

The Evaluation of Screening, Treatment and Vaccination of HIV-infected women

World STI @ HIV Congress 2015

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HPV and cervical lesions in HIV-seropositive women: What we know

- HIV seropositive women:
 - Higher prevalence, incidence and persistence of HPV
 - Higher risk of squamous intraepithelial lesions (SIL) and invasive cervical cancer
 - Higher rates of recurrent high-grade lesions

All of these associations are stronger in HIV+ women with lower CD4 counts.

De Vuyst H. et al. Eur J Cancer Prev, 2008;17(6):545-54

South Africa

Dr. Cindy Firnhaber
Dr. Ian Sanne

WITS,
Johannesburg



South Africa: Collaborative Results

- Prevalence of high-grade cervical lesions and HPV infection is notably higher among HIV-infected women with lower CD4 counts¹.
- HAART use appears to approximately halve the combined incidence and progression rates of cervical lesions in prospective analyses².

¹Firnhaber et al., Cancer Causes Control. 2010. ²Firnhaber et al., J Int AIDS Soc. 2012.

Methods



- 1,202 HIV-seropositive women screened in an HIV treatment clinic in Johannesburg
- Women had Digene HC-II HPV testing, conventional Pap smear and VIA screening.
- All women with positive Pap smears and VIA had colposcopy
- ~25% women with negative Pap and VIA results were referred for colposcopy to control for verification bias

Plos One, 2013

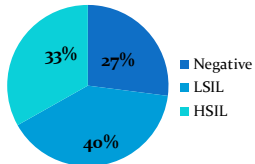
Quality Control



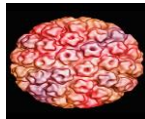
Results of 1,202 HIV-seropositive women screened in an HIV treatment clinic in Johannesburg

➤ **VIA + 55.7%**

Pap smear

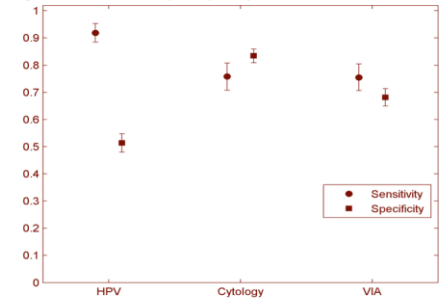


➤ **HC-II HPV DNA 60.9%**

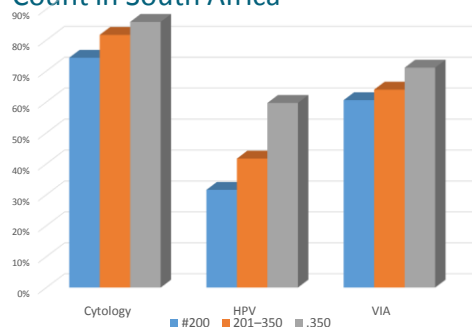


Sensitivity /Specificity among HIV-seropositive in South Africa

Figure 2. Estimated Sensitivity and Specificity for CIN2+ and 95% Confidence Interval



Specificity Estimates, Stratified by CD4 Count in South Africa



Coptic Hope Center for Infectious Diseases in Nairobi, Kenya, Michael Chung et al.

- 500 HIV-positive patients enrolled from Coptic Hope Center, a PEPFAR-funded HIV clinic based in Nairobi, Kenya since 2004



- Eligible if HIV-positive, ≥18 years, intact cervix, never received cervical treatment

Detection of CIN3 by immune status and CD4 count in HIV-seropositive women in Nairobi, Chung et al.

	CD4 <350	CD4 >350	p-value
Sensitivity			
Pap (HSIL+)	78.6%	84.2%	0.7
VIA	67.9%	73.7%	0.7
HPV	89.3%	100%	0.3
Specificity			
Pap (HSIL+)	85.2%	89.3%	0.2
VIA	56.6%	67.0%	0.03
HPV	40.7%	58.9%	<0.001

	Off ART	On ART	p-value
Sensitivity			
Pap (HSIL+)	66.7%	85.7%	0.2
VIA	66.7%	71.4%	0.7
HPV	100%	91.4%	0.6
Specificity			
Pap (HSIL+)	89.5%	86.7%	0.5
VIA	62.9%	62.1%	0.9
HPV	46.7%	52.2%	0.3

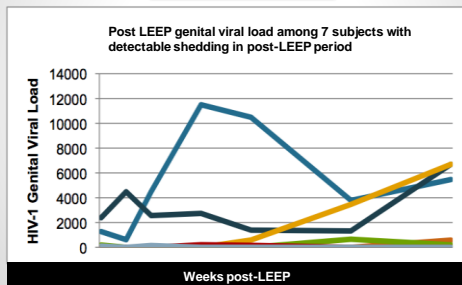
HIV-shedding pre and post treatment in Kenya


- HIV+ women with CIN 2/3, on HAART treated LEEP
- HIV-1 genital shedding samples collected at baseline and weeks 1, 2, 4, 6, 10 and 14
- Blood serum testing for HIV-1 viral load at baseline
- HIV-1 tear flo strips processed and analyzed at UCSF-GIVI lab using Abbott RealTime Viral Load Assay, lower detection limit < 40 copies/mL




Huchko et al. BIOG 2013:120:1233-9.

No pattern was observed among the seven women who demonstrated HIV-1 genital shedding





THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL



Right
to care
TREATING AIDS SERIOUSLY

**Upcoming this week at IPV Lisbon 2015:
A Randomized Trial Comparing Cervical
Dysplasia Treatment Modalities in HIV-
Seropositive Women from Johannesburg,
South Africa**

http://www.gagen.com

**Busola Sanusi (speaker), Jennifer Smith, Avril Swarts, Mark Faesen,
Simon Levin, Bridgette Goeleman, Sibongile
Ramotshela, Ntombiyenkosi Rakhombe, Anna Lise Williamson, Pam
Michelow, Tanvier Omar, Michael Hudgens, Cindy Firnhaber**

CFAR Meeting in Cape Town, South Africa
Research Priorities

- What are the optimal screening strategies for cervical cancer precursors in setting of HIV
 - Potential role of self-collection; use of HPV RNA Aptima testing
- What are the optimal treatment methods for cervical cancer precursors in setting of HIV
- Does screening or treatment effectiveness vary by CD4/CD4 nadir or ART status
- What are the determinants of recurrence and what are best strategies to identify recurrences

CFAR Meeting in Cape Town, South Africa
Research Priorities

- How can high-grade recurrences be prevented
- What is role of male circumcision in cervical cancer prevention (and programmatic implications)
- What are effects of treatment (cryotherapy vs LEEP, others?) on HIV shedding and what are the determinants
- What are the most effective strategies to incorporate cervical screening and treatment into HIV care
 - Models of integration
 - Systems issues
 - Quality control: training, pathology, etc

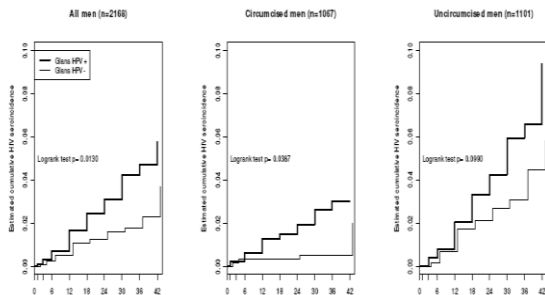
CFAR Meeting in Cape Town, South Africa
Research Priorities, continued

- How to evaluate and manage ICC in setting of HIV
- What is efficacy and effectiveness of HPV vaccine in the setting of HIV to prevent HPV-related cancers
- Implementation issues
- What is natural history of other HPV-related cancers and precursors (anal, oral) and what are effective screening, treatment and longitudinal follow-up of precancerous lesions in these sites

HPV Vaccination in HIV-seropositive

- High neutralizing antibody titers following HPV vaccination in HIV-seropositive individuals
- No data yet available on vaccine efficacy

Results: Cumulative HIV Seroincidence Across Follow-up Visits by HPV Positivity in the Glans



Thank you!

Let's work to be Cervical Cancer Free
www.Cervicalcancerfreeorganization.org

JenniferS@unc.edu

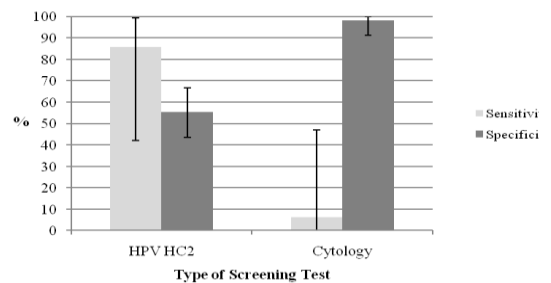
Intraepithelial neoplasia among HIV-infected women in Yunnan Province



The Women and Children's Hospital Luxi County, Mangshi, Yunnan Province

Zhang HV et al., Asian Pac J Cancer Prev. 2012;13(1):91-6.

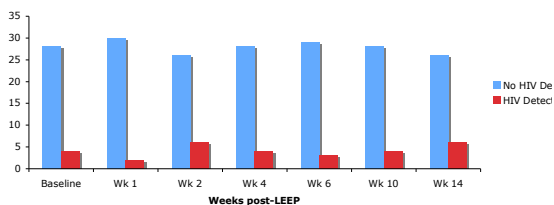
Sensitivity and Specificity for CIN2+ of HPV DNA (Hybrid Capture 2) Testing vs. Cytology among HIV-infected women in Yunnan, China



Zhang HV et al., Asian Pac J Cancer Prev. 2012;13(1):91-6.

The majority of women had no detectable HIV-1 genital shedding

Participants with Detectable Shedding at Each Visit



Huchko et al, BJOG 2013;120:1233-9.