

A Population-based study of Point-of-Care HPV Testing, Visual Inspection with Acetic Acid, and Cervical Cytology in Rwandan Women of Known HIV-Serostatus

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Women's Equity in Access to Care and Treatment

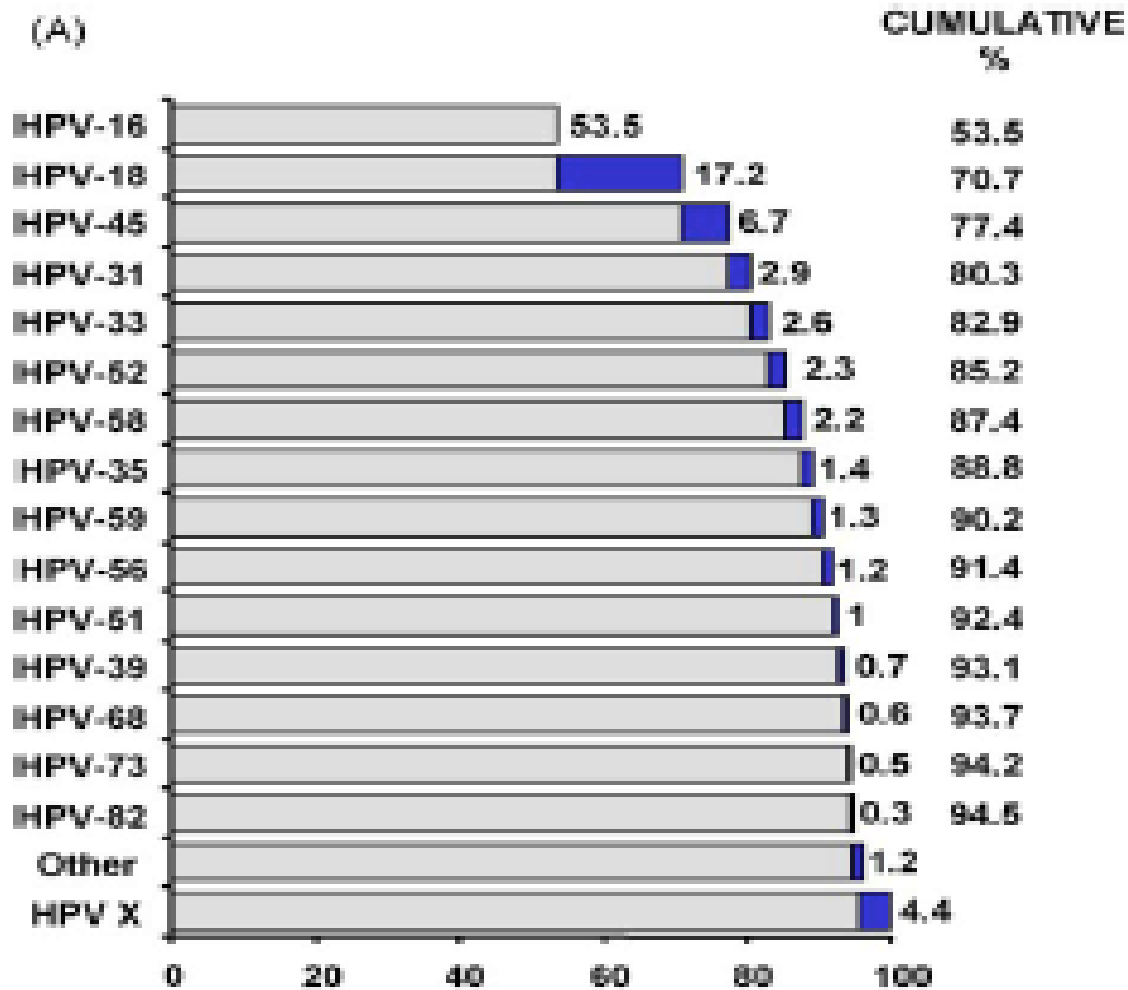
(WE-ACTx) Kigali, Rwanda



EPIDEMIOLOGY

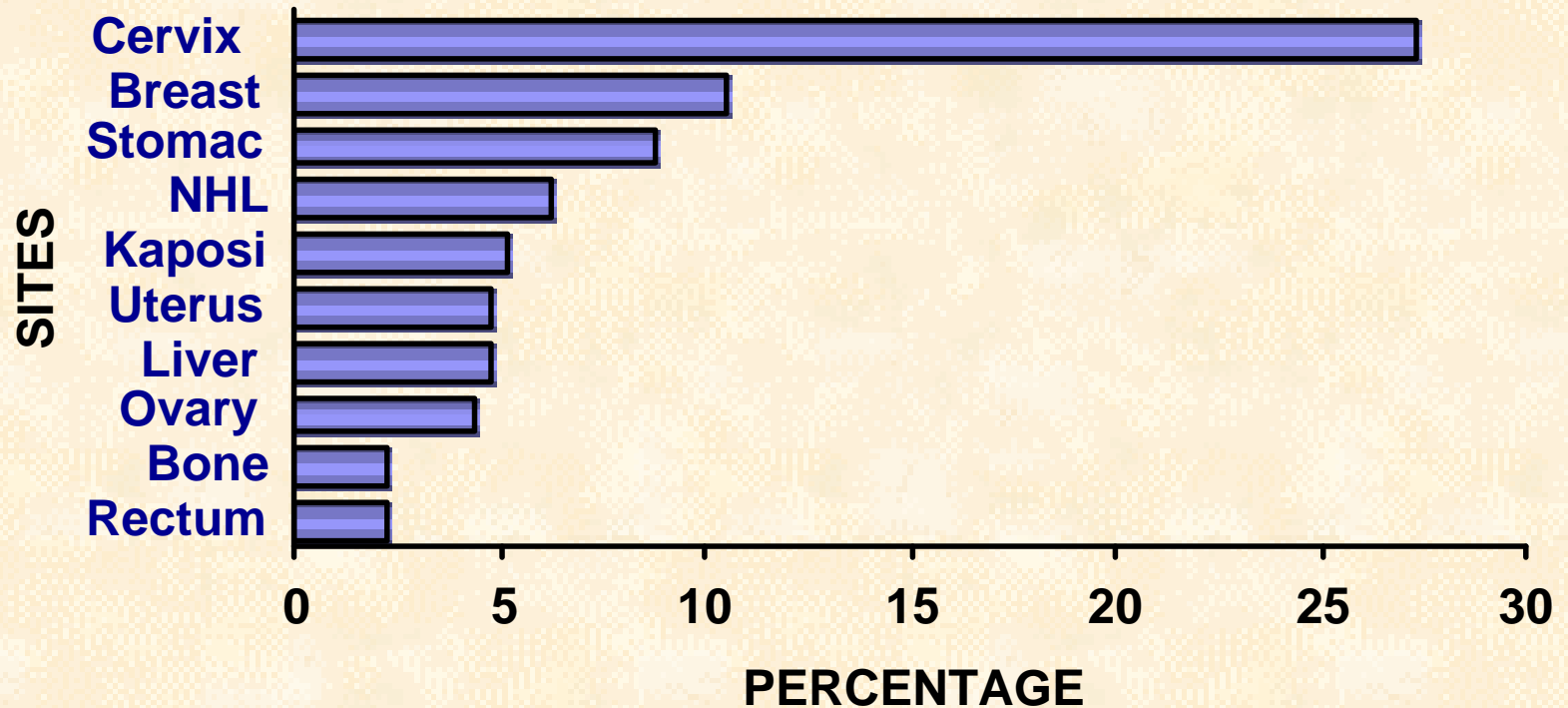
- # Cervical Cancer is most common cause of cancer deaths in African and Rwandan women
- # 80% of cervical cancer deaths occur in lower-income nations
- # In higher-income countries cervical cancer mortality reduced 90% through cytology-based screening and treatment
- # HPV is the etiologic agent of cervical cancer
 - ~15 HPV types causes nearly all cervical cancer

Percent of worldwide cervical cancer caused by HPV Types



Cancers in Rwandan Women, 2001-2005

10 MOST FREQUENT CANCERS IN WOMEN



Principles of Screening

- # Significant burden of disease in the community-- high prevalence, bad outcomes
- # There must be an asymptomatic (preclinical) period in which disease can be detected and treated
- # Early detection must improve outcomes
- # Screening test(s) must be acceptable to the population, inexpensive and relatively accurate
- # There must be an effective and acceptable treatment

The Ideal Screening Test

- # Should be inexpensive, easy to administer (low risk) and with minimal discomfort
- # There should be a Gold Standard based on the evidence
- # Results should be accurate/valid and reliable/reproducible/precise

Screening tests for cervical cancer

- ✦ Cytology (pap smears)
- ✦ HPV testing
- ✦ Visual inspection with acetic acid (VIA)
- ✦ Screen and treat protocols can be performed with VIA and with a rapid HPV test

Specific Aims

- 1) To compare the sensitivity of a rapid point-of-care HPV test (*careHPV*) and VIA in identifying high-grade squamous intraepithelial lesions (HSIL) or cancer.
- 2) To assess possible differences in test performance in HIV+ and HIV- women

RESEARCH DESIGN AND METHODS

- # Cross-sectional study
 - # Population based recruitment
 - # Oversampled for HIV+ women
 - # Screen and treat protocol
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POPULATION

- # 2000 population-based participants in Nduba and Jabana sectors (semi-urban)
 - Offered participation through Nyacyonga Health Center, mobile VCT teams, and Community Health Workers
 - Expected 3% would be HIV+ (population prevalence)
- # 1000 HIV+ women receiving care at WE-ACTx
 - Offered participation by WE-ACTx clinical staff

Primary Outcomes and Predictors

Outcome variables

- High-grade squamous intraepithelial neoplasia, or higher-grade lesion, on cytology (HGSIL+)
- Cancer diagnosed by biopsy

Primary predictor Variables

- Rapid HPV point-of-care, positive vs. negative
- VIA, positive or negative
- HIV serostatus

Inclusion Criteria

- # 30 - 65 years of age;
- # Have never been screened for cervical cancer
- # Are willing and able to give consent for study procedures;
- # Agree to HIV-testing and
- # If HIV-positive, agree to CD4 cell count determination.

Research Procedures

- # Informed Consent (video)
- # A short interview (15 minutes)
- # Cervical cancer screening: pelvic exam with:
 - Endocervical specimen for *care*HPV
 - Standard cervical cytology
 - Visual Inspection with Acetic Acid

Research Procedures cont'd.

- # HIV-testing for community-based participants
- # HPV testing run same day, batch testing, 2 hour test

Research Procedure: Screen and Treat

Immediate Treatment during VIA

- cryotherapy of identified treatable lesions by standard VIA protocol
- lesions not amenable to cryotherapy referred for appropriate further treatment (colposcopy, LEEP, biopsy)
- Cryotherapy for HPV+ if not treated during VIA
- Women newly found HIV+ referred to HIV care services (WE-ACTx)

Didactic and Practical Training on Visual Inspection with Acetic Acid (VIA) & Cryo



Training
for all
staff--15



Population

- # 3018 women recruited
 - 1707 HIV-negative
 - 1311 HIV-positive

- # Reported cytology results available (n=1996):
 - 1300 HIV-negative
 - 696 HIV-positive

Demographic Characteristics

Characteristic Mean (SD)	HIV-negative n=1300	HIV-positive n=696	P-value
Age	41.9 (8.1)	39.8 (6.7)	<0.0001
Age at first intercourse	18.7 (4.0)	17.4 (4.1)	0.0015
Age at first birth	21.2 (3.8)	20.1 (3.6)	<0.0001
BMI, Mean	22.0 (3.8)	22.5 (4.5)	0.0129
CD4 count		485 (232)	

Demographic Characteristics

Characteristic n (%)	HIV-negative n=1300	HIV-positive n=696	P-value
# of sexual partners			<0.0001
0- 1	931 (72.1)	172 (25.2)	
2	238 (18.4)	207 (30.3)	
>2	123 (9.5)	304 (44.5)	
# of pregnancies			<0.0001
0-2	149 (11.6)	145 (21.6)	
3-4	324 (25.3)	233 (34.8)	
5-6	366 (28.5)	182 (27.2)	
>=7	444 (34.6)	110 (16.4)	
Hormonal Contraception Use			
Ever	387 (29.9)	163 (23.4)	0.002
Last six months	308 (23.8)	123 (17.7)	0.002

Demographic Characteristics

Characteristic n (%)	HIV-negative n=1300	HIV-positive n=696	P-value
Marital Status			
Married/Partner	867 (66.9)	319 (46.0)	<0.0001
Widowed	300 (23.2)	240 (34.6)	
Divorced	129 (10.0)	135 (19.5)	
Number of Children			
0	28 (2.2)	45 (6.7)	<0.0001
1-2	289 (22.5)	245 (36.6)	
3-4	499 (39.0)	265 (39.6)	
5 +	467 (36.4)	115 (17.2)	
Post-menopausal	211 (16.3)	67 (9.64)	<0.0001
Use Tobacco	210 (16.2)	41 (5.9)	
Take ARV		496 (72.6)	

Cytology findings

	Total	HIV-negative # (%)	HIV-positive # (%)	P-value
Normal	1791 (89.7)	1179 (90.7)	612 (87.9)	0.0011
ASCUS	119 (6.0)	82 (6.3)	37 (5.3)	
Low grade SIL*	29 (1.5)	14 (1.1)	15 (2.2)	
High grade SIL+	57 (2.9)	25 (1.9)	32 (4.6)	

*Squamous Intraepithelial Lesion

Prevalence by Each Screening Test

Finding	HIV-negative n=1300 % (n)	HIV-positive n=696 % (n)	P-value
High grade cytology	1.9% (25)	4.6% (32)	0.001
HPV-positive	9.9% (128)	30.0% (209)	<0.0001
VIA positive	8.1% (105)	11.6% (81)	0.012

Sensitivity and Specificity in detecting HGSIL+

	Sensitivity	Specificity
HIV-positive	% (95% CI*)	% (95% CI*)
VIA	43.8 (26.4, 62.3)	89.9 (87.6, 92.2)
HPV	71.9 (56.3, 87.5)	72.0 (68.6, 75.4)
HIV-negative		
VIA	8.0 (1.0, 0.19)	91.9 (90.4, 93.3)
HPV	40.0 (0.20, 0.59)	90.8 (89.0, 92.3)

*CI=confidence Interval

Projected proportion of those with disease detected if screening repeated

TEST	Screen once	Screen Twice	Screen three times
HIV-positive			
HPV	71.9%	92.1%	97.8%
VIA	43.8%	72.8%	84.7%
HIV-negative			
HPV	40.0%	64.0%	78.4%
VIA	8.0%	15.4%	22.2%

Conclusions

- ✦ Rapid point-of-care HPV test significantly more sensitive than VIA in predicting HGSIL
- ✦ Both HPV and VIA were more sensitive in HIV+ compared to HIV-negative women
- ✦ Repeated testing is desirable (if sensitivity is similar in predicting invasive cancers)
- ✦ VIA in HIV-negative women had a low sensitivity and did not predict HGSIL+

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WE-ACT_x

Women's Equity in Access to Care and Treatment for HIV



www.we-actx.org

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Predictors of HGSIL+: all women

	Univariate	Multivariate
Variable	OR (CI)	OR (CI)
Age (Per 10-Year)	1.40 (1.01- 1.95)*	2.06 (1.44- 2.95)***
HIV Status (+ vs. -)	2.46 (1.44- 4.18)***	1.50 (0.83- 2.70)
VIA Status (+ vs. -)	4.04 (2.22- 7.36)***	2.95 (1.52- 5.74)**
HPV Status (+ vs. -)	7.40 (4.31-12.69)***	6.88 (3.73-12.71)***
Sexual Partners		
=2 vs. 0-1	2.05 (1.07- 3.92)*	
>= 3 vs. 0-1	2.27 (1.20- 4.30)*	
Age at First Birth	0.89 (0.82- 0.97)*	
Menopause	2.27 (1.24- 4.15)**	
Rape	1.98 (1.11- 3.53)*	

CI=95% Confidence Interval; *p<0.05; **p<0.01; ***p<0.001

Predictors of HGSIL+:HIV-negative women

	Univariate	Multivariate
Variable	OR (C.I.)	OR (C.I.)
Age (Per 10-Year)	1.42 (0.88- 2.28)	1.72 (1.03- 2.87)*
VIA Status (+ vs. -)	0.98 (0.23- 4.23)	0.82 (0.18- 3.80)
HPV Status (+ vs. -)	6.54 (2.87- 14.88)***	8.53 (3.59-20.23)***
Sexual Partners		
2 vs. 0-1	1.99 (0.84- 4.71)	
≥3 vs. 0-1	0.47 (0.06- 3.57)	
Age at First Birth	0.94 (0.83- 1.06)	
Menopause	2.47 (1.05- 5.81)*	
Rape	1.07 (0.31- 3.60)	

CI=95% confidence interval; *p<0.05; ***p<0.001

Predictors of HGSIL+: HIV-positive women

	Univariate	Multivariate
Variable	OR (C.I.)	OR (C.I.)
Age (Per 10-Year)	1.73 (1.07- 2.80)*	2.22 (1.31- 3.75)**
VIA Status (+ vs. -)	6.93 (3.30-14.57)***	5.72 (2.43-13.49)***
HPV Status (+ vs. -)	6.57 (2.98-14.46)***	5.12 (2.17-12.10)***
Sexual Partners		
2 vs. 0-1	1.52 (0.50- 4.62)	
≥3 vs. 0-1	1.98 (0.72- 5.46)	
Age at First Birth	0.89 (0.78- 1.00)	0.90 (0.79- 1.02)
Menopause	2.81 (1.17- 6.78)*	
Rape	1.83 (0.89- 3.74)	
Taking ART	2.74 (0.95- 7.91)	2.79 (0.90- 8.65)
CD4 Count (per 100)	0.94 (0.81-1.11)	1.09 (0.91- 1.30)

Most common in all parks
(lovely animals)



Rwanda: Tourism

Nyungwe park in Rwanda



Rwanda: Tourism Akagera Park

