HPV DNA and VIA-DC Co-testing for 'Screen-and-Treat' Cervical Cancer Prevention: Initial Screening and 1-year Follow-up

Preetam Cholli, MS3
University of Massachusetts Medical School
Worcester, MA United States

Disclosures

- No financial relationships or conflict of interest to disclose
- *care*HPV DNA tests for initial screening were purchased; follow-up tests donated by Qiagen

Background

Invasive cervical cancer (ICC) is the second leading cause of cancer mortality among Cameroonian women

If women aged 35 years are screened a single time, lifetime risk of ICC is reduced >25%

WHO advocates a same-day ‘screen-and-treat’ approach to reduce loss to follow-up

Role of HIV status in the performance of screening modalities lacks evidence

Globocan 2012 (2013) IARC Cancer Base
Goldie et al. (2005) NEJM 353: 2158

Background: Screen-and-treat

Different screening modalities available:

- Visual inspection with acetic acid (VIA)
  - Can be enhanced by digital cervicography (VIA-DC)
- Pap test – not feasible in resource poor countries
- HPV DNA testing
  - *care*HPV: tests for 14 high-risk HPV subtypes; designed for low-resource settings

Perham et al. (2015) PLoS One. 2015, 17;10(4):e0122169.

World Health Organization, 2013. Guidelines for screening and treatment of precancerous lesions for cervical cancer prevention

Objectives

Role of Co-testing in Enhancing Screening, Triage for HIV+ and HIV- Women

1. Is integrating VIA-DC with HPV DNA feasible for same-day co-testing? What can co-testing tell us about VIA-DC's efficacy?

Future Projections

2. For women who screen VIA-DC positive or HPV positive, how does their status change in one-year's time? How can this inform screening, treatment and follow-up algorithms?

Methodology:
Screening by Cameroon Baptist Convention Health Services (CBCHS)

Initial screening 2015: 2 CBCHS clinics piloted co-testing (HPV, VIA-DC) with HIV testing if status unknown

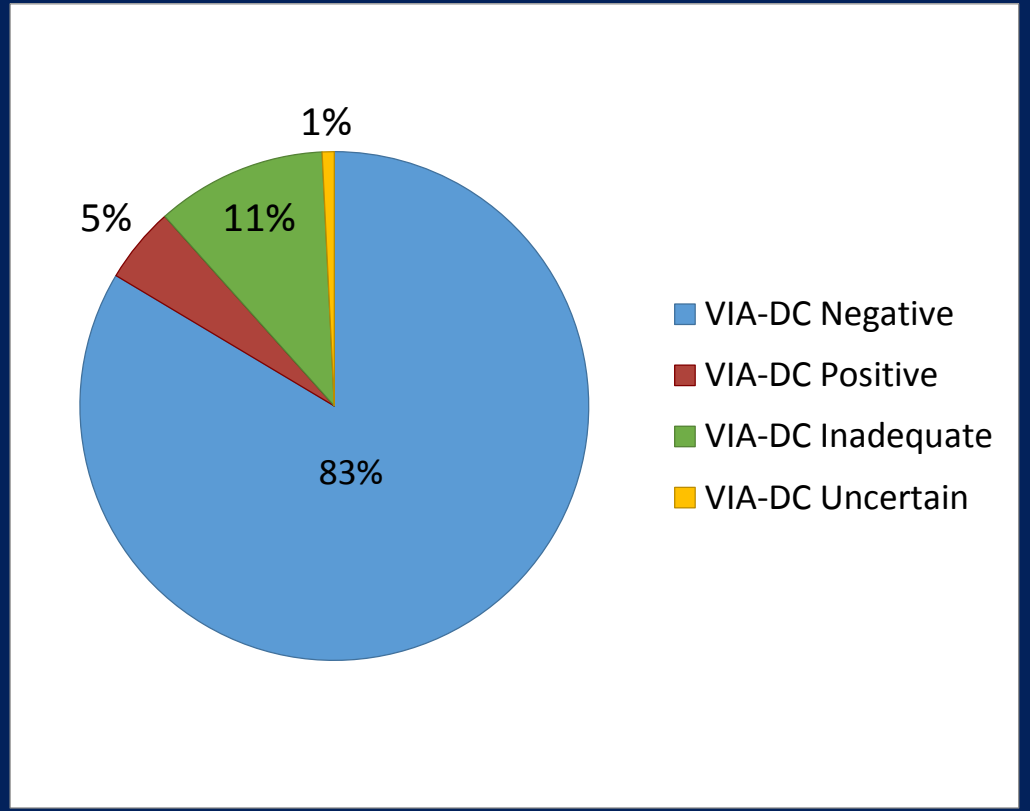
- 913 women met inclusion criteria (age 30-65 years, previously unscreened, confirmed HIV status); 42% HIV positive
- Same-day cryotherapy, thermal coagulation or referral for Loop Electrical Excision Procedure (LEEP) offered to VIA-DC positive women per WHO criteria

Follow-up screening 2016: Repeat co-testing

- Target: all previously VIA-DC positive and HPV positive women
- Same-day treatment or referral offered to all VIA-DC and HPV positive women

Results: Initial Screening 2015

- VIA-DC results: 5% positive, 11% inadequate*
- HPV results: prevalence 24%
  - HIV positive subgroup: 41% HPV positive
  - HIV negative subgroup: 17% HPV positive
- In total: 245 women initially HPV or VIA-DC positive
- Treatment uptake, VIA-DC positive women:
  - 27% received same-day intervention
  - 11% returned for LEEP

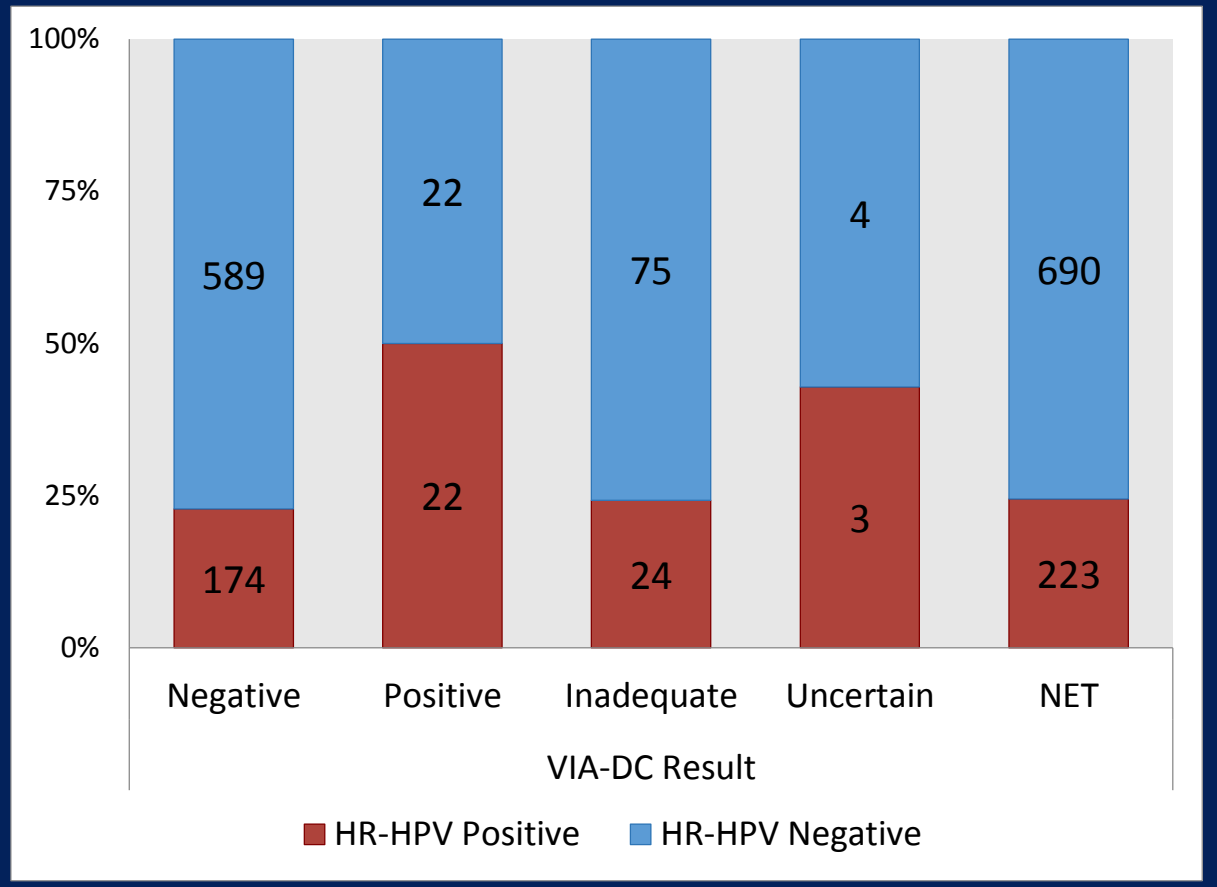


* VIA-DC Inadequate: squamocolumnar junction could not be fully visualized

Results: Initial Screening 2015

What did HPV DNA co-testing teach us about VIA-DC?

- 50% of VIA-DC positive women were HPV positive
  - Remaining women: implications for same-day 'screen-and-treat'
- Among VIA-DC positive women:
  - HIV positive: 65% had HPV infection
  - HIV negative: 20% had HPV infection

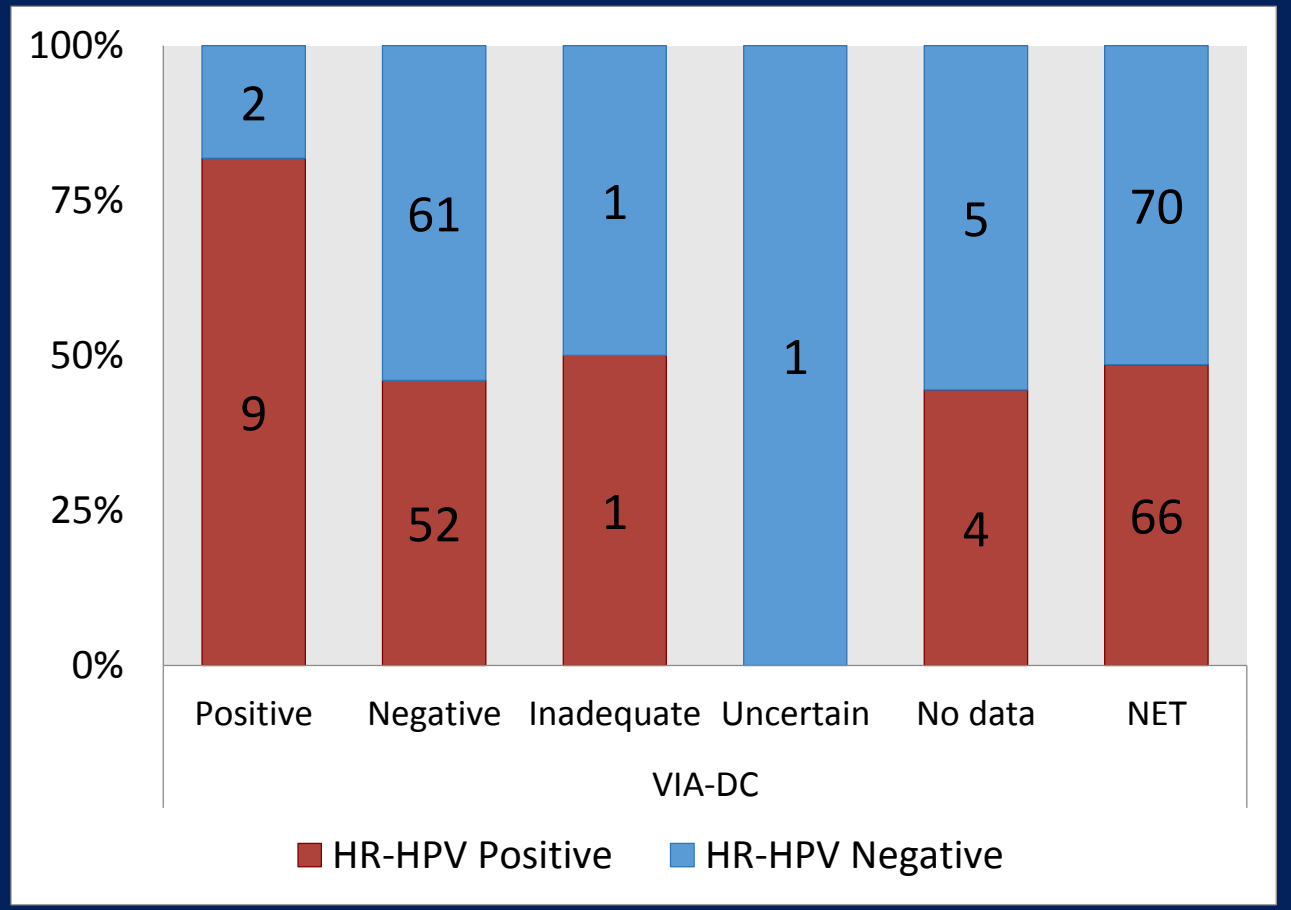


Results: 1-year follow-up

Target: re-screen all VIA-DC positive and HPV positive women after 1 year (n=245)

136 (55.5%) of indicated women returned for follow-up

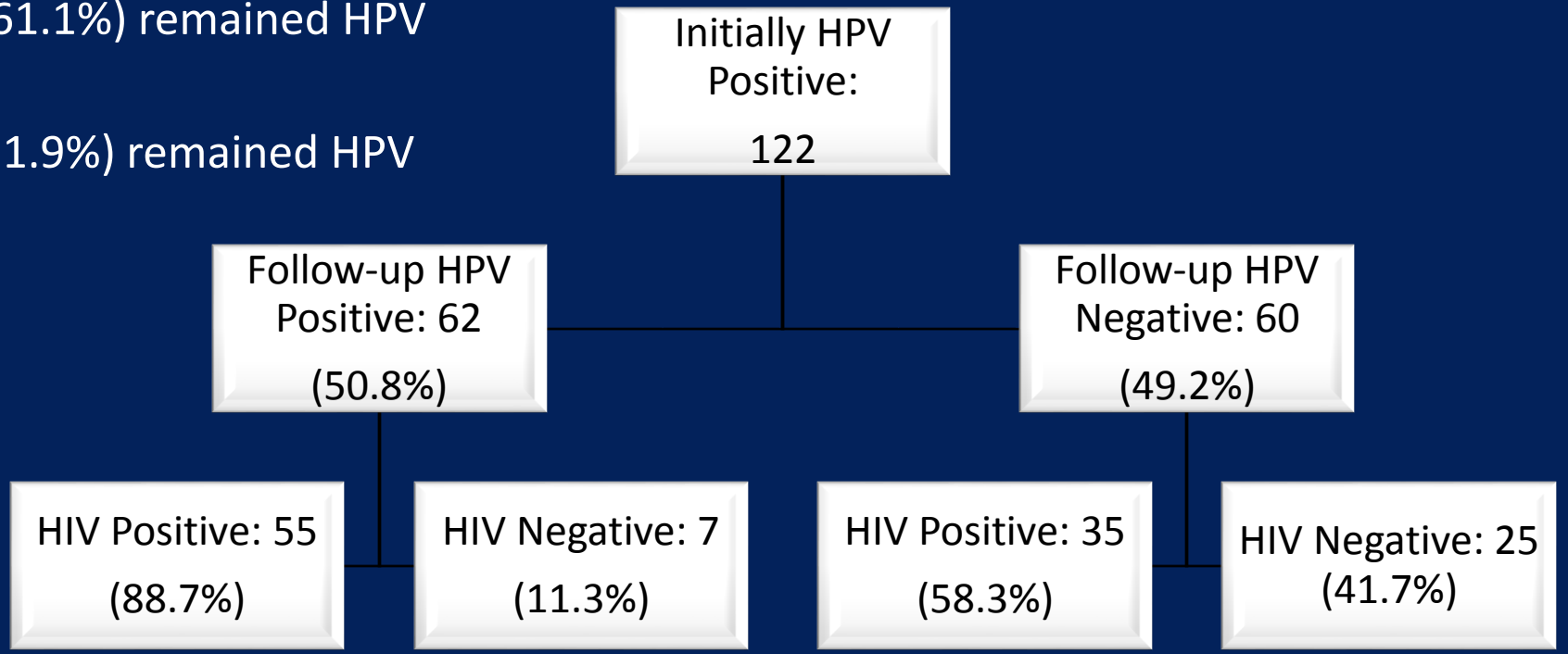
- HIV Prevalence: 69.85%
- Figure: follow-up VIA-DC and HPV results



Results: 1-year follow-up – HPV Positive

HPV clearance and HIV status

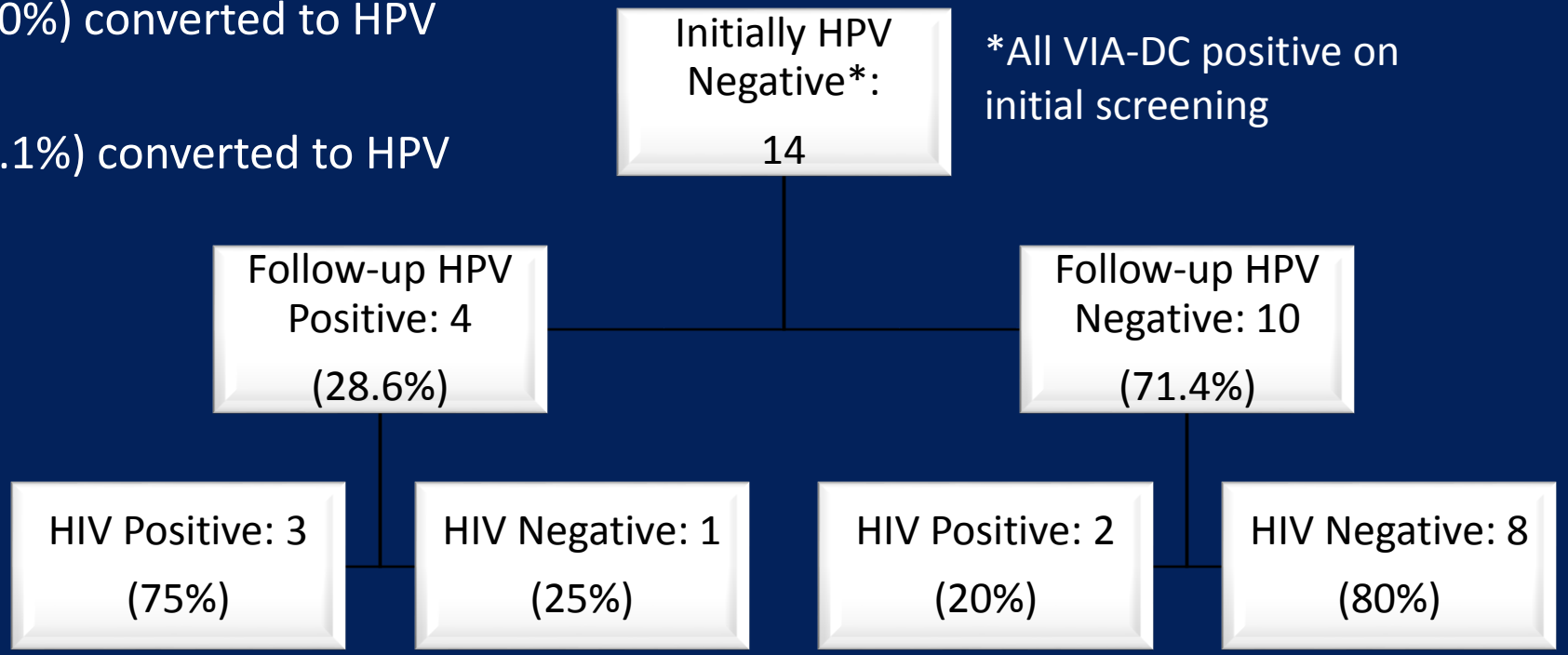
- For women HPV **positive** on initial screening:
  - HIV positive: 55/90 (61.1%) remained HPV positive
  - HIV negative: 7/32 (21.9%) remained HPV positive



Results: 1-year follow-up – HPV Negative

HPV clearance and HIV status

- For women HPV **negative** on initial screening:
  - HIV positive: 3/5 (60.0%) converted to HPV positive
  - HIV negative: 1/9 (11.1%) converted to HPV positive



Results: 1-year follow-up

Treatment uptake: intended for all women who were either VIA-DC positive or HPV positive

- Number of women who qualified: 68
  - Available treatment data for 36 women: all received treatment (cryotherapy, thermal coagulation, or LEEP)
  - No data for 32 women
  - Confirmed treatment uptake: 52.9%

Discussion

What did we learn about VIA-DC and HPV DNA co-testing?

- HPV DNA testing can be a valuable tool to identify false positives and avoid overtreatment
  - VIA-DC had a 50% false positive rate (i.e. no concurrent HPV infection)
- Pairing HPV DNA testing with confirmed HIV status may help guide decisions for treatment and surveillance
- *care*HPV batching requirements (90-well plate) led to ~1-week delay
  - Too late to inform same-day treatment and avoid loss to follow-up
- Co-testing is implementable and acceptable, but an affordable point of care test is needed for HPV results to guide same day treatment

Discussion

What did we learn from trends with 1-year follow-up?

- Loss to follow-up less than expected; **55.5%** of women returned after 1 year
- Strong correlation between HIV status and HPV persistence
- Using HPV results alone under same-day screen-and-treat: would lead to **49.2%** overtreatment, since they cleared their HPV spontaneously.
  - Vs. 50% overtreatment with VIA-DC alone
- Triaging same-day treatment based on **HIV status** and HPV results:
  - Treating HIV positive, HPV positive women: **38.9%** overtreatment
  - Treating HIV negative, HPV positive women: **78.1%** overtreatment

Discussion

Strengths

- 'Triple-screening' with VIA-DC, HPV DNA, and HIV status
- Successful follow-up after 1 year (55.5%)

Limitations

- Population ages were not normally distributed
- Insufficient power to identify definitive trends
- HPV DNA results were delayed due to batching limitations (results in 7-10 days) – could not guide same day treatment

Acknowledgements

UMass:

- UMass Office of Global Health
- Leslie Bradford, MD
- Javier Gordon Ogembo, PhD (currently at Beckman Research Institute of City of Hope)

CBCHS:

- Thomas Welty, MD
- Edith Welty, MD
- Simon Manga, MSc (currently doctoral student at UMass, Boston)
- Kathleen Nulah, MSc

All Cameroonian women who participated in the screening program

Reference:
Results: 1-year follow-up

Comparing rates of VIA-DC persistence and conversion based on HPV status:

- Persistently HPV **positive** after 1 year, and…
  - VIA-DC positive on initial screening (n=8): 25% remained VIA-DC positive
  - VIA-DC negative on initial screening (n=48): 8.3% converted to VIA-DC positive
- Cleared HPV infection in 1 year, and
  - VIA-DC positive on initial screening (n=7): 0% remained VIA-DC positive
  - VIA-DC negative on initial screening (n=48): 2.1% converted to VIA-DC positive

Reference:
Results: 1-year follow-up

Comparing rates of VIA-DC persistence and conversion based on HPV status:

- Persistently HPV **negative** after 1 year, and…
  - VIA-DC positive on initial screening (n=10): 10% remained VIA-DC positive
  - VIA-DC negative on initial screening: not indicated for follow-up
- Converted to HPV **positive** in 1 year, and
  - VIA-DC positive on initial screening (n=4): 75% remained VIA-DC positive
  - VIA-DC negative on initial screening: not indicated for follow-up