Global Health: Role of HPV Testing in Resource Poor Environment

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Global Health: Role of HPV Testing in Resource Poor Environment

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Abstract
Eighty-five percent of cervical cancer deaths occur in the developing world. While cervical cancer is only the tenth most common cancer in women in developed countries, it is the leading cause of cancer related deaths in women in low and middle-income countries (LMICs). Despite this, there is a disproportionate allocation of cervical-cancer related resources in countries with the highest burden. Cervical cancer is preventable and amenable to early detection and treatment. Over the past two decades, large-scale data investigating low cost screening interventions have demonstrated efficacy of cervical cancer prevention in many continents. Further, use of HPV vaccine alone has the potential to reduce cervical cancer deaths by 50% over several decades. Decreased overall prevalence of HPV in conjunction with the development of new testing for high risk HPV subtypes has the potential to improve the predictive ability of a single negative HPV test for up to a decade. Nonetheless, in LMICs cervical cancer remains a leading cause of cancer-related morbidity and mortality affecting women. This suggests the focus must shift towards novel and innovative techniques that are widely acceptable and will have a positive impact on access to cervical cancer screening, improved diagnosis, treatment and survival.

Keywords
Human papillomavirus; HPV; Low and middle income countries; LMIC; HPV testing; Cervical cancer screening

Discussion
There have been numerous efforts directed at improving primary and secondary prevention of cervical cancer. Clinical trials have found that HPV vaccination (Gardasil, Gardasil 9, Cervarix) is at least 95% effective in preventing HPV-16 or -18 persistent infection, and at least 93% effective in preventing vaccine-type specific lesions when given to girls prior to onset of sexual activity, or to those without prior infection with these subtypes [1-3]. The data also demonstrates that the HPV vaccine is widely accepted in LMICs. Vaccine coverage ranging from 55-75% can be achieved with a positive impact on access to cervical cancer screening, improved diagnosis, treatment and survival.

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The specific high-risk HPV subtype varies by continent and by ethnic group. One large retrospective analysis of 8977 paraffin specimens of invasive cervical cancer from six different continents identified HR-HPV subtypes by PCR analysis [17]. HPV-16 associated cancers ranged from 66 % to 72% in Europe and North America, while in South America and Oceania it was 59%, 60% in Asia, and 48% in Africa. The greatest proportion of HPV -18 associated cervical cancers (23%) occurred in Africa. HPV-45 was an important high-risk subtype involving 10% of cancers in Africa, and 4-7% of cancers on other continents. HPV-33 was another significant minor high-risk subtype involving 10% of cancers in Africa, and 4-7% of cancers in South America with 4% while it involved less than 3 percent in other continents. The remaining eight HR-HPV subtypes were associated with less than four percent of cancers. In Bhutan, 70% of cervical cancers contain HPV-16, and -18 [18].

Africa has the highest regional prevalence of HPV overall with 22% of women with HPV infections [17]. In Uganda, HPV -52 and -51 are more common than HPV -16 and -18 with detection rates of 12-13 percent versus 11 percent respectively [19]. In a study of 135 smears in Sudan, HPV 16 and 58 were the predominant HR-HPV subtypes [20].

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An international cost-effective analysis evaluated several strategies for cervical cancer screening in Thailand, India, Peru, Kenya, and South Africa [21]. If women are screened once in their lifetime at around age 35 years with either Visual Inspection with Acetic acid (VIA) or HPV testing, a 25 to 36 % reduction in lifetime risk can occur. Risk is reduced further with a 40 % reduction for two screenings.

Women in rural India were randomized to HPV testing with Hybrid Capture® 2 High-Risk HPV DNA Test ™ (HC-2) or no risk can occur. Risk is reduced further with a 40 % reduction for two screenings.

In general, HPV tests are too expensive for a low resource setting. However, one less expensive kit, care HPV (Qiagen Inc Gaithersberg MD) costs USD $5.00. In a study of 2388 women between the ages of 30 and 54, VIA, cytology, HPV testing with HC-2 and care HPV was performed. Colposcopy with biopsy was done as needed. The sensitivities and specificities of CIN2/3 were 41.4/94.5 for VIA, 85.3/87.5 for cytology, 97.1/85.6 for HC2, and 84.3/87.7 for care HPV [23]. In another cross sectional study of 5032 women in rural India, care HPV was superior to VIA and Pap testing for the detection of high-grade preinvasive cervical lesions [24]. An innovative digital diffraction analysis using a smartphone is being currently evaluated to detect HPV DNA and may be another low cost approach to screening [25].

IARC is creating a electronic directory of global screening programs through their IARC screening group http://screening.iarc.fr/cervicalindex.php [15]. There is also a coalition of healthcare advocacy organizations reports on cervical cancer screening efforts and disseminates lectures and pamphlets on screening in developing countries [26]. As more complete data emerges about worldwide cervical cancer rates and outcomes, HPV prevalence by region, and screening programs, it will be possible to fashion interventions of low cost screening and vaccination programs that are region and ethnic group appropriate.

References