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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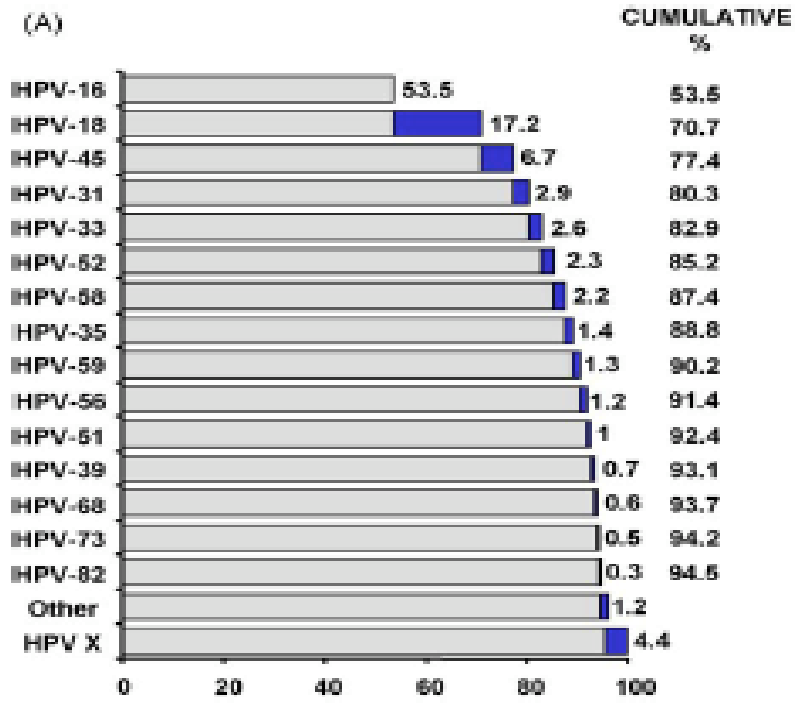
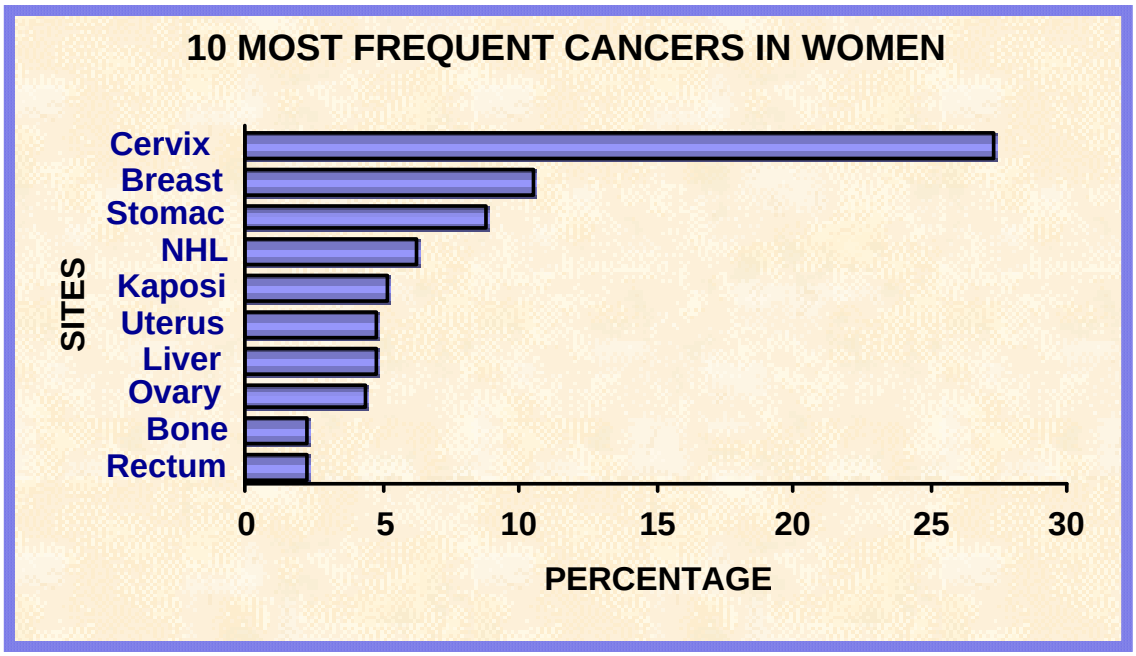
EPIDEMIOLOGY

- 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 mortalityreduced 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



Ngendahayo L. 2006

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 rapidpoint-of-care HPV test (careHPV) andVIA in identifying high-grade squamousintraepithelial lesions (HSIL) or cancer.
2) To assess possible differences in testperformance in HIV+ and HIV-women

RESEARCH DESIGN AND METHODS

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

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 careHPV
    - Standard cervical cytology
    - Visual Inspection with Acetic Acid

Research Procedures cont'd.

- HIV-testing for community-basedparticipants
- HPV testing run same day, batch testing,2 hour test
- Research Procedure:
- Screen and Treat

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 0-2			<0.0001
3-4	149 (11.6)	145 (21.6)	
5-6	324 (25.3)	233 (34.8)	
>=7	366 (28.5)	182 (27.2)	
	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

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

Positive and negative predictive value in detecting HGSIL+

	PPV	**NPV**
HIV-positive		
VIA	17.3%	97.1%
HPV	11.3%	98.2%
HIV-negative		
VIA	1.9%	98.1%
HPV	7.8%	98.7%

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-ACTx
Women's Equity in Access to Care and
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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)

CI=95% confidence interval; ART=antiretroviral therapy; *p<0.05; **p<0.01; ***p<0.001

Thank you