



HPV and Cervical Cancer: Unique Challenges and Opportunities for Disease Prevention

According to the most recent global annual estimates, nearly 500,000 women will develop cervical cancer and some 275,000 will die of this preventable disease.¹ The vast majority of cervical cancer cases and deaths occur in developing countries where women have little or no access to effective disease prevention services. The population of older women—women at greatest risk for cervical cancer in the absence of effective screening—is growing rapidly in these countries. By the year 2020, three of four women older than 50 years will live in developing countries.² Cervical cancer tends to disproportionately affect the lowest-income women within most developing countries and the disease is the number-one cause of cancer-related deaths among women in these countries.¹

HPV and cervical cancer: natural history and burden of disease

Human papillomavirus (HPV) infection has been clearly established as the necessary (but not solely sufficient) cause of invasive cervical cancer. HPV is the most common sexually transmitted infection (STI) worldwide, and developed-country studies suggest that it infects an estimated 50 to 80 percent of sexually active women at least once in their lifetime.^{3,4} Women are usually infected with HPV in their teens, 20s, or early 30s, although these infections are typically transient or become undetectable over time.

Not all HPV types cause cervical cancer

More than 100 HPV types have been identified, and of these, more than 30 types are known to cause genital infection. These types are broadly classified as high or low risk for cervical cancer, and some 18 types are considered high-risk or oncogenic. Approximately 5 to 10 percent of women infected with oncogenic HPV types develop persistent infections; these women have an increased risk of developing precancerous cervical lesions. If untreated, the lesions can progress to cancer over a period of years. Cervical cancer occurs most commonly among women in their 40s and 50s.

This 20-year time frame from HPV infection to development of cervical cancer provides a window of opportunity during which screening programs can be most effective. An array of environmental and host immunological factors are believed to influence whether and how progression occurs, although the associated mechanisms are not currently well understood.

Two HPV types account for about 70 percent of HPV infections

Six types of HPV account for about 85 percent of cervical cancer cases worldwide; two of these types—16 and 18—account for some 70 percent of cases. There are regional and country variations in the distribution of HPV types in cervical cancers, however. For instance, an International Agency for Research on Cancer (IARC) analysis found that in sub-Saharan Africa, HPV 16 and 18 account for 64 percent of cancers, and HPV 45 accounts for almost 14 percent. In Central and South America, HPV 16 and 18 account for 65 percent of the total, and HPV 31 accounts for over 7 percent.⁵ More data are needed to clarify these differences. Another analysis of 42 studies in 22 countries found that HPV 16 and 18 account for 10 percent less cancer in developing countries in comparison to developed countries.⁶

Integrating vaccines into the prevention equation

Although there are many options for preventing HPV infection, all have limitations. Preventing HPV infection is challenging because the virus is easily transmitted and generally does not produce any symptoms. Genital warts caused by some types of HPV can be treated, but no therapies can eliminate the underlying infection and the virus can remain infectious for years. Condom use has been shown to have limited preventive effect because HPV can reside throughout the anogenital region. Nonetheless, women can protect themselves from HPV infection to some degree by using condoms regularly and limiting the number of sexual partners.



Secondary prevention of cervical cancer through screening for precancerous lesions and offering treatment as appropriate has proven to be an effective public health strategy. While well-organized cytology programs have significantly reduced the burden of disease in developed countries, infrastructure and other requirements make cytology difficult to implement in many low-resource settings. Alternative screening methods such as visual inspection with acetic acid (VIA) or with Lugol's iodine (VILI) offer promise as simple, rapid, and effective means of identifying precancerous cervical changes; evidence regarding their impact on burden of disease, when combined with simple outpatient treatment as needed, will be available in the near future. In addition, HPV DNA testing is more objective and generally performs better than other tests in women 30 years and older. However, as currently formulated, the test requires considerable infrastructural and technical capacities that make it difficult to implement in low-resource areas.

The development of prophylactic HPV vaccines offers new hope for primary prevention of cervical cancer. Clinical trials of the two first-generation vaccines—one for HPV types 16 and 18 and the other for types 16, 18, 6, and 11—have shown that they conferred high levels of protection against incident and persistent infections.^{3,7} Decision-science modeling suggests that an HPV 16/18 vaccine—if 98 percent effective at preventing persistent HPV infection—would reduce the total burden of cervical cancer by 51 percent over several decades.⁸

Unique challenges remain

While recent progress in vaccine development is exciting, the natural history of HPV and cervical cancer and variations in the type-specific global prevalence of HPV present unique challenges with regard to introducing vaccines. It may be difficult to communicate the public health benefit of preventing a very common, albeit usually harmless, STI that has only a remote possibility many years in the future of progressing to cervical cancer. The impact of a vaccine, particularly if administered to young adolescents, will not be measurable for decades to come—the amount of time it would take for girls to reach an age when they might otherwise have developed cancer. Administering an HPV vaccine at

early adolescence (prior to sexual debut) will pose challenges related to vaccine acceptability, awareness raising, and logistics (see the factsheet *Accelerating HPV Vaccine Access in Developing Countries*, PATH 2005). Further, a vaccine's impact on burden of disease will vary according to HPV type prevalence; even vaccines that are 100 percent effective will have limited impact in regions with high prevalence of high-risk HPV type(s) not protected against by the vaccines. While it is clear that vaccines will not eliminate the need for effective cervical screening and treatment for many years to come, they can substantially reduce the burden that cervical cancer imposes on women and health services.

References

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