

Evaluation of an artificial intelligence (AI)-powered cervical precancer screening tool in Zimbabwe





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Introduction

- Cervical cancer is preventable, yet claims 300,000 lives annually, primarily in countries where access to preventive services is limited like Zimbabwe¹. Commonly used screening methods like visual inspection with acetic acid (VIA) and even improved-upon VIA with cervicography (VIAC) have suboptimal accuracy².
- Despite World Health Organization (WHO) recommendations to transition to Human Papilloma Virus (HPV)-based screening, these tests remain expensive and limited in access in many low- and middle-income countries (LMICs).
- As a result, visual inspection methods like VIA will continue to play a critical role in cervical cancer screening programs in resource-limited settings, but there is a pressing need to explore alternative solutions that can enhance the reliability and performance of visual inspection.
- Artificial intelligence-powered tools like Automated Visual Evaluation (AVE) represent a promising option, with the potential to provide affordable and more accurate visual cervical precancer screening in LMICs. An internally validated novel AI-based tool³, Automated Visual Evaluation (AVE), to improve VIAC was externally evaluated for accuracy

1. <https://gco.iarc.who.int/media/globocan/factsheets/cancers/23-cervix-uteri-fact-sheet.pdf>

2. Bateman AC, Parham GP, Sahasrabudhe VV, et al. Clinical performance of digital cervicography and cytology for cervical cancer screening in HIV-infected women in Lusaka, Zambia. *J Acquir Immune Defic Syndr*. 2014;67(2):212-215. doi:10.1097/QAI.0000000000000270

3. Hu L, Bell D, Antani S, Xue Z, Yu K, Horning MP, et al. An Observational Study of Deep Learning and Automated Evaluation of Cervical Images for Cancer Screening. *J Natl Cancer Inst [Internet]*. 2019 Jan 10 [cited 2024 Aug 14]. <http://www.ncbi.nlm.nih.gov/pubmed/30629194>





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What is machine learning

Machine learning is a branch of artificial intelligence in which computers learn from data, identify patterns, and develop the ability to recognize and classify new inputs

The first step of developing a machine learning algorithm is to **train** it to distinguish between different types of images – analogous to teaching it to tell dogs from cats.

We tell the algorithm.....



After the algorithm is trained, the second step is to show pictures of dogs and pictures of cats (pictures not used in the training phase) to test or “**validate**” its performance.

We ask the algorithm.....



*Based on the algorithm's performance, during the validation phase adjustments are made **until the algorithm is identifying dogs vs. cats – or pre-cancer vs. control – with high accuracy.***



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8K women were enrolled
2020-2021 at 8 sites

~8K participants
~4K controls
828 precancer cases

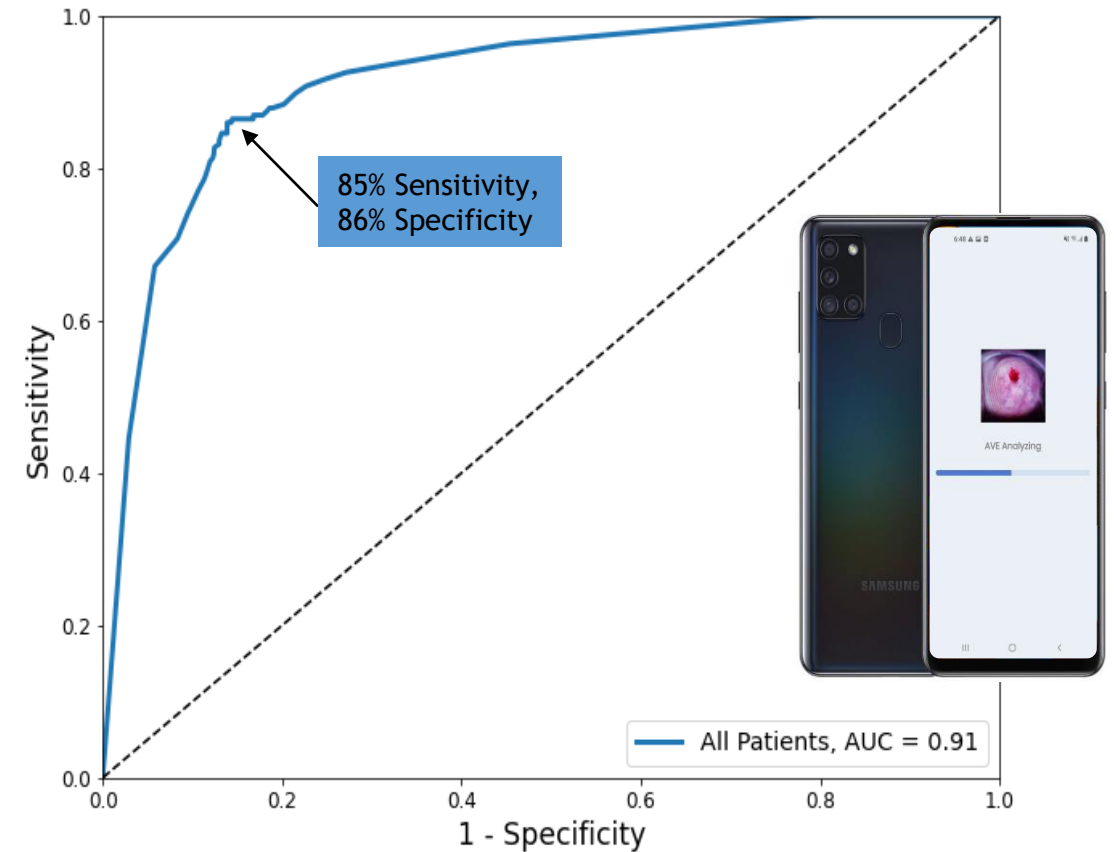
(remainder excluded due to no usable A21s image, missing data, etc)

Images divided into three sets:

- **Training set:** ~65% of images, roughly equal proportion of cases and controls. This is what the algorithm uses to 'learn' how to best separate cases from non-cases.
- **Validation set:** ~10% of images, roughly equal proportion of cases and controls. This set is used to monitor accuracy; training is considered complete when the validation accuracy plateaus.
- **Test set:** ~25% of images, **not seen by the algorithm** during training & validation. Performance on this test set informs whether the process should be concluded or if more training is needed, which can involve increasing the amount of training data or using alternative algorithm approaches.

The algorithm was trained and validated using smartphone images conducted under a study protocol in Zambia

AVE performance in machine learning lab



Hu et al. 2024. doi:[10.1002/cam4.7355](https://doi.org/10.1002/cam4.7355)

Based on the results of the Zambia validation study, a prospective observational study was conducted in 5 countries including Zimbabwe to measure AVE's accuracy in a real-world clinical setting



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Methods : The AVE tool was subjected to an external validation in an observational study in Zimbabwe as part of a five-country study.

The study aimed to evaluate the accuracy of AVE in identifying CIN 2+ in a real-world setting relative to VIAC, the standard of care by:

1. determining the sensitivity and specificity of AVE and
2. comparing the sensitivity of AVE and VIAC, using histologically confirmed cervical intraepithelial neoplasia grade 2 or higher (CIN2+) cases as reference standard.

		<u>AVE Result</u>		
		Positive	Negative	
<u>Histopathology Result</u>	CIN2+	TP	FN	<i>Missed cases of precancerous/cancerous lesions: under-treatment</i>
	<CIN2	FP	TN	

Incorrect cases of precancerous/cancerous lesions: over-treatment

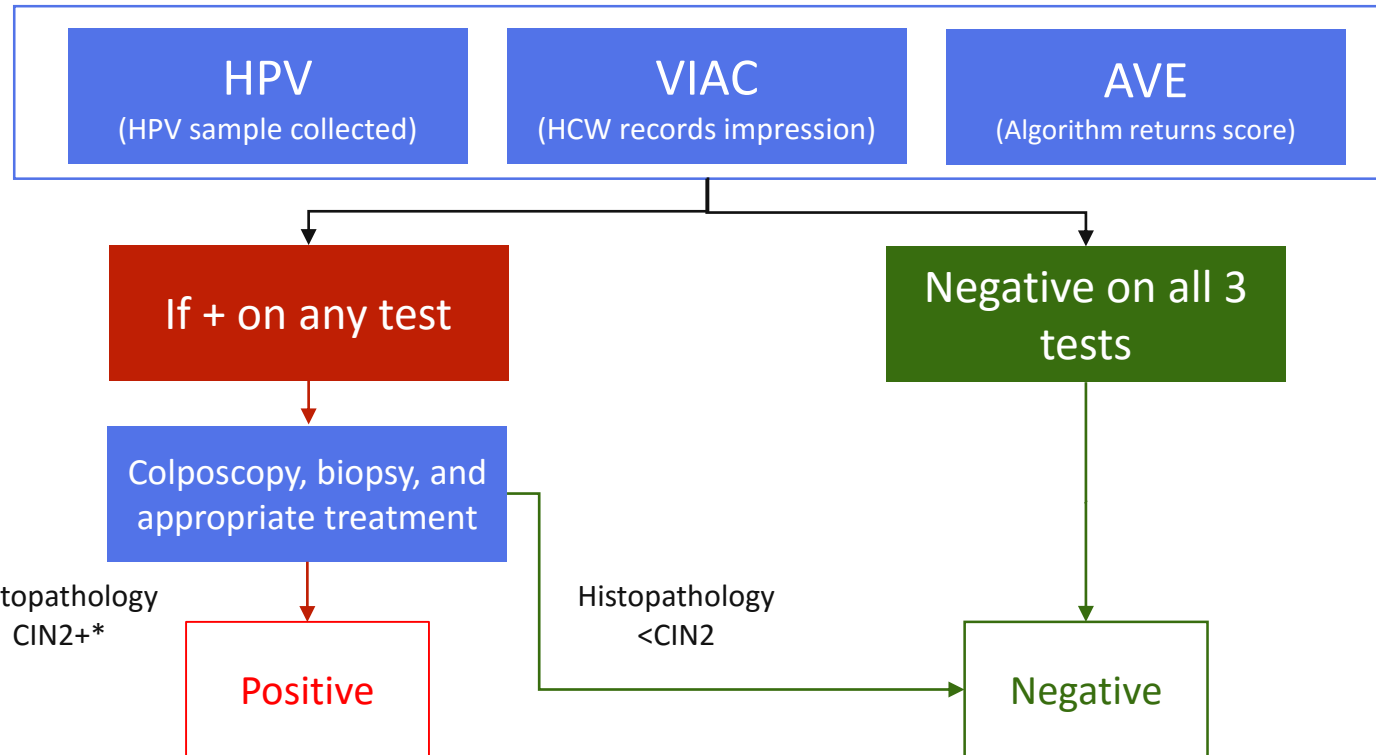
Definitions:
Sensitivity= $TP/(TP+FN)$
Specificity= $TN/(FP+TN)$
Positive predictive value= $TP/(TP+FP)$
Negative predictive value= $FN/(FN+TN)$



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Overview of AVE study methods



Five participating countries: Malawi, Rwanda, Senegal, Zambia, and **Zimbabwe**



Enrollment occurred from July 2022-January 2023



Data collected across 16 sites, 19 providers



All CIN2+ pathology results confirmed by two or more pathologists



Data collection through smartphone (for AVE exam) and web-based server

*CIN2+: Cervical intraepithelial neoplasia 2 and beyond, which includes CIN2, CIN3, carcinoma in situ and invasive cervical cancer





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Results: AVE cascade

	Malawi	Rwanda	Senegal	Zambia	Zimbabwe	Total
Enrolled	4,619	4,454	3,067	6,066	6,908	25,114
Age-ineligible	1 (0%)	643 (14%)	0 (0%)	0 (0%)	23 (0%)	667 (3%)
VIA-Indeterminate or TZ3	35 (1%)	62 (1%)	195 (6%)	1,645 (27%)	249 (4%)	2,186 (9%)
Total in final analysis	4,583 (99%)	3,749 (84%)	2,872 (94%)	4,421 (73%)	6,636 (96%)	22,261 (89%)
Screen Result						
Screen-positive	2,256 (49%)	1,494 (40%)	1,021 (36%)	2,177 (49%)	3,550 (53%)	10,498 (47%)
Triple-negative	2,320 (51%)	2,254 (60%)	1850 (64%)	2,094 (47%)	2,968 (45%)	11,486 (52%)
Screen –inconclusive	7 (0%)	1 (0%)	1 (0%)	150 (3%)	118 (2%)	277 (1%)
Biopsy						
Biopsy collected	1,796 (80%)	1,303 (87%)	976 (96%)	1,658 (76%)	2,582 (73%)	8,315 (79%)
Biopsy attempted	62 (3%)	6 (0%)	2 (0%)	0 (0%)	165 (5%)	235 (2%)
Biopsy not taken	399 (18%)	187 (13%)	55 (5%)	532 (24%)	818 (23%)	1,991 (19%)
Confirmed CIN2+	109	44	27	128	168	476



Results: The study demonstrated AVE's increased sensitivity as compared to VIA, though AVE's sensitivity was not as high as in the internal validation study

Key findings: HPV positivity was 40.7%, VIAC positivity 7.6% and AVE positivity 26.0%.

168 (3.4%) women had confirmed disease status of CIN2+.

AVE demonstrated statistically significant improved sensitivity compared to VIAC ($p < 0.001$).

"AVE-assisted VIA" (AVE or VIA positive), the planned application of AVE, has improved sensitivity compared to both AVE and VIAC but a lower specificity compared to both.

HPV has the highest sensitivity, though with some trade-off in risk of client loss to follow up

Table 1: Sensitivity and specificity for AVE, VIAC, and AVE-assisted VIA.

	N	Sensitivity (95% CI)	N	Specificity (95% CI)	P-Value*
AVE	168	54.8(46.9%-62.4%)	4840	81.5% (80.4%-82.6%)	
VIAC	168	26.2% (19.7%-33.5%)	4840	95.8(95.2%-96.4%)	<0.001
AVE-assisted VIA ⁺	168	63.7(55.9%-71.0%)	4840	79.6% (78.5%-80.8%)	
HPV	168				

*p- value represents comparison of AVE with VIAC for sensitivity only

+ AVE-assisted VIA: treating a participant as positive when neither VIA or AVE results are positive



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Discussion and conclusions: AVE-assisted VIA offers potential to feasibly and affordably increase precancer detection in resource-limited settings

Study results show higher-than-expected positivity rates across tests, underscoring the importance of a strong cascade of care

The trade-off between sensitivity and specificity observed in this study highlights the importance of considering the intended use and context of the screening technique.

The increased sensitivity of AVE could feasibly and cost-effectively enhance precancer detection. Additionally, the improved specificity of AVE through combination of AVE and VIA (AVE-assisted VIA) will greatly improve detection of precancerous lesions and has the potential to minimize unnecessary interventions.

Given the substantial disease burden, scaling up quality preventive services like AVE-assisted VIA is essential for cervical cancer elimination in Zimbabwe.



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Discussion and conclusions

These results show that there is need for further research building on the current results as well as research on the primary screening methods that can be implemented in Zimbabwe taking into consideration the available resources

In addition to the existing VIAC program we suggest adoption of AVE assisted VIA to increase access to cervical cancer screening in Zimbabwe

There is need for further analysis to evaluate how AVE could fit in the National Screening Algorithms

Depending on local context other options for different screening approaches may be more feasible

- Where HPV testing is not accessible: AVE + VIA as sole screening test
- Where HPV testing is available: HPV primary, AVE + VIA as triage
- Where all options are possible: HPV + AVE + VIA together

Thank you

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