Human papillomavirus (HPV), one of the most common sexually transmitted infections (STIs), is the primary cause of cervical cancer.1 HPV infection is a necessary but not sufficient precursor to cervical cancer. While the cumulative lifetime incidence of acquiring HPV is 70 to 80 percent in many countries, the vast majority of women with HPV infection will not develop cancer (see PATH’s fact sheet, Natural History of Cervical Cancer).2,3 Worldwide, interest is growing in the potential uses for HPV DNA testing in cervical cancer prevention programs (see Table 1). HPV testing indicates whether a woman is infected with high-risk HPV types and thus at increased risk of cervical cancer. The test’s relatively high sensitivity for detecting high-grade squamous intraepithelial lesions (HSIL) makes it particularly appealing.4-6

**Techniques for Detecting HPV**

HPV cannot be cultured reliably in a laboratory setting; therefore, HPV testing relies on molecular techniques that detect HPV DNA in cervical samples. Because there are so many HPV types with differing carcinogenic potential, HPV tests are designed to determine if one or more high-risk types are present in a specimen. Descriptions of two broadly recognized techniques for detecting specific HPV types follow.

**Signal-Amplified Nucleic Acid Assay**

The one commercially available HPV test, Digene Corporation’s Hybrid Capture II (HC II) assay, uses signal amplification to detect HPV DNA. It provides sensitivity approaching that of polymerase chain reaction (PCR) (see below). HC II detects 13 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) and is standardized and highly reproducible.

Performing the HC II test involves a laboratory process that produces light signals roughly proportional to the amount of HPV DNA present in the specimen. The process requires equipment ranging from basic laboratory supplies to technologically advanced equipment, such as a special computer. These requirements currently make the use of HC II too costly and difficult to implement in many low-resource settings.

**Target-Amplified Techniques**

Target-amplified HPV assays, such as PCR, produce highly concentrated samples of a specific DNA genetic sequence. The DNA samples are then

### Table 1. Possible Uses of HPV Testing

Optimal uses of HPV testing in cervical cancer prevention programs are not yet clear, but proposed uses include:

<table>
<thead>
<tr>
<th>Triage</th>
<th>Surveillance</th>
<th>Primary Screening</th>
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<tbody>
<tr>
<td>Where Pap smear screening is the norm, HPV testing could be used as a</td>
<td>HPV testing could be used as a means of surveillance of women after treatment for high-grade</td>
<td>HPV testing could be used as a primary screening method for high-grade lesions</td>
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<tr>
<td>triage for women with Pap smear findings of atypical squamous cells of</td>
<td>lesions or microinvasive cancer. Those who test positive for high-risk HPV types would be</td>
<td>among women aged 30 to 35 or older. Those who test positive for high-risk HPV</td>
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<tr>
<td>unknown significance (cells that are atypical but not definitely</td>
<td>monitored more closely than those who test negative.4</td>
<td>would undergo diagnosis via colposcopy or another visualization technique.4,7</td>
</tr>
<tr>
<td>dysplastic). Those who test positive for high-risk HPV types would be</td>
<td></td>
<td></td>
</tr>
<tr>
<td>monitored closely or referred for colposcopy.4</td>
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The cost-effectiveness and clinical usefulness of these approaches have not been clearly outlined and require further research.
probed to identify which specific HPV genotypes are present. PCR is the most common target-amplified technique; its inherent strength lies in its capacity to detect very small amounts of HPV DNA. The considerable skills, equipment, and costs involved, however, generally make PCR inappropriate for large screening programs in low-resource settings.

**Test Performance**

Research suggests that HPV DNA testing may eventually have potential as a primary screening method among women aged 30 to 35 or older. Among these women, the sensitivity of a single lifetime HC II test for detection of high-grade dysplasia has been about 80 to 90 percent (higher than for cytology), and specificity has ranged from 57 to 89 percent.\(^5\)\(^6\)\(^8\) In addition, HC II may be more effective than conventional cytology or visual inspection with acetic acid for screening post-menopausal women. When used to detect HSIL, however, the test is only moderately specific at best, particularly among women younger than age 30.

**Programmatic Issues**

Women who test positive for carcinogenic types of HPV may experience great anxiety about developing cancer despite being at very low risk. There currently is no cure for HPV infection, prevention is very difficult, and there is no way to clearly predict which HPV-infected women are likely to develop cancer. In addition, cervical cancer’s association with sexual activity carries a stigma in many parts of the world, and women may be reluctant to seek screening if it is associated with taking what could be seen as an STI test. A desire to avoid unnecessary client concern may leave providers with difficult decisions regarding how they should describe the test to women. These issues must be taken into account when considering initiating HPV testing. Qualitative research on women’s information needs may help address these concerns and guide the development of culturally appropriate counseling messages.

**Key Recommendations**

- Further research is needed to develop HPV test technologies that are feasible for use in low-resource settings and that accurately predict a woman’s risk of developing high-grade lesions and need for further testing. Ideally, an HPV diagnostic would require minimal supporting equipment and would provide inexpensive, accurate, and rapid detection.
- Further research and education on self-collection and other sampling methods are needed so that providers and women perform the procedures correctly.
- Effective education and counseling messages need to be developed for providers to use when counseling women who are at risk of or are diagnosed with HPV infection.

**Self-Collection of Samples**

Studies indicate that women can successfully obtain self-collected vaginal specimens for use in HPV DNA detection. This has important implications for programs located where cultural and program barriers may limit acceptability of and access to vaginal examination. Self-sampling may be more acceptable to women, resulting in increased program effectiveness due to better population coverage. A South African study evaluating the HC II test found that self-collected samples were less specific but as sensitive as conventional cytology for detecting HSIL in women aged 35 or older.\(^6\) A Canadian study assessing the effectiveness and acceptability of different sampling methods found that self-collection was acceptable to women and showed sufficient sensitivity to warrant further evaluation.\(^9\)

**References**