Results of LuViva Test with Comparisons to Other Tests -
Cytology, HPV, VIA and Histopathology

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Part I. Results of Cytology, HPV, VIA and Histopathology

Observations from Table 1: Sixty-five of the 100 women in the study were referred to colposcopy on the basis of either an abnormal Pap result or a positive VIA. VIA+ was able to identify seven CIN1 and five CIN2, but only one CIN3, which is the goal of screening. Referral Pap at the LSIL threshold identified five of 10 CIN1 as positive, missed one CIN2 and identified three of five CIN3 as positive for a sensitivity of 60%. At the CIN3 threshold, the yield of positive biopsies for VIA was 3% (1/36) and was 12% (3/25) for Pap at the LSIL threshold.

Table 1: Cytology and VIA+ results as a function of histopathology

	Histology				
Cytology	**Normal**	**CIN1**	**CIN2**	**CIN3**	
Negative	29	4	1	1	35
ASC-US	1	0	0	1	2
AGC	2	0	0	0	2
LSIL	13	5	0	2	20
ASC-H	0	0	0	0	0
HSIL	3	1	0	1	5
VIA +	23	7	5	1	36
Total	**71**	**17**	**6**	**6**	**100**

Observations from Table 2: Positive HPV results were lower in number than expected based on the population of referred women. Overall, 11% (11/98) of all women in the study were positive for high risk HPV. This included only one of six with CIN2 and three of six with CIN3 (sensitivity = 50%). The reasons for this are not completely clear but could include sampling issues, labeling issues and/or degradation due to environmental conditions. Another possible explanation is that the average age of women in the study was 45 years. It is known that HPV infection rates can be much lower in women above the age of 40 and that the sensitivity of HPV is also lower in this age group. In support of this, we found that HPV false negatives were more likely to occur in older Nigerian women (median age 51.5 years) compared with women having true positive HPV results (median age 43.0 years), although sample sizes are small.

Table 2: HPV results as a function of histopathology

	Histology				
Histopathology	**Normal**	**CIN1**	**CIN2**	**CIN3**	
HPV+	5	2	1	3	11
HPV-	64	15	5	3	87
HPV (no result)	2	0	0	0	2
Total	**71**	**17**	**6**	**6**	**100**

Part II. Results of LuViva Test with Comparisons to Other Tests

***Triage Performance*:**
Of the 100 women enrolled in the study, 24 qualified as LuViva triage patients based on referral Pap results of ASC-US/AGUS (n = 4) or LSIL (n = 20). An additional five patients with HSIL Paps were tested, but HSIL is contra-indicated for LuViva due to the high likelihood of significant cervical disease.

Of the 24 women with abnormal Paps (excluding HSIL), three were found to have CIN2+ at histopathology. All three recorded RED (high likelihood of CIN2+) by LuViva for a sensitivity of 100%. It is of interest that HPV was negative for all three of these patients (sensitivity = 0%).

Of the remaining 21 women without CIN2+, five were found to have CIN1. LuViva recorded four of these as RED and one as YELLOW (moderate likelihood of CIN2+). Fifteen referred patients were found to have cervicitis (n = 9) or normal histology (n = 6) (but no dysplasia upon biopsy). Of these 15 patients, five were recorded as GREEN (low likelihood of CIN2+) and two were recorded as YELLOW by LuViva. The remaining eight were recorded as RED by LuViva.

Finally, one patient with metaplasia could not be analyzed due to lack of contact between the cervical guide and the cervix.

Therefore, the sensitivity and specificity of the triage patients were as follows:

Table 3: Sensitivity and Specificity of LuViva at the *Green/Yellow* Threshold

Sensitivity CIN2+	Specificity CIN1	Specificity No Dysplasia
100% (3/3)	**0% (0/5)**	**33% (5/15)**

Table 4: Sensitivity and Specificity of LuViva at the *Yellow/Red* Threshold

Sensitivity CIN2+	Specificity CIN1	Specificity No Dysplasia
100% (3/3)	**20% (1/5)**	**40% (6/15)**

Image 1—LuViva MHS Device

***Screening Performance*:**

Because the prevalence of CIN2 and especially CIN3 is very small in the population of women normal Pap results (see Table 1 above) we chose to compare the LuViva results for women screened positive by Visual Inspection with Acetic Acid (VIA+; n = 36) vs. those with Negative Pap results (n = 35). Using the LuViva algorithm developed for triage of HPV+ (but Pap negative) referred patients, 26 of the 35 women (74%) with negative Pap results produced a LuViva result in the GREEN or YELLOW zone, while only one of the 36 VIA+ women did (3%). Thus LuViva was able to differentiate VIA+ from Pap negative women at a sensitivity of 97% and a specificity of 74%. Additional work with larger populations is needed in order to re-calibrate LuViva's algorithms to pick out the CIN3+ cases within screened populations.

***Conclusions*:**

1. LuViva would have reduced the percentage of unnecessary colposcopy and biopsy by between 33% and 40% without any false negatives. This is consistent with other triage studies conducted in North America.

2. LuViva was able to differentiate between VIA+ vs. Pap Negative women at the high level of confidence.

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