we will apply lessons learned from our cervical cancer work to related women’s health needs across the developing world.

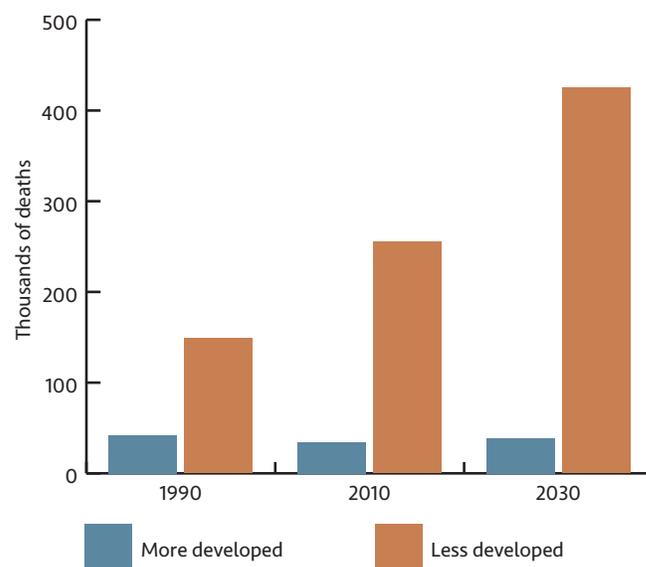
### PATH’S COMMITMENT AND CONTRIBUTIONS

PATH has produced and assessed important cervical cancer innovations; accelerated the integration of new primary and secondary prevention approaches nationally and internationally; disseminated critical evidence; advocated for action based on the evidence; and formed and supported diverse partnerships to enhance and accelerate program impact.

We began our work in 1991, with a focus on landscaping cervical cancer burden and existing prevention programs in the developing world. This work led to a series of publishing, convening, and advocacy efforts that raised awareness of the problem and promoted investment in solution-oriented activities. In parallel, PATH steadily increased our activities in developing, assessing, testing, and piloting new screening and preventive treatment approaches (treatment of *precancer* as opposed to advanced cancer) in low-resource settings. We made certain that the needs and concerns of women, communities, and primary providers were considered throughout. As we steadily broadened our portfolio of cervical cancer activities, we engaged key donors in the field, including the US Agency for International Development (USAID), the Soros Foundation, the World Bank, and the Bill & Melinda Gates Foundation.

From 2000 to 2008, PATH led the Alliance for Cervical Cancer Prevention (ACCP) and other critical partnerships, including a public-private partnership (PATH and Digene Corporation) to develop an HPV test designed specifically for use in low-resource settings (see box on page 5). The ACCP (a partnership of PATH, EngenderHealth, the International Agency for Research in Cancer [IARC], Jhpiego, and the Pan American Health Organization [PAHO]) worked in 13 countries in Africa, Asia, and Latin America and the Caribbean, developing evidence on screening and treatment approaches, service delivery needs, community engagement requirements, and advocacy priorities for preventing cervical cancer. Based on the extensive evidence base generated by ACCP, in 2008, the partnership made recommendations that upended traditional Pap smear-based screening strategies that had been promoted for years, but were rarely successful in low-resource settings. The new focus was on simple, inexpensive methods such as visual inspection with acetic

**FIGURE 1. Estimated global deaths from cervical cancer over time, by country level of development as defined by GLOBOCAN (from Tsu et al 2013).**



acid, or VIA. The World Health Organization (WHO) has since adopted and expanded this guidance, and use of VIA for screening has become a norm in low-resource settings.

As PATH was working to build the evidence and experience for new approaches to screening and preventive treatment, pharmaceutical companies were moving HPV vaccines through the development pipeline, with positive results. As these exciting new health tools neared approval in the developed world, vaccine companies and the global health community recognized the need to accelerate access to HPV vaccines in low-resource settings. Based on PATH’s extensive experience in cervical cancer prevention and in vaccine development and introduction, we were selected by the Bill & Melinda Gates Foundation to lead the first comprehensive, multi-country assessment to build evidence regarding how licensed HPV vaccines can be introduced efficiently and effectively in the poorest settings. Data on service delivery issues, community engagement needs, costs, and more were used to develop guidance for countries and international agencies. PATH continues to provide support to countries introducing HPV vaccine through projects supported by Gavi, the Vaccine Alliance.

PATH’s work in supporting screening and preventive treatment efforts continues, with a focus both on developing and refining new technologies and on accelerating use of proven technologies for public health impact. PATH’s work to develop and support introduction of the *careHPV™* test has been groundbreaking. PATH led the establishment of regional training facilities for screening and preventive treatment in Africa and Latin

## Aisha's tragedy and Uganda's promise



girls and screening and preventive treatment services available to all adult women. With government commitment, international funding, and technical help from PATH and other organizations, Uganda has the capacity to make deaths from cervical cancer a rare event, just as they are in most western countries.

A BBC film, *The Real Lady Killer*, tells Aisha's story and explores Uganda's efforts to prevent the tragedy her family experienced. To view the film online, see "For more information" at the end of this paper.

Cervical cancer has profound impacts on women and their families in the developing world. Take the example of Aisha, a 10-year-old girl who PATH met in 2009 when working with the Ugandan government to explore how best to provide HPV vaccine in settings like rural Nakasongola District. Aisha received HPV vaccine through a PATH-led demonstration project at her school—she now is protected against the most common types of HPV that cause cervical cancer.

Tragically, Aisha lost her mother to cervical cancer just two years before she was vaccinated. This left her family economically and socially vulnerable, given their reliance on small-scale farming to meet daily needs.

Recognizing that women like Aisha's mother remain at high risk of cervical cancer, Uganda is working hard to make vaccine available to all

America and the Caribbean, aimed at accelerating scale-up of secondary prevention (screening and preventive treatment) programs. PATH was also among the first organizations to build evidence for use of self-collected vaginal samples for molecular testing, an approach that has the potential to increase access to effective screening programs for women around the world. In addition, vaginal self-sampling holds promise for overcoming cultural and implementation barriers (shyness and cultural stigma against presenting to a male provider). PATH also is pioneering market-based analysis of factors affecting access to preventive treatment—including cryotherapy and thermal coagulation—around the world.

Over the years, PATH has provided an evidence-based advocacy voice for addressing cervical cancer. Our early publications on the burden of disease and available screening/preventive treatment programs in low-resource settings established the groundwork for extensive, systematic documentation of ACCP evidence and recommendations. Our landmark documents outlining experience in HPV vaccine introduction have been used by policymakers and planners worldwide. We maintain an extensive web resource of cervical cancer information ([www.rho.org](http://www.rho.org)); provide leadership to the Cervical Cancer Action coalition, a global partnership focused on maximizing the impact of those working to stop cervical cancer ([www.cervicalcanceraction.org](http://www.cervicalcanceraction.org)); and contribute to a range of working and expert groups based at WHO and other agencies, with the goal of providing an integrated

evidence- and equity-based perspective to discussions about how to measurably reduce the toll of cervical cancer worldwide.

### IMPRESSIVE PROGRESS, BUT WE ARE NOT DONE YET!

The progress we have seen over the past two decades is remarkable and clearly provides a platform for changing the picture of cervical cancer worldwide in the coming years. That said, there is still much to be done:

- Women in low-resource settings continue to die from cervical cancer at much higher rates than their counterparts in wealthier countries.
- VIA-based and HPV-DNA test-based screening programs—while expanding—still are not available to the vast majority of women who need them.
- Shortages of trained providers and lack of adequate laboratory and referral options limit the ability of countries to scale programs for impact.
- For women who develop cervical cancer, treatment options are often unavailable or require travel that presents insurmountable challenges.
- Financial resources are still woefully inadequate.

To help bridge these gaps, and to ensure that all women are protected, PATH will continue to expand our cervical cancer program, building on pillars of innovation, integration, information, and partnerships.

## Global progress in cervical cancer prevention

PATH has been an important contributor to changing the face of cervical cancer prevention over the past 25 years.

	In 1990	In 2015
Disease burden	<ul style="list-style-type: none"> <li>• Many countries did not prioritize—or even speak about—the high burden of cervical cancer among their citizens.</li> <li>• No solid agreement as to whether cervical cancer was caused by an infectious agent, or what that agent might be.</li> <li>• Widespread pessimism regarding feasible solutions to the problem.</li> </ul>	<ul style="list-style-type: none"> <li>• Cervical cancer is broadly recognized as a critical health problem that can be prevented.</li> <li>• The natural history of the disease is well understood to be caused by HPV infection.</li> <li>• Optimism for eradication of cervical cancer. There are numerous resources for and support to countries seeking to build or strengthen cervical cancer prevention programs.</li> </ul>
Screening and treatment	<ul style="list-style-type: none"> <li>• Cytology-based programs (Pap smear) were the only screening options worldwide.</li> <li>• Preventive treatment for even low-grade precancer was often limited to surgical interventions (including cervical conization and hysterectomy).</li> <li>• These approaches were uniformly unsuccessful in reducing disease burden in low-resource settings, and often harmed women.</li> </ul>	<ul style="list-style-type: none"> <li>• Countries have a range of screening approaches including VIA, HPV-DNA testing, colposcopy, and Pap smear.</li> <li>• Hysterectomies are no longer needed to treat low-grade precancer. Safe and effective evidence-based options for preventive treatment include cryotherapy, thermal coagulation, and more.</li> <li>• Documented experience on how to introduce and sustain these approaches in the poorest settings is available.</li> </ul>
Vaccination	<ul style="list-style-type: none"> <li>• No HPV vaccines for women or girls.</li> </ul>	<ul style="list-style-type: none"> <li>• Two highly effective HPV vaccines are available worldwide, due in large part to a sustained development partnership between public-sector research agencies and pharmaceutical companies.</li> <li>• PATH’s work to demonstrate how these vaccines can be provided most efficiently—and cost-effectively—in the lowest-resource settings has been instrumental in expanding access in poor countries.</li> </ul>
Policies and guidelines	<ul style="list-style-type: none"> <li>• Policies and guidelines were not yet established by WHO, the United Nations Population Fund (UNFPA), and most other global agencies, in part because of the paucity of evidence for successful, sustainable approaches to reducing disease burden.</li> </ul>	<ul style="list-style-type: none"> <li>• Established policies and guidelines are available from WHO, UNFPA, Gavi, and other agencies that are providing critical leadership in advancing evidence-based programs to address cervical cancer inequities.</li> <li>• PATH has collaborated with all of these agencies over the course of our cervical cancer program to advance policies, financing decisions, and practical program guidance.</li> </ul>
Public awareness	<ul style="list-style-type: none"> <li>• There was little, if any, information on how well women, communities, or primary providers in low-resource settings understood cervical cancer or how lack of understanding might inhibit access to screening, preventive treatment, or invasive cancer treatment.</li> </ul>	<ul style="list-style-type: none"> <li>• There is extensive documentation of the issues that need to be addressed with local stakeholders as new programs are launched and scaled.</li> <li>• There are many success stories demonstrating strong demand for both vaccination and screening/preventive treatment services, including among the poorest and most disenfranchised populations. PATH has been a major contributor to this knowledge base.</li> </ul>

We are convinced that the evidence, experience, and commitment demonstrated by PATH teams over the past two decades will accelerate and expand prevention programs in the future. We have excellent tools in hand (and some exciting new ones on the horizon), and we have the understanding necessary to introduce such tools for measurable health impact. Now is the time to scale programs and systems and improve the lives of women, their families, and communities across the globe.

As we continue working toward our overriding goal of expanding access to evidence-based primary prevention, screening, and preventive treatment approaches in low-resource settings, we also will leverage PATH's broad capacity and program portfolio to apply our experience to inform and accelerate work in related global health challenges, including breast cancer and other noncommunicable diseases (NCDs). Our cervical cancer portfolio has given us important insights into addressing the growing burden of NCDs worldwide, including how to build prevention/downstaging services for cancers in low-resource settings, how to address "older women's" health concerns through existing health services, understanding the costs and impact of integrating new services into existing systems, and more.

## FOR MORE INFORMATION

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### CareHPV: Innovation to reduce cervical cancer prevention inequities



demanding for broad-scale use in the developing world. To respond to this need, we established a partnership with Digene (now QIAGEN), the developer of the first HPV test, to develop a robust, affordable, and accurate test designed for use in low-resource settings.

PATH worked with the manufacturer and other partners to design the new test (*careHPV*, pictured above), validate it in a range of settings, demonstrate how it can be used as part of a cervical cancer prevention program, and support commercialization efforts in developing countries. PATH's work through the Bill & Melinda Gates Foundation-funded START-UP project (Screening Technologies to Advance Rapid Testing for Cervical Cancer Prevention—Utility and Program Planning) has shown that *careHPV* is more sensitive than VIA or Pap screening in all project sites (India, Nicaragua, and Uganda), including when using self-collected vaginal samples, which often are more acceptable to women, and can increase uptake of the test and reduce program costs.

While funding for systematic use of *careHPV* in large-scale programs is still a concern, the work that PATH led to develop, assess, demonstrate, and support the introduction of *careHPV* has laid the groundwork for use of effective molecular tests for cervical cancer prevention programs around the world.

Over a decade ago, PATH set our sights on developing an HPV-DNA test appropriate for low-resource settings. While visual screening (VIA) is a great step forward in increasing access to cervical cancer prevention services in these settings, strong evidence has demonstrated that HPV testing, paired with effective preventive treatment, can have the largest impact.

When PATH began this work, HPV-DNA tests were available but they were too costly and technically

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CareHPV is a trademark of QIAGEN.

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

PATH is the leader in global health innovation. An international nonprofit organization, we save lives and improve health, especially among women and children. We accelerate innovation across five platforms—vaccines, drugs, diagnostics, devices, and system and service innovations—that harness our entrepreneurial insight, scientific and public health expertise, and passion for health equity. By mobilizing partners around the world, we take innovation to scale, working alongside countries primarily in Africa and Asia to tackle their greatest health needs. Together, we deliver measurable results that disrupt the cycle of poor health. Learn more at [www.path.org](http://www.path.org).

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