Randomized comparison of two vaginal self-sampling methods for human papillomavirus detection: dry swab versus FTA cartridge

Rosa Catarino
Research Resident
Department of Gynecology & Obstetrics
## Faculty Disclosure

<table>
<thead>
<tr>
<th>Company Name</th>
<th>Honoraria/Expenses</th>
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<td>BÜHLMANN Laboratories AG</td>
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<td>Anyplex II HPV28 tests were provided gratis</td>
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<td>GE Healthcare</td>
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<td>FTA cards were provided gratis</td>
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<td>Rovers Medical Devices B.V</td>
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<td>Rovers® Viba-Brushs were provided gratis</td>
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No, nothing to disclose

X Yes, please specify:
HPV self-sampling (self-HPV) is valuable in **cervical cancer screening** and overcomes inherent barriers of cytological screening;  
HPV testing is usually performed on physician-collected cervical smears stored in **liquid-based medium**;  
The need for **stable transport and storage temperatures** makes such testing methods difficult and costly to provide in LMIC;  
**Dry filters** and **swabs** are an alternative.
Objectives

To evaluate the adequacy of self-HPV using two dry storage/transport devices, the FTA cartridge (s-FTA) and swab (s-DRY) comparing them with the current standard of HPV testing using physician-collected samples and specimen transport medium (Dr-WET).

FTA™ Cards (GE Healthcare)  
FLOQSwabs™ (COPAN Italia)
**Material and Methods**

130 Patients (>30 years)
- Attending Colposcopy clinic
- Completing eligibility criteria
  - Completing an ICF

**Randomization**

- S-FTA then s-DRY
- s-DRY then s-FTA

Gynecologist
- Dr-WET
- Colposcopy (+- biopsy and CEC)

All vaginal specimens collected by the 3 methods will be tested for the same pathogens (HR-HPV), using the same diagnostic test (*The Anyplex II HPV28*, Seegene)
Material and Methods – Laboratory analysis

**Elution from FTA card**: 3 circles of ~3mm diameter were cut from the center section of the card with a disposable sterile surgical blade, and placed into a 1.5ml microfuge tube. Further procedure was done according to manufacturer.

**Material recovery from s-DRY**: Each sample was placed into 1ml of sterile PBS, and each tube was pulse vortexed 3x15s before removing and discarding the swab.

**Material recovery from Dr-WET**: Tubes containing the Dr-WET sample were also pulse vortexed 3x15 s.
Material and Methods – Laboratory analysis

**DNA extraction:** The entire volume of recovered material was transferred into appropriate tubes and the volume adjusted to 600 µl with PBS. DNA was then extracted on an **m2000sp instrument** (Abbott Molecular, Des Plaines, IL, USA), according to manufacturer instructions.

**HPV detection:** HPV analyses were performed using the **Anyplex II HPV28 (H28) Detection test** (Seegene, Seoul, South Korea), which allows the detection of 19 high-risk HPVs and 9 low-risk HPVs.
Results – Sample characteristics

- The median age of the participants was 42 years (34–50);
- 77.7% had a partner;
- Number of children (mean ± sd): 1.3 ± 1.1;
- The majority of women had secondary/tertiary education (78.6%);
- The median delay between sampling and laboratory processing was 44 days (IQR = 26–60).
Results – hr-HPV genotypes distribution

HPV prevalence for high-risk types was 62.3% detected by s-DRY, 56.2% by Dr-WET, and 54.6% by s-FTA.
Results - Agreement between collection methods according to cytological results

- 119 patients had cytological diagnoses (61 normal, 1 carcinoma, 5 HSIL, 20 LSIL, 9 ASC-H, 3 AGC and 20 ASC-US);
- Agreement between s-FTA and s-DRY samples when LSIL+ was present was 69.2% (κ = 0.27), and the PPA was 78.9%;
- Agreement between self-HPV and Dr-WET when LSIL+ was present was 89.7% (κ = 0.61), and the PPA was 93.0%.
Results - Agreement between number of oncogenic HPV genotypes

✓ Agreement between s-FTA and Dr-WET was 70.8% (k=0.56);
✓ Agreement between s-DRY and Dr-WET was 72.3% (k= 0.61);
✓ Agreement between s-FTA and s-DRY was 54.6% (k=0.35);
✓ Detection of ≥ 3 oncogenic HPV types was more common in s-DRY samples (17.7%) relative to s-FTA and Dr-WET samples (4.6% and 8.4%, respectively).
Results - Clinical performance of self-HPV and Dr-WET and women’s preferences

<table>
<thead>
<tr>
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<th>s-FTA and s-DRY performances, using Dr-WET results as gold-standard</th>
<th>s-FTA, s-DRY and Dr-WET performances, using LSIL+ as gold-standard</th>
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<tbody>
<tr>
<td></td>
<td>Sensitivity (95% CI)</td>
<td>Sensitivity (95% CI)</td>
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<td></td>
<td>p value*</td>
<td>Specificity (95% CI)</td>
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<tr>
<td>s-FTA</td>
<td>85.4 (76.4-91.5)</td>
<td>64.0 (44.5-79.8)</td>
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<tr>
<td>s-DRY</td>
<td>96.5 (90.1-98.8)</td>
<td>84.6 (66.5-93.9)</td>
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<td>0.02</td>
<td>0.06</td>
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<td>82.2 (68.7-90.7)</td>
<td>39.1 (29.8-49.4)</td>
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<td>0.05</td>
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*The p-value was calculated with McNemar's test.

The preferred self-collection method was s-DRY (40.8% vs. 15.4%);

90% of women affirmed that they were prepared to do self-HPV at home.
Discussion - Highlights

FTA card may have some advantages such as the assurance of correct test performance by means of the color indicator. Although:

- HPV detection was significantly less with the s-FTA relative to s-DRY or Dr-WET, using the same test for HPV detection (H28), as well its sensitivity compared to s-DRY with use of cytological results as the gold standard (64.0% vs. 84.6%);
- FTA card has a higher cost;
- Involves additional costs (brush for collection and puncher for extraction);
- s-FTA would be difficult to implement in LMIC context, owing to laborious sample processing.
Conclusion and recommendations

- The benefits of dry carriers are appealing, owing to accessibility and simplicity.
- We found that the FTA cartridge is not only less sensitive than swabs but is also more expensive than other methods.
- In our view, the FTA method is inappropriate for use in low-resource settings and may only be slightly appealing for self-HPV testing in developed countries.
- Dry swabs should be adopted in future projects within low-resource settings, where it may be a great asset for CC screening.
Acknowledgments

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