Feasibility, validity and acceptability of self-collected samples for human papillomavirus (HPV) testing in rural Malawi

Allahna Esber¹, Alison Norris¹, Enock Jumbe², Jonathan Kandodo³, Patrick Nampandeni², Patricia Carr Reese³, Abigail Norris Turner⁴

1. Division of Epidemiology, The Ohio State University, Columbus, USA
2. Child Legacy International, Umoyo wa Thanzi Research, Lilongwe Malawi
3. School of Medicine, The George Washington University, Washington, DC, USA
4. Division of Infectious Diseases, Department of Internal Medicine, The Ohio State University, Columbus, USA

Abstract

Aim
The World Health Organization (WHO) recently endorsed human papillomavirus (HPV) testing as a cervical cancer screening method in countries without established programs. Self-collection for HPV testing may be an effective way to expand screening. Our objective was to assess the feasibility, validity, and acceptability of self-collection for HPV testing in a population of care-seeking, unscreened women in rural Malawi.

Methods
We enrolled women reporting to a rural Malawian clinic from January to August 2015. Participants were offered the option to self-collect a vaginal sample and the study clinician collected a cervical sample for HPV testing. Using the clinician-collected sample as the reference standard, we calculated a kappa statistic, sensitivity, and specificity by hr-HPV type. Participants also received a brief survey assessing acceptability of the procedure.

Results
Among the 199 enrolled women, 22% had any high risk-HPV. Comparing self- and clinician-collected samples for HPV testing, we found generally high agreement (κ = 0.66–0.90) and high specificity (98%–100%), but varied sensitivity (50%–91%) for different types of hr-HPV. We also found that self-collection was acceptable, with 98% of women reporting it was easy to do and 99% reporting willingness to do so again.

Conclusions
WHO guidelines recommend that treatment is available immediately after a positive screening test for clinic-based cervical cancer screening programs. Our findings demonstrate that self-collection of samples for HPV testing is a feasible and acceptable method of cervical cancer screening in this rural Malawian population. High agreement between the self- and clinician-collected samples and high levels of acceptability among women in the study suggest that self-collection of vaginal samples for HPV testing may be effectively incorporated into screening programs among rural, largely unscreened populations.

Introduction
Effective and widespread cervical cancer screening has greatly reduced cervical cancer incidence and related morbidity and mortality. The most commonly used cervical cancer screening method worldwide is a Pap test, which involves the collection of cervical cells for examination under a microscope by a cytopathologist. Pap testing detects abnormal cells in the cervix and enables early detection and treatment of cervical cancer. However, Pap screening programs have low feasibility in limited-resource settings owing to a lack of infrastructure and trained personnel, limited health budgets and competing healthcare priorities.

To address these barriers, some national screening programs use alternatives to traditional cytology (Pap testing), such as visual inspection of the cervix with acetic acid (VIA). VIA involves unaided (naked eye) inspection of the cervix after application of acetic acid to identify abnormal tissue. While VIA eliminates some constraints of Pap testing, such as cost and need for multiple visits, there can be high variability by provider in the quality of VIA screening.

DNA testing for human papillomavirus (HPV) offers an accurate alternative to VIA. The WHO recommends hr-HPV DNA testing as the primary cervical cancer screening approach in places where Pap testing has not been established. Similar to other screening methods, cervical samples are typically gathered by a clinician during the course of a pelvic examination, but samples can also be self-collected by women themselves with a swab. WHO recommends screening with an HPV test and treatment over screening with VIA and treatment where feasible. HPV testing is also recommended as first line screening followed by VIA and treatment.

When successfully introduced, self-collection of samples for HPV testing can increase screening for hard to reach women or women who do not come in for screening tests. Self-collected samples have been shown to perform comparably to clinician-collected samples, but published findings suggest that the population and method of collection or testing are important to consider when assessing the utility of self-collected samples.
The recently lowered costs of HPV DNA testing may make this method of cervical cancer screening a viable screening tool. Combined with self-collection, such a method could be used to increase access to screening, even in settings with limited resources. Previous research suggests that many women in rural Malawi would be willing to self-collect a sample at home, yet no research has examined self-collection in a clinical setting or whether women’s hypothetical willingness would translate into actual behavior if offered an opportunity to provide a self-collected sample. We sought to assess the validity, feasibility and acceptability of using the GeneXpert HPV Assay to test self-collected vaginal samples in a rural clinic in Lilongwe District, Malawi.

Methods

Study setting and population

Women were recruited for this study as part of a larger clinic-based study examining sexual and reproductive tract infections. Briefly, from January to August 2015, any woman who presented to the study clinic in rural Lilongwe District, Malawi, with any genitourinary symptom (including abdominal menstrual cycle or patterns of bleeding; pain with urination, pain during sex, abdominal pain, lower back pain, or any type of pelvic pain; incontinence or unusual urinary odour, frequency or colour; unusual vaginal discharge in terms of quantity, odour, colour or consistency) was referred to study staff to be assessed for eligibility. Women were eligible to participate if they were 18-49 years of age, spoke Chichewa, had at least one genitourinary symptom consented to be examined and give biological specimens for testing, and resided in Lilongwe District. Women who were pregnant or menstruating were ineligible. Women provided written informed consent to participate either by signature or thumbprint.

Data collection

Screening

Women were examined in a private clinic room by the study clinician. At the start of the exam, each woman was offered the option to self-collect a vaginal sample for HPV testing. If she agreed, she was given a sterile, cotton-tipped swab and instructions on how to collect the vaginal sample. The clinician remained in the study room, on the other side of a privacy screen, in case the participant had any questions about collecting the sample. After collection, the clinician placed the swab in 20 ml of Preservcyst solution (Hologic, Bedford, Massachusetts) and proceeded to perform a pelvic examination. The clinician used an endocervical brush to collect the sample for HPV testing. Following collection, he swirled the cervical brush in 20 ml of Preservcyst solution. Both clinician- and self-collected samples were stored between 2°C and 8°C and were tested using the GeneXpert HPV assay at the end of the study (Cepheid, Sunnyvale, California).

The GeneXpert technology was developed to identify multi-HPV, and its use is supported by the Malawi Ministry of Health. The GeneXpert HPV test yields results in four categories: (a) negative for hr-HPV; (b) positive for hr-HPV (but no additional hr-HPV type(s) detected); (c) positive for any hr-HPV type(s) detected; and (d) positive for hr-HPV type(s). All 11 pooled hr-HPV types (31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68; Figure 1). The GeneXpert also includes quality assurance channels for sample adequacy control and a probe check control.

Data analysis

We first described the prevalence of hr-HPV in the study population, overall and by the four separate GeneXpert result categories, for both self- and clinician-collected samples. We then calculated the sensitivity and specificity of self-collected samples, using the clinician-collected samples as a reference standard. In order to assess agreement between the two sampling methods, we calculated a kappa statistic for overall hr-HPV type (positive for any hr-HPV vs. hr-HPV negative) and by the 3 GeneXpert hr-HPV categories (HPV 16, HPV 18/45, additional hr-HPV types). As HPV testing is recommended only in women over 30 years of age due to the transient nature of HPV infections in younger women, we also conducted analyses restricting our sample to women over 30 years (n=126). Finally, using questionnaire data, we calculated frequencies to describe abnormality of self-collection among participants. All analyses were done using Stata 14.0 (StataCorp, College Station, TX).

Ethical approval

This project received ethical approval from the Ohio State University Institutional Review Board and the University of Malawi College of Medicine Research and Ethics Committee.

Results

Study population and prevalence of hr-HPV infections with clinician-collected sampling

We screened 234 women to enroll 200 in the parent study, 199 of whom consented to HPV testing. Women without hr-HPV were slightly older than women with hr-HPV (median age 34 vs. 32 years) and more likely to be married (97% vs. 77%; Table 1). Sixteen women (8%) were initially noted as having a positive VIA screen although two of these were later determined to be false positives. Of the remaining women, 10 presented with abnormality of self-collection and four with inconclusive results that required additional screening. All 14 women were referred to the district hospital.

Table 1: Participant characteristics of 199 care-seeking women by clinician-collected HPV results

We found high agreement between HPV results from self- and clinician-collected samples as measured by the kappa statistic, which measures agreement beyond chance alone. The highest agreement between self- and clinician-collected samples was for HPV 16 at 95% (95% CI: 90%). The agreement between self- and clinician-collected samples for any type of hr-HPV and the additional hr-HPV types were similar (κ=0.77, κ=0.74; Table 3). Overall compared to clinician-collected samples, categories of hr-HPV and the additional hr-HPV types were similar.

Table 2: HPV results, by collection modality

We did not inform women if they had hr-HPV. However, women found to have hr-HPV were referred to VIA and all participants in the research study underwent VIA as part of the research protocol. Treatment for abnormal lesions was not available at the study clinic, and thus women with abnormal VIA results were referred to secondary care at one of two district hospitals in Lilongwe. The referral appointments were scheduled within a week of the study visit, and participants were provided with funds to facilitate travel to and from Lilongwe. Study clinicians requested records documenting care received at the district hospitals.

Acceptability

Overall, women found the self-collection procedure easy to perform (98%), reported that the instructions were easy to understand (100%), and were confident they did it correctly (98%; Table 5). Most women

https://dx.doi.org/10.4314/mmj.v30i2.2
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Self-collected samples for HPV testing:

### Table 4: Concordance between HPV test results by self- and clinician-collected samples in women older than 30 years of age

| Test   | Sensitivity (95% CI) | Specificity (95% CI) | Kappa 1 (95% CI) |
|--------|----------------------|----------------------|------------------|
| All types of hr-HPV | 99 (57, 93) | 99 (95, 100) | 0.83 (0.71, 0.96) |
| HPV 16 | 75 (19, 99) | 100 (97, 100) | 0.85 (0.57, 1.0) |
| HPV 18/45 | 83 (36, 100) | 99 (95, 100) | 0.82 (0.59, 1.0) |
| Other hr-HPV | 75 (18, 93) | 98 (94, 100) | 0.77 (0.60, 0.95) |

1Kappa measures expected vs. observed agreement

### Table 5: Acceptability of self-collection

| Acceptability | n (%) | Very or somewhat easy to understand self-collection instructions | 197 (100) |
|---------------|-------|------------------------------------------------------------------|-----------|
| Might not | 194 (98) | Very or somewhat easy to do self-collection of samples | |
| Might not | 186 (95) | Would use self-collection for HPV testing in the future | |
| Might not | 119 (61) | Very or somewhat certain self-collected correctly | |

Concerns about self-collection

| Concerns | 138 (74) | Collection | 22 (12) |
|----------|----------|------------|--------|
| Might not | 114 (61) | Might not be accurate | 20 (11) |
| Might not | 14 (7) | Might not do it correctly | |

Women would select multiple concerns, reported they would recommend self-collection for HPV testing to a friend (99%) and more women preferred self-collection compared to clinician-collection (61% vs. 39%).

Discussion

To our knowledge, this is the first study to examine self-collected samples for HPV testing using the GeneXpert HPV assay. Our findings suggest that self-collection of samples for HPV testing is a feasible and acceptable method of cervical cancer screening in this rural, Malawian population. While the specificity was high, the sensitivity was lower for all HPV types compared to clinician-collected samples, which might limit the ability to detect HPV-positive women using self-collected samples. This may indicate that younger women were excluded from the sample, and the sensitivity was lower compared to the different types of hr-HPV, although the sensitivity for detection of HPV 18/45 was slightly reduced. Our findings also align with previous research that suggests agreement in HPV results from self- and clinician-collected samples varies by HPV type.

For example, in our study, the study clinician found it easy and fast to test using the self-collection procedure to women, suggesting that a future screening program must provide detailed instructions or have a healthcare provider to answer questions. The laboratory technician found it easy to interpret the results and was able to incorporate the self-collection procedure into their workflow. However, some samples required a repeat test due to machine error and added costs of HPV testing. We also experienced challenges in procuring the transport medium as an expensive part of the testing procedure, and this supply issue must be addressed before a larger rollout of any HPV testing program is possible in this region. Studies of other polymerase chain reaction (PCR)-based HPV DNA tests suggest that more commercially-available and inexpensive transport media (e.g. Scope mouthwash) or the collection and storage of dry swabs, may perform comparably, although these approaches have not been validated for the GeneXpert HPV DNA test.

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Conflict of interest

Authors have no conflicts of interest to disclose.

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