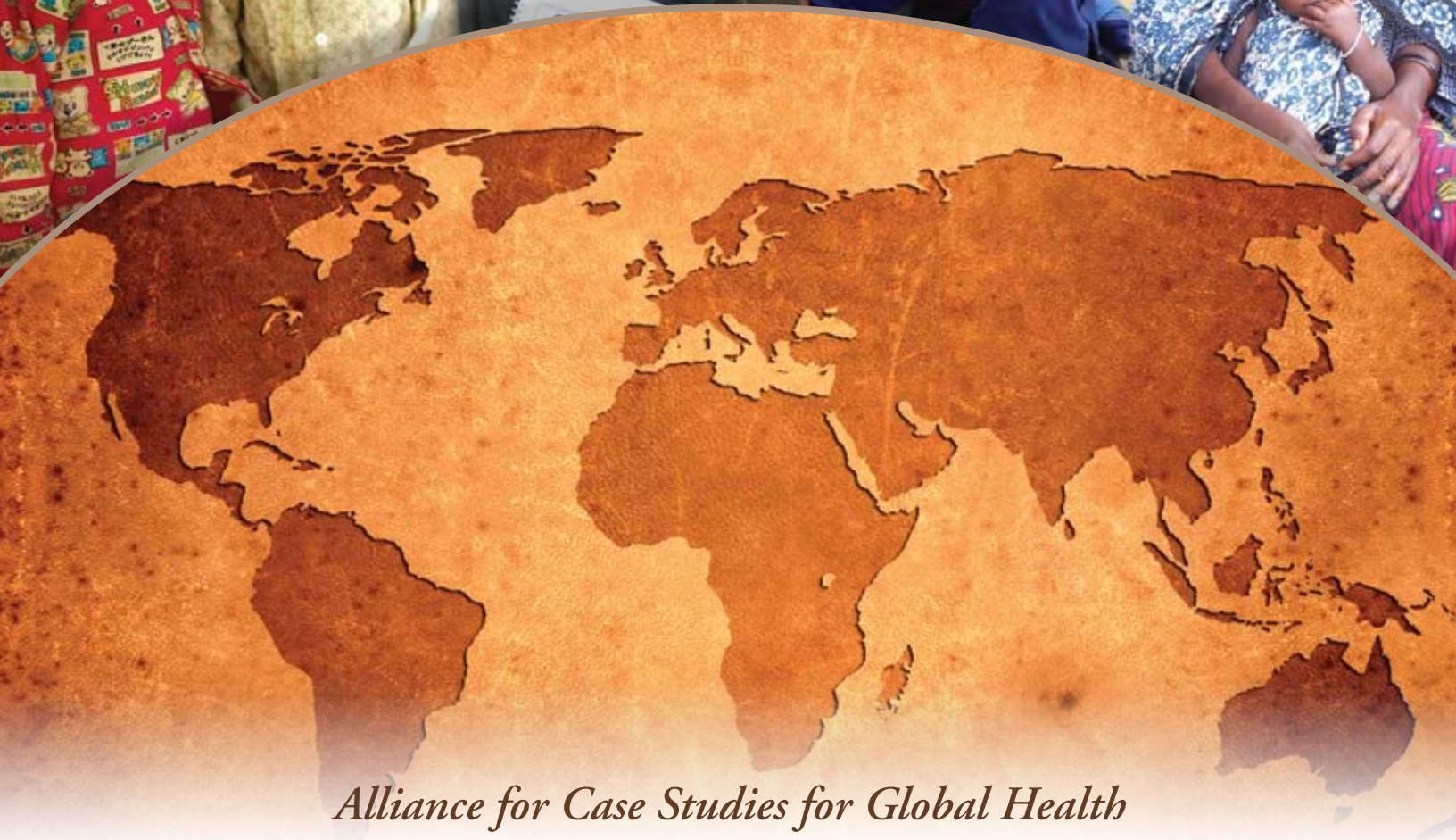


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Multi-Pronged Attack on Cervical Cancer Detection Seeks to Speed Detection and Treatment in Resource-Constrained Countries



Lessons Learned:

- *Because of differences in stakeholders' organizational styles and cultures, agreement on a clear, common purpose is critical to a successful collaboration and ongoing knowledge sharing may require continuous effort.*
- *Inadequate funding can leave individual partners stretched too thin and thus slow results.*
- *Helping local medical communities recognize the advantages of new health care technologies will enable effective rollout.*



ACCP, CCA, PATH and others agree that the best strategy for rapidly reducing deaths due to cervical cancer is a comprehensive prevention approach, focusing both on screening of adult women and vaccination of adolescent girls.

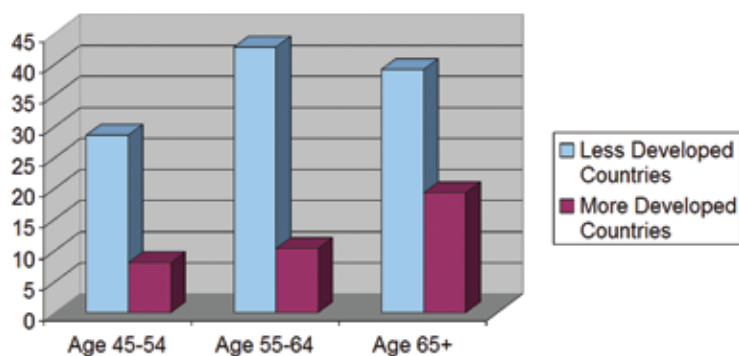
Cervical cancer kills approximately 270,000 women each year with nearly 85 percent of those deaths in resource-poor settings. Routine cytological screening of women, commonly known as the Pap smear, has resulted in a dramatic decline in cervical cancer deaths over the past four decades in wealthier regions. However, screening has been much less successful in developing regions. A key reason for continuing high mortality in the developing world is the shortage of practical and cost-effective, yet still high-quality, precancer screening programs. Existing tests are prohibitively expensive and too technical for low-resource settings.

New technologies that allow alternative screening methods could help overcome this obstacle. To this end, PATH developed close partnerships with several, very different organizations to launch a multi-pronged approach to solving the problem.

In 2000, an effort to investigate sustainable alternatives to Pap became the Alliance for Cervical Cancer Prevention (ACCP); member organizations included EngenderHealth, the International Agency for Research on Cancer (IARC), Jhpiego, the Pan American Health Organization (PAHO) and PATH, which acts as the coordinator. Recently the alliance expanded to include three additional members. The ACCP, with support from the Bill & Melinda Gates Foundation, worked closely with the World Health Organization, Harvard University, and governmental and nongovernmental partners in Africa, Asia and Latin America on a coordinated research agenda aimed at assessing a variety of approaches to cervical cancer screening for low-resource settings. The goals were to improve service delivery systems, ensure that community perspectives and needs were incorporated into program design, and heighten awareness of cervical cancer and effective prevention strategies.

After initial friction generated by competitive natures and role misunderstandings, the details of a clear, common purpose and

Age-Specific Cervical Cancer Mortality Rates per 100,000 Women



Source: Globocan 2002

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

roles for each partner were negotiated and carefully articulated over the first couple of years to help coalesce the ACCP. Trust between the partners built over time, making it easier to resolve issues as they arose. The group also agreed early on to operate under the single Alliance logo, rather than vie for positioning of their separate logos, which has helped build cohesiveness. Even so, partners are listed individually in the body of documents and printed materials so that some individual recognition is retained.

In the nine years since inauguration of the project, the ACCP partners conducted studies comparing a number of screening techniques including cytology (Pap), visual inspection methods with acetic acid (VIA) or Lugol's iodine, and a HPV DNA test. The tests were evaluated in more than 20 low-resource settings around the world.

VIA and HPV DNA testing have proven to be of special interest. The ACCP found that VIA compares well to cytology in terms of sensitivity for disease detection, yet presents clear advantages because it requires fewer specialized personnel and less infrastructure, training and equipment. Cervical cancer screening using VIA can be offered in remote, less-equipped clinics, thereby reaching more women. Another important advantage is that VIA provides immediate results, making it possible to screen and treat women during the same visit. Immediate treatment means that women do not have to make an extra visit to the health center — this reduces the number of women who are lost to treatment

because they cannot return for one reason or another. Even so, recent data suggest that a new, low-cost HPV test specifically designed for low-resource settings has much better performance than either cytology or VIA (see below).

In 2003, PATH launched a second related initiative: the Screening Technologies to Advance Rapid Testing (START) project designed to develop two different biochemical HPV screening methods appropriate for use in the developing world, including the low-cost HPV DNA test previously mentioned. It was important that the tests be acceptable to women and their providers, relatively simple to use, accurate, and affordable; cultural sensitivities to medical tests being performed on the genitals or by male doctors on female patients were of concern, therefore the testing method had to be made acceptable to the population. In addition, diagnosis and treatment, if indicated, should be possible during the same screening visit.

In this effort, PATH developed close partnerships with the commercial medical diagnostics company Digene, since purchased by QIAGEN, and the World Health Organization (WHO). Digene/QIAGEN needed access to cervical smear samples from countries of interest, and needed PATH to manage field research with local institutions.

PATH needed an industry partner to develop the technology and for future manufacturing and distribution of the test. WHO, a research and advocacy partner, was keenly interested in technologies that could bring precancer screening to poor women. Further, WHO plays a regulatory role, and will assess the new test

ACCP project areas



for international procurement by United Nations (UN) agencies, such as the United Nations Population Fund, and will prequalify the manufacturer of the product — thus significantly increasing access to the test worldwide.

PATH is also partnering with Jhpiego, a not-for-profit agency affiliated with The Johns Hopkins University, to lay the foundation for future introduction of the new test through creation of a network of in-country training excellence centers focused on VIA and cryotherapy.

By early 2007, PATH and QIAGEN had developed and field-evaluated a new, highly sensitive HPV DNA test that is portable, could be powered with rechargeable batteries and uses reagents that do not require refrigeration. Test results are available in less than two-and-a-half hours, facilitating immediate treatment or referral in the same visit.

In developing countries, however, several challenges impede widespread adoption of new technologies. Before incorporating the HPV DNA test into national cervical cancer prevention strategies and plans, ministries of health need evidence that the new test is feasible and appropriate for their health system infrastructure and their geographic, cultural and economic circumstances. In addition, private industry needs guidance in navigating the complexities of product introduction in the public sector of developing countries, which are generally perceived as high-risk, low-return markets. To address these issues, in November 2007, PATH inaugurated a follow-up project to START, called START-UP.

And Then There Were Three

Cervical Cancer Action (CCA) is yet a third coalition of organizations with diverse connections to the prevention of cervical cancer in the developing world, specifically to immunization, cancer, sexually transmitted diseases and reproductive health, women's health, and HIV/AIDS. This group coalesced to advocate for equitable and rapid access to new lifesaving technologies to prevent cervical cancer in these countries, specifically better and less expensive methods of screening adult women for signs of pre-cancer and provision of HPV vaccines to protect girls.

CCA was created in 2006; founding members include PATH, PAHO, the American Cancer Society, the International Planned Parenthood Federation, Cancer Research UK, the International Union Against Cancer, the AIDS Vaccine Advocacy Coalition, the International AIDS Vaccine Initiative, and the International Federation of Gynecology and Obstetrics. CCA has been designed to avoid duplicating the activities of any member organization or taking

on activities that member organizations, or other groups, are better able to fulfill. The work of CCA is grounded in public health science, but also evokes arguments related to economics and global equality of access.

The CCA partners recognized that, unless there is coordination and cooperation on a common, forward-looking mission to ensure access to the new tools, the potential for real progress in reducing the global burden of disease will be unfulfilled.

Certain conditions must be in place for these new prevention technologies to become available and be effectively used in developing countries:

- Strong scientific and public health leadership by leading international health agencies and organizations
- Sustained political leadership and financial commitment for a comprehensive approach to appropriately and effectively vaccinate girls and screen and treat women
- Partnership among diverse constituents of civil society, health professionals, medical associations, researchers, donors and governments to support widespread access to these new tools
- Adequate supplies of the full range of HPV and cervical cancer prevention tools from the manufacturers at affordable prices
- Leadership and action by multi-lateral agencies, including rapid prequalification, issuance of international guidelines and large-scale procurement for developing countries.

CCA activities have been limited by its funding model. It has not been able to raise external funding but instead functions on cash and in-kind contributions from CCA Governing Council members. Lack of external funds may be, in part, a result of the decision early on not to solicit or accept funding from the pharmaceutical industry, even though CCA members felt that such funding may have been relatively easy to access. The Governing Council adopted this position to avoid any perception of conflict of interest in its mission.

The funding CCA has obtained from some of the nine Governing Council members over the past two years has been used to support a small but very active secretariat. CCA members recognize the utility of maintaining a dedicated secretariat, but it is unclear how sustainable this shoestring budget system will be in the future.

Aside from the efforts of the secretariat, all CCA work is carried out by members of the CCA Governing Council. These volunteers have primary duties that sometimes force them to put CCA tasks at lower priority. It is more difficult for some members to allocate time to CCA than for others.

Challenges of the Three Efforts

The three initiatives share goals but incurred separate challenges; some obstacles were due to the nature of the partnership, others were due to the nature of the work.

In the case of the Alliance for Cervical Cancer Protection, the groups were brought together because of their interest in cervical cancer prevention in the developing world, but not necessarily because they were driven to work as part of a strong alliance. A lack of attention to the collaborative/coordinated work of the alliance in the early days led to friction — ACCP scientific and programmatic discussions often were contentious and maintaining the partnership seemed in doubt on several occasions.

For example, while some of the partners had more of a research perspective, others were more focused on practical programmatic approaches. This led to different tolerances for uncertainty in the data related to use of visual inspection as a primary screening method and use of a single-visit approach to screening and treatment. Partners were also influenced in part by the prevailing opinions and political climate of the regions where they worked. It is possible that ACCP achievements could have been more extensive had the partners agreed at the start to a coordinated research agenda. However, given early differences in organizational visions, the ways that the funding was dispersed and individual personalities, agreement on an overall agenda did not seem likely.

Over time collaboration became easier. As the evidence base grew during the following years, the partners defined their respective roles and became accustomed to working together. In short, trust levels increased, and the ACCP's collective vision became more aligned. By 2007, ACCP partners were able to articulate and broadcast a clear set of 10 recommendations endorsed by all.

The ACCP is now exploring how a cervical cancer screening visit can serve as a core building block for a broader menu of health services needed by women in their 30s and 40s, such as screening for cardiovascular disease, breast cancer, and diabetes; management of symptoms of menopause; and other services largely unavailable in developing countries, but which address increasingly important public health problems.

The START program initiative and its sequel, START-UP, faced a number of obstacles. A key challenge for QIAGEN, the industry partner, is to develop a business model that allows the marketing of two types of HPV DNA tests — one more technologically complex than the other and, thus, with different pricing tiers — in different parts of the world.

Another key challenge came from medical communities. One aspect of country mobilization is engagement of the community of reproductive health care providers in the country, including the obstetrics-gynecological community. These clinicians and researchers, many of whom are very comfortable with Pap smear testing in urban settings, may see Pap and subsequent diagnosis as gold standard medicine and may, in fact, make a living from cytology. Many have not seen the results of alternative strategies with their own eyes and remain skeptical about those alternatives.

To address these needs, PATH, Jhpiego and WHO are continuing to promote their findings in professional journals, at international meetings and through personal contacts in the hopes of moving influential professionals towards a new paradigm of cervical cancer screening in low-resource settings.

For Cervical Cancer Action, progress toward comprehensive prevention and control has been substantial, despite key challenges including the high current price of HPV vaccine in the private sector and lack of global success implementing large-scale cervical cancer screening in low-resource settings. However, the GAVI's recent interest in subsidizing HPV vaccine and encouraging results using less-expensive and more rapid screening tests is galvanizing the effort. The global conversation has evolved to the point that country-focused discussions can become a major theme over the next few years.

Coming to Agreement

Some member organizations are constrained in the kinds of agreements they can sign with others. This is especially true of UN agencies. It is for this reason that neither WHO nor IARC felt they were able to join the coalition. UN member PAHO was able to join, but cannot enter into some of the agreements shared by all other groups. The coalition has had to craft agreements to accommodate these circumstances accordingly.

By Pam Baker