**Title**: HPV self-sampling acceptability and preferences among women living with HIV in Botswana

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**Keywords:** cervical cancer prevention; HPV testing; self-sampling; patient preferences; acceptability; HIV; sub-Saharan Africa

**Synopsis:** HPVself-sampling is acceptable in Botswana; however, preferences vary by education and residence. Interventions increasing HPV knowledge and self-efficacy will be critical to program success.

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**Abstract (199/200)**

**Objective**: To assess the acceptability and preferences of human papillomavirus (HPV) screening with self-sampling and mobile phone results delivery among women living with HIV (WLWH) in Botswana, as an alternative to traditional speculum screening.

**Methods**: We report acceptability, experiences, and preferences from a cross-sectional study among WLWH ≥25 years attending an infectious disease clinic in Gaborone March-April 2017. Women self-sampled with a flocked swab, had a speculum exam, and completed an interviewer-administered questionnaire.

**Results**: Of 104 recruited, 98 (94%) had a history of traditional screening. Over 90% agreed self-sampling was easy and comfortable. Ninety-five percent were willing to self-sample again; however, only 19% preferred self-sampling over speculum exam for future screening. Preferences differed by education and residence with self-sampling being considered more convenient, easier, less embarrassing, and less painful. Speculum exams were preferred because of trust in providers’ skills and women’s low self-efficacy to sample correctly. Almost half (47%) preferred to receive results via mobile phone call. Cervical cancer knowledge did not affect preferences.

**Conclusion**: HPV self-sampling is acceptable among WLWH in Botswana; however, preferences vary. Although self-sampling is an important alternative to traditional speculum screening, education and support will be critical to address women’s low self-efficacy to self-sample correctly.

**Introduction**

Cervical cancer is the second most common cause of female cancer death in Africa resulting in over 60,000 deaths across the continent[1]. Women living with HIV (WLWH) are at increased risk of human papillomavirus (HPV) infection, developing cervical cancer, and worse outcomes[2] despite access to antiretroviral therapy. High regional HIV prevalence underscores the importance of cervical cancer prevention.

Although screening for and treating pre-cancerous lesions can prevent cervical cancer, cytology-based screening programs face challenges in most African countries due to inadequate infrastructure and human resources, especially in rural settings[3]. Instead many countries rely on visual inspection with acetic acid (VIA), which is recommended in settings with limited resources to build capacity for HPV testing. However, HPV testing is recommended over VIA and cytology because of its superior performance, which also allows for longer screening intervals[4]. HPV testing can also increase participation through self-sampling[5], especially among first-time screeners, women in remote areas, and those reluctant to have a speculum exam. However, self-sampling program success depends on women’s acceptance and preferences, which vary across countries, contexts, and cultures.

In Botswana cervical cancer is the leading cause of female cancer deaths[1], with more than two-thirds of cases occurring among WLWH[6]. Although the national prevention plan endorsed VIA in 2011, Pap screening remains a large part of the program and overall coverage is poor[6, 7]. Low cervical cancer knowledge and perceived risk are notable drivers of poor participation. Additionally, few women understand the causal link between HPV and cervical cancer[8], all of which can affect screening behaviors.

Botswana’s national program will eventually shift to HPV testing, including options to self-sample. Therefore, the objective of this study was to describe HPV self-sampling acceptability, experiences, and preferences among WLWH to inform national program planning and implementation.

**Materials and Methods**

This cross-sectional study was conducted at the infectious disease care clinic (IDCC) in Gaborone, which is an outpatient HIV clinic at a tertiary public hospital. The IDCC also provides reproductive health services including cervical cancer screening[9]. The catchment area covers Gaborone, Botswana’s capital and largest city.

We recruited WLWH ≥25 years of age attending the IDCC for routine health care appointments. Women were not eligible to participate if they were currently pregnant, menstruating or had persistent vaginal discharge; those with a history of cervical cancer or total abdominal hysterectomy were also ineligible.

The protocol was reviewed and approved by the Health Research Development Committee of Botswana Ministry of Health, Research Ethics Committee at University of Botswana, and Research and Ethics Committee of Princess Marina Hospital. Only eligible women who provided written informed consent were enrolled.

We recruited from March-April 2017. We did not conduct any prior community advertisements. Two trained staff, including a nurse coordinator, recruited participants in the local language, Setswana. Staff informed women about a cervical cancer screening study; women expressing interest were given an information sheet. Staff answered questions from potential participants and assessed eligibility. Women ineligible because of abnormal vaginal discharge or menstruation were advised to return another day.

In a private exam room, staff verbally described how to use the self-sampling kit and distributed pictorial instructions (Figure 1). The Cepheid patient-collected vaginal swab instructions were adapted for the local language, reading level, and supplies used. Staff gave each participant a kit and escorted her to the clinic bathroom where she used a flocked swab unsupervised and returned the PreservCyt transport medium to study staff.

Participants completed an interviewer administered survey including sections on demographic characteristics, sexual health behaviors, cervical cancer knowledge, and self-sampling. Phone numbers were obtained to communicate results. After the self-sample and initial questionnaire, all women had a speculum exam with provider-collected cervical sample for clinical performance evaluation described elsewhere[10]. Then women answered questions regarding the speculum exam. After both samples had been collected we assessed preferences for future screening.

Samples were tested within 24 hours of collection using GeneXpert HPV (Cepheid, Sunnyvale, California, USA) in the National Laboratory. Xpert HPV is a polymerase chain reaction amplification assay which detects 14 types of high-risk (hr) HPV and offers limited genotyping of HPV16, HPV18/45, and other hr-HPV (31/33/35/39/51/52/56/58/59/66/68)[11]. Results are available within one hour of testing. Staff communicated HPV results to participants via mobile phone call within 24 hours of availability. Participants testing positive for any hr-HPV (from self- or provider-sample) were counseled over the phone and scheduled for follow-up colposcopy. All colposcopies included histopathology. Study data were collected using REDCap hosted by University of Pennsylvania[12].

Women were asked about previous Pap or VIA screening. We cross-checked self-reported screening when data were available in the hospital’s electronic health record (EHR). Uncomfortable, painful, scary, or embarrassing responses were collapsed into one “negative experience” category.

To determine cervical cancer knowledge, we measured previous HPV awareness and whether participants knew the cause of cervical cancer. We included an open-ended question about risk factors of cervical cancer and categorized responses as correct or misconceptions.

Based on a review of the self-sampling literature in other countries, we included multiple acceptability measures. Usability included questions on instruction comprehension as well as difficulty using swab and transport medium. To capture overall acceptability, we assessed ease and comfort of using the self-swab and willingness to use it again. Self-efficacy for sampling correctly was measured using a confidence scale. Perceptions of privacy, physical discomfort, and embarrassment were collected for both self- and provider-sampling. We assessed stated preferences for self-sampling as a future screening method as well as preferred results communication channels.

Descriptive statistics examining frequencies and percentages were conducted on survey responses using the appropriate statistical tests (Pearson’s chi squared, Fischer’s exact, Wilcoxon rank sum tests). Open-ended questions were reviewed and thematically categorized (REK and PC) and compared across demographic characteristics and behavioral risk factors. We used STATA version 13 (Stata Corporation, College Station, Texas, USA) for statistical analyses and a *p*-value of 0.05 for statistical significance.

**Results**

All 104 participants were HIV-positive and on antiretroviral therapy. Most (94.2%) women self-reported a history of VIA or Pap screening, but only 66 (63.5%) were confirmed in the EHR. Thirty-nine (37.5%) reported a previous negative experience with a speculum exam (Table 1). Overall hr-HPV prevalence was 30.0%.

Nineteen percent of the sample had previously heard of HPV. Among those 20 who were aware, 13 reported learning about HPV through the media, usually the radio. Six women reported hearing about HPV at a health facility. One learned about it from a school HPV vaccination campaign. We found no differences in willingness to self-sample or preferences by HPV awareness.

Two-thirds (69) reported they did not know the cause of cervical cancer. Among those who thought they knew about the cause (n=35), 25 (71%) correctly identified at least one risk factor though 12 (34%) believed misconceptions about cervical cancer risk (Table 2).

Nearly all agreed that self-sampling was easy and comfortable (Figure 2). Ninety-four women (90.3%) expressed they were somewhat or extremely confident in doing it correctly, which was different by screening history (97.0% screened vs. 78.9% unscreened, *p*=0.002). Nearly all women (99, 95.2%) were willing to self-sample again.

Although 12 women reported a problem handling the swab or transport medium, only three samples were inadequate. A few mentioned it was difficult to hold the swab while sampling, locate the right place to insert it, and open/close the container.

Most women (93, 89%) indicated they understood the instructions well. Four with less understanding explained it was their first time using such a device and therefore unsure how to insert it. The majority (77, 74%) found the combination of verbal explanation and handout most helpful compared to the explanation alone. One quarter (26, 25%) noted the importance of the nurse’s sex: they felt more comfortable asking questions to a female and trusted her explanation better.

Twenty women (19%) stated their preference for future screening was self-sampling over speculum exam. We found no differences in preference by screening history (EHR confirmed and self-reported), knowledge, or self-sampling confidence. Urban-residing women (*p*=0.019) and those with higher education (*p*=0.040) were more likely to prefer self-sampling.

We categorized open-ended responses about preference rationale, allowing more than one response per participant. Self-sampling was preferred because it was easier (15), less painful (11), less embarrassing (7) and more convenient (3). Speculum exams were preferred because of trust in providers’ skills (24), women’s low confidence to sample correctly (24), and providers being able to visualize the cervix/see where to sample (15). Six women also mentioned the novelty of the self-swab or the familiarity of routine screening as reasons for their choices.

Majority WLWH (78, 76%) reported they wanted to use the self-swab at the clinic versus at home. There were no differences in preferred location by sociodemographic characteristics or screening history. Women preferring clinic-based self-sampling wanted access to a nurse or other assistance (36), were concerned about sample transportation/delivery logistics with home-based self-sampling (33), and thought the clinic was a cleaner environment (10). Women preferring home-based self-sampling thought it would be more comfortable or convenient (11) and more private (11).

Phoning HPV results was feasible and acceptable. Most (84%) were reached on the first call attempt, and 89% of results were delivered within 24 hours of availability. Two women were unreachable and lost to follow-up. Twenty-two percent of calls took >3 minutes; there was no difference in call length by HPV result.

Almost half (49, 47.1%) preferred to receive HPV results solely over the phone, largely due to convenience (29.8%) (Table 3). Ten women were interested in text messaging and two suggested email. Ninety (86.5%) preferred that a doctor or nurse communicate the results, while the rest were indifferent. Fewer (43, 41.7%) wanted to hear from a provider they had previously seen. When asked about an acceptable timeframe to receive results, 40.4% (42) women preferred within 48 hours, 34.6% (36) women indicated within a week, and the rest said within one month or more.

**Discussion**

In this HPV self-sampling study, we found that self-sampling was acceptable among WLWH in Botswana. Despite understanding the instructions and finding the swab easy to use, more women preferred a speculum exam for future screening. Low self-efficacy and strong trust in providers were driving factors for the speculum exam preference in our sample of routinely screened women. Because of potential access to health care provider assistance, more women preferred to self-sample at a clinic instead of at home.

Over 95% of our sample was willing to self-sample again. Acceptance was much lower among WLWH in Uganda – only 46% of women agreed to use the self-sampling device while seeking care at the HIV clinic[13].

Despite acceptability of self-sampling being generally high across Southern Africa, the literature on preferences is mixed. Similar to our findings, women in Cameroon preferred traditional screening over self-sampling (62 vs. 29%) largely because they did not trust self-sampling and did not believe they performed the test properly[14]. Self-swab preference was correlated with higher education just as it was in our sample; however, cervical cancer knowledge and HPV awareness did not affect preferences in our sample like it did in Cameroon. Conversely in Nigeria, where 19% preferred self-sampling, higher socioeconomic status and increased spirituality were associated with lower odds of self-sampling preference, though women were asked about screening hypothetically[15]. In a study of Ghanaian women who experienced both screening approaches, more than half (58%) preferred self-sampling over provider screening and 62% felt it would increase the likelihood of them screening at all [16].

Similar to our findings, important themes of embarrassment, lack of privacy at home, handling the swab, and novelty of the self-swab have been linked to unwillingness to self-sample[17, 18]. Teng and colleagues found that community/social embarrassment and personal/individual discomfort were barriers in Uganda, though they decreased over time with education and increased knowledge[17]. However, women in our sample did not confuse HPV self-collection with HIV testing, which was a concern in Uganda.

Our sample had low self-efficacy to correctly self-sample, which is a common concern[18, 19], especially among women with low education. This highlights the importance of having clear instructions and providing support in future interventions. Women in our study valued verbal explanations of how to self-sample, but still liked the handout with pictures. In a separate study in Cameroon with high preference for self-sampling, women noted written instructions and diagrams were helpful aspects of an educational intervention; however, there were no changes in acceptability or preferences after an educational session[20]. And despite a more resource-intensive intervention in Uganda with visual plus verbal instructions and access to a provider in the exam room if help was needed, 47% were still concerned about not getting a good sample[21]. Our sample was highly engaged in HIV care, so participants may have been more accustomed to pelvic exams, which could have influenced confidence and preferences. Although women who had screened previously had higher self-sampling confidence, participants experienced both collection modalities during the study encounter, potentially affecting their perceptions of self-sampling.

Lack of confidence and strong desire for provider assistance were the most common reasons for choosing self-sampling in clinics versus at home. Our participants were also concerned about transporting the sample from home and thought having to drop it off at the clinic would be inconvenient; however, we failed to explain how home-based self-sampling might work (e.g., a community health worker transporting samples). Our findings are similar to those from Uganda where self-sampling in clinics was preferred because of access to provider assistance and having a clean, private environment[21]. However, a majority (84%) of WLWH in Kenya preferred to screen at home versus in a clinic[22].

We also found that communicating results over the phone was feasible. Convenient, fast results were desired with nearly half of our participants preferring to get a phone call instead of picking-up results in person, which is current practice. Women also preferred having a familiar health care provider make the call, suggesting they value continuity of care.

Although results were available within 24 hours and multiple attempts were made, we were unable to reach 2 women, underscoring the importance of getting multiple, reliable phone numbers and confirming them. In a trial comparing VIA and self-HPV in Uganda, more than half of the women in the HPV arm could not be contacted by phone and did not receive their HPV results, which affected triage attendance. The authors posited that lab delays influenced result delivery and emphasized quick result turnaround time and intense tracing efforts to ensure women follow-up[23].

Our study has some limitations, including that we recruited from a clinic which provides women’s health care including cervical cancer screening. Although we could only confirm screening among 66/98 (67%) who self-reported a previous Pap/VIA, this is much higher than regional screening prevalence estimates of the general population. . Preferences for self-sampling generally, and at-home self-sampling in particular, may be different among women who have never been screened and those not regularly accessing the health system[24]. Although integrating HPV-testing into HIV care is an important consideration to reach high-risk women and leverage existing resources, HIV-negative women in Botswana are less likely to ever screen[8], which may affect self-sampling uptake. Future studies investigating the potential of self-sampling outside the clinical setting and in unscreened populations are also needed as these key factors to expanding access to those at high-risk of cervical cancer.

Despite these limitations, this study provides local contextual data that HPV self-sampling is an acceptable alternative to provider screening in Botswana. Patient-centered interventions designed to give women screening choices and increase HPV knowledge and self-efficacy to self-sample will be critical to program success. Given interest in m-health interventions, additional research is needed to ensure results are effectively delivered with appropriate counseling to ensure women with hr-HPV follow-up.

Author Contributions

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Design | Planning | Conduct | Analysis | Manuscript |
| Racquel E. Kohler | X | X | X | X | X |
| Tamara Elliott | X | X | X | X | X |
| Barati Monare | X | X | X |  | X |
| Neo Moshashane  |  | X | X |  | X |
| Keumelile Ramontshonyana |  |  | X |  | X |
| Pritha Chatterjee |  |  |  | X | X |
| Doreen Ramogola-Masire | X | X | X | X | X |
| Chelsea Morroni | X | X | X | X | X |

Conflicts of Interest

All authors report no conflicts of interest.

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**Figure 1. Self-sampling instructions distributed to women in Botswana**



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| **Table 1. Characteristics of WLWH by preferred HPV screening method (n=104)** |

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|  | **Speculum exam****84 (81%)** | **Self-sample****20 (19%)** | **Total****N (%)****104 (100%)** | ***p*-value** |
| Age, mean (sd) | 45.2 (8.4) | 44.8 (8.3) | 45 (8.3) | 0.431 |
| Education |  |  |  | 0.040 |
| None or primary | 33 (39.3) | 3 (15.0) | 36 (34.6) |  |
| Secondary or higher | 51 (60.7) | 17 (85.0) | 68 (65.4) |  |
| Marital status |  |  |  | 0.924 |
| Single | 60 (71.4) | 14 (70.0) | 74 (71.1) |  |
| Divorced or widowed | 10 (11.9) | 2 (10.0) | 18 (17.3) |  |
| Married | 14 (16.7) | 4 (20.0) | 12 (11.5) |  |
| Urban residence | 43 (51.2) | 16 (80.0) | 59 (56.7) | 0.019 |
| Previous screening history (self-reported) | 80 (95.2) | 18 (90.0) | 98 (94.2) | 0.367 |
| Previous screening history (EHR confirmed) | 51 (60.7) | 15 (75.0) | 66 (63.5) | 0.233 |
| Previous negative pelvic exam experience a | 29 (34.5) | 10 (50.0) | 39 (37.5) | 0.199 |
| Confident about sampling |  |  |  | 0.146 |
| No or little  | 10 (11.9) | 0 (0.0) | 10 (9.6) |  |
| Somewhat | 15 (17.8) | 2 (10.0) | 17 (16.3) |  |
| Extremely  | 59 (70.2) | 18 (90.0) | 77 (74.0) |  |
| *Notes*: WLWH, women living with HIV; sd, standard deviation; EHR, electronic health recorda reported uncomfortable, painful, scary or embarrassing experience  |

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| **Table 2. Cervical cancer knowledge and misconceptions among WLWH in Botswana**  |
| *Correctly identified risk factors*  | *n\** |
| Multiple sex partners  | 13 |
| Unprotected sex | 8 |
| STIs | 6 |
| Smoking | 4 |
| Early sexual debut | *3* |
| HPV | 2 |
| HIV | 2 |
| Multiple births | 1 |
|  |  |
| *Misconceptions*  |  |
| Personal hygiene and intravaginal practices | 5 |
| Sperm left inside  | 4 |
| Diet and drinking alcohol  | 3 |
| Increased sex frequency, rough acts | 2 |
| *Notes*: \*among 35 women who reported knowing something that can increase the chances of getting cervical cancer  |



**Figure 2. HPV self-sampling acceptability among WLWH in Botswana (n=104)**

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| **Table 3. Preferred results communication channels and rationale** |
| *Preference* | n=104 | %  |  |
| Phone call only | 49 | 47.1% |  |
| Call/text and facility pickup | 28 | 26.9% |  |
| Facility pickup only  | 25 | 24.0% |  |
| Text only | 2 | 1.9% |  |
|  |  |  |  |
| *Rationale* |  |  |  |
| Convenience  | 31 | 29.8% |  |
| Counseling service availability  | 30 | 28.8% |  |
| Transportation challenges | 12 | 11.5% |  |
| Accessing results faster | 11 | 10.6% |  |
| Poor mobile phone connectivity | 4 | 3.8% |  |
| Continuity of care | 4 | 3.8% |  |
| Privacy  | 1 | 1.0% |  |
|  |  |  |  |