

Novel screening and triage approach to detect cervical precancer with HPV extended genotyping and AI-automated visual evaluation (PAVE)

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Background

Cervical cancer remains a leading cause of death among women in low- and middle-income countries. Limited access to cervical screening demands accurate, scalable strategies to impact the target population effectively. The PAVE Consortium validated a cervical screening approach to detect precancer CIN3 or worse (CIN3+) in resource-limited settings with varying HIV prevalence.

Methods

Participants aged 25–49 were enrolled before April 2025 from clinical sites across Brazil, the Dominican Republic, El Salvador, Honduras, Cambodia, Malawi, Nigeria, Tanzania, and Eswatini (N= 50,450). Self-collected vaginal samples (FLOQSwab) were tested using a low-cost HPV extended genotyping assay (ScreenFire), providing results in four risk-based channels: HPV16, HPV18/45, HPV31/33/35/52/58, HPV39/51/56/59/68. HPV channels were analyzed hierarchically by carcinogenicity. All HPV-positive participants were referred for cervical imaging using a mobile colposcope (IRIS) and biopsy. An earlier AI algorithm was trained and validated to classify images into three categories of Automated Visual Evaluation (AVE): Normal, Indeterminate, and Severe. The algorithm is tested on IRIS images for external validation. Among HPV-positive women, we assessed the performance of HPV extended genotyping combined with AVE, to estimate absolute risk for confirmed CIN3+.

Results

HPV prevalence was 27% among HIV negative/unknown status and 36.1% among women living with HIV (WLHIV). HPV-negative women were reassured. Among HPV-positive participants with complete data (N=7,535), 6,113 were HIV-negative/unknown and 1,422 WLHIV. CIN3+ background risk was 5.9% in HIV-negative and 12.2% in WLHIV. HPV genotype and AVE classification independently predicted CIN3+ risk and improved when combined. Risk of CIN3+ ranged from 1.8% (HPV39/51/56/59/68-positive with Normal AVE) to 42.6% (HPV16-positive WLHIV with Severe AVE).

Conclusion

The PAVE study showed feasibility of HPV screening across diverse settings. The PAVE strategy provided remarkable CIN3+ risk stratification. The combination of HPV extended genotyping and AVE enables targeted management for HPV-positive women at greatest risk of precancer, regardless of HIV status.

This multi-country study confirmed that combining HPV genotyping with AI-aided visual evaluation is an accurate, low-cost solution to expand screening while directing limited resources to women most at risk.