



# Southern African HIV Clinicians Society 3rd Biennial Conference

13 - 16 April 2016  
Sandton Convention Centre  
Johannesburg

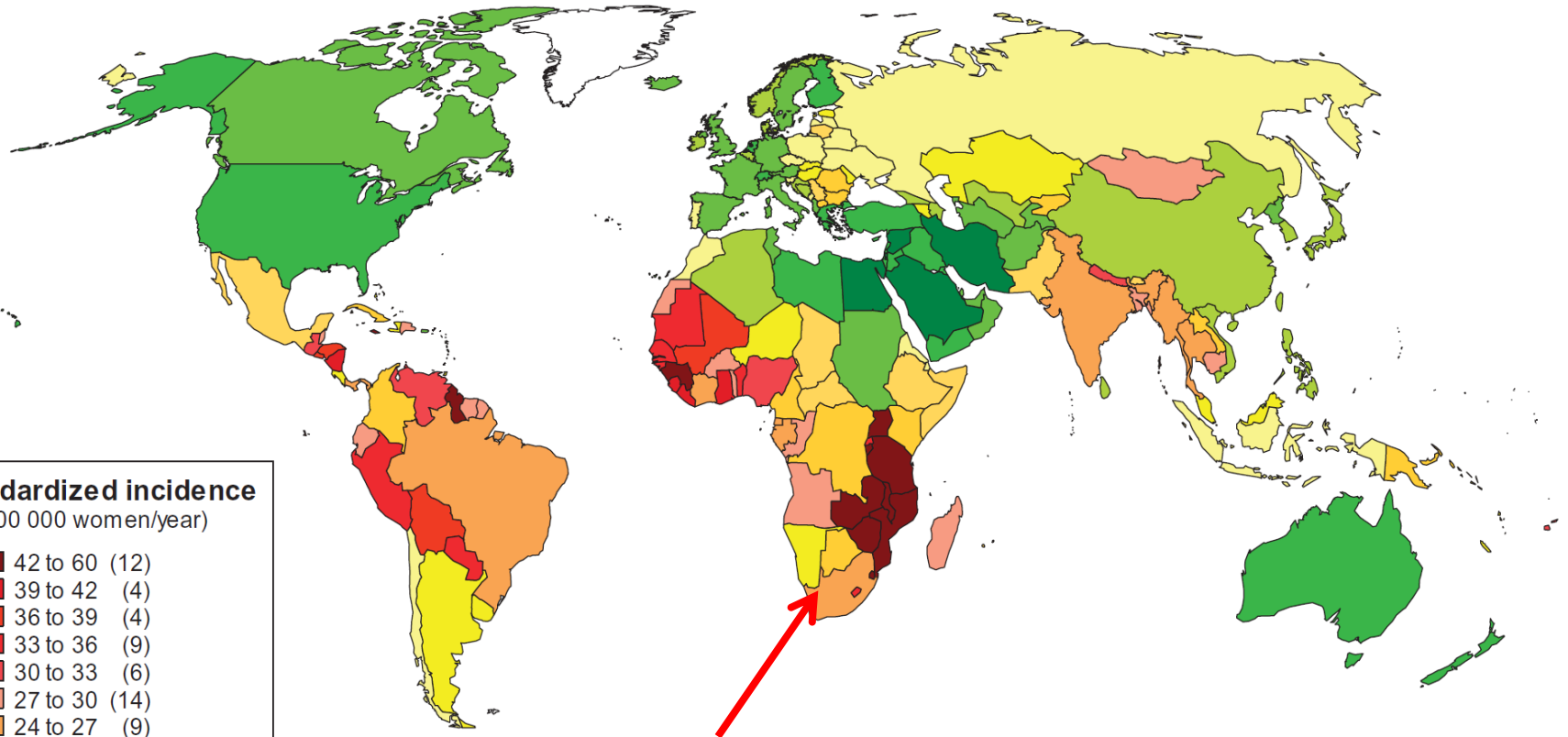
**Our Issues, Our Drugs,  
Our Patients**

[www.sahivsoc.org](http://www.sahivsoc.org)  
[www.sahivsoc2016.co.za](http://www.sahivsoc2016.co.za)

# Cervical Cancer and HIV

Prof Cynthia Firnhaber  
South African Clinician HIV Society  
April 2016

# Age-standardized incidence rate of cervical cancer



**Age-standardized incidence**  
(per 100 000 women/year)

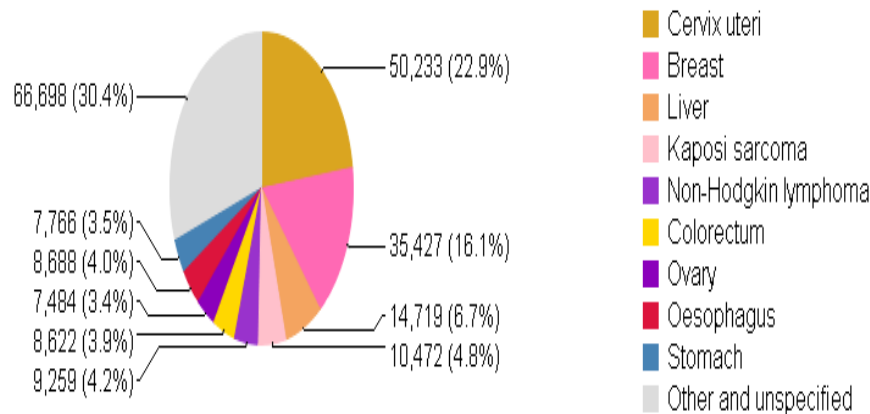
- 42 to 60 (12)
- 39 to 42 (4)
- 36 to 39 (4)
- 33 to 36 (9)
- 30 to 33 (6)
- 27 to 30 (14)
- 24 to 27 (9)
- 21 to 24 (12)
- 18 to 21 (12)
- 15 to 18 (20)
- 12 to 15 (16)
- 9 to 12 (19)
- 6 to 9 (23)
- 3 to 6 (16)
- 0 to 3 (6)

# Cancer Mortality in Sub-Saharan Africa

International Agency for Research on Cancer



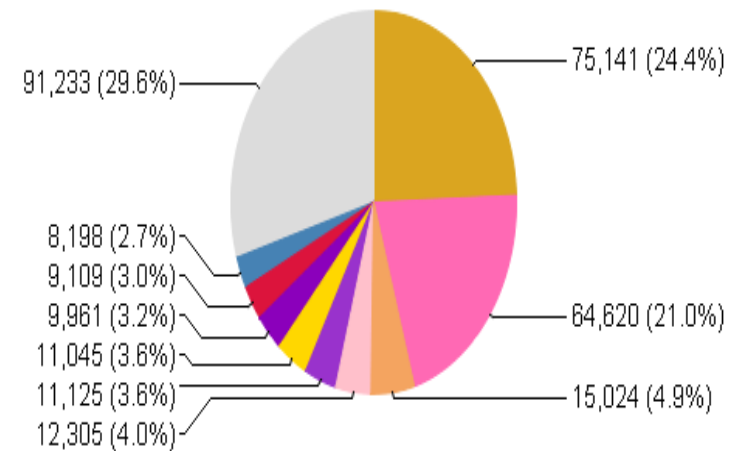
## Mortality



International Agency for Research on Cancer

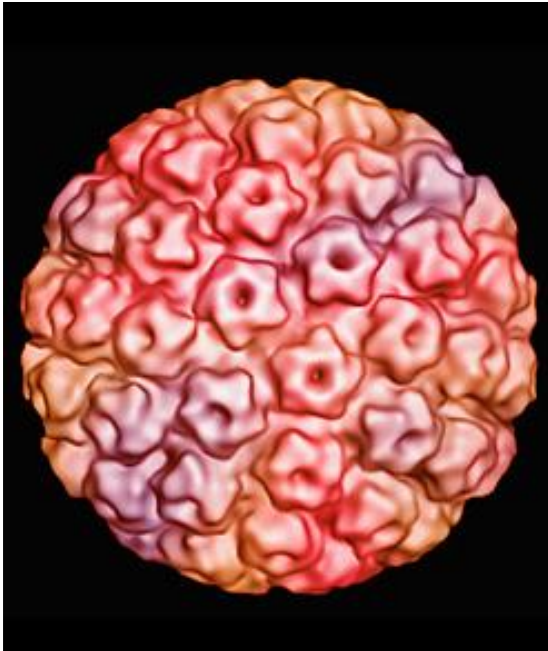


## Incidence



2016

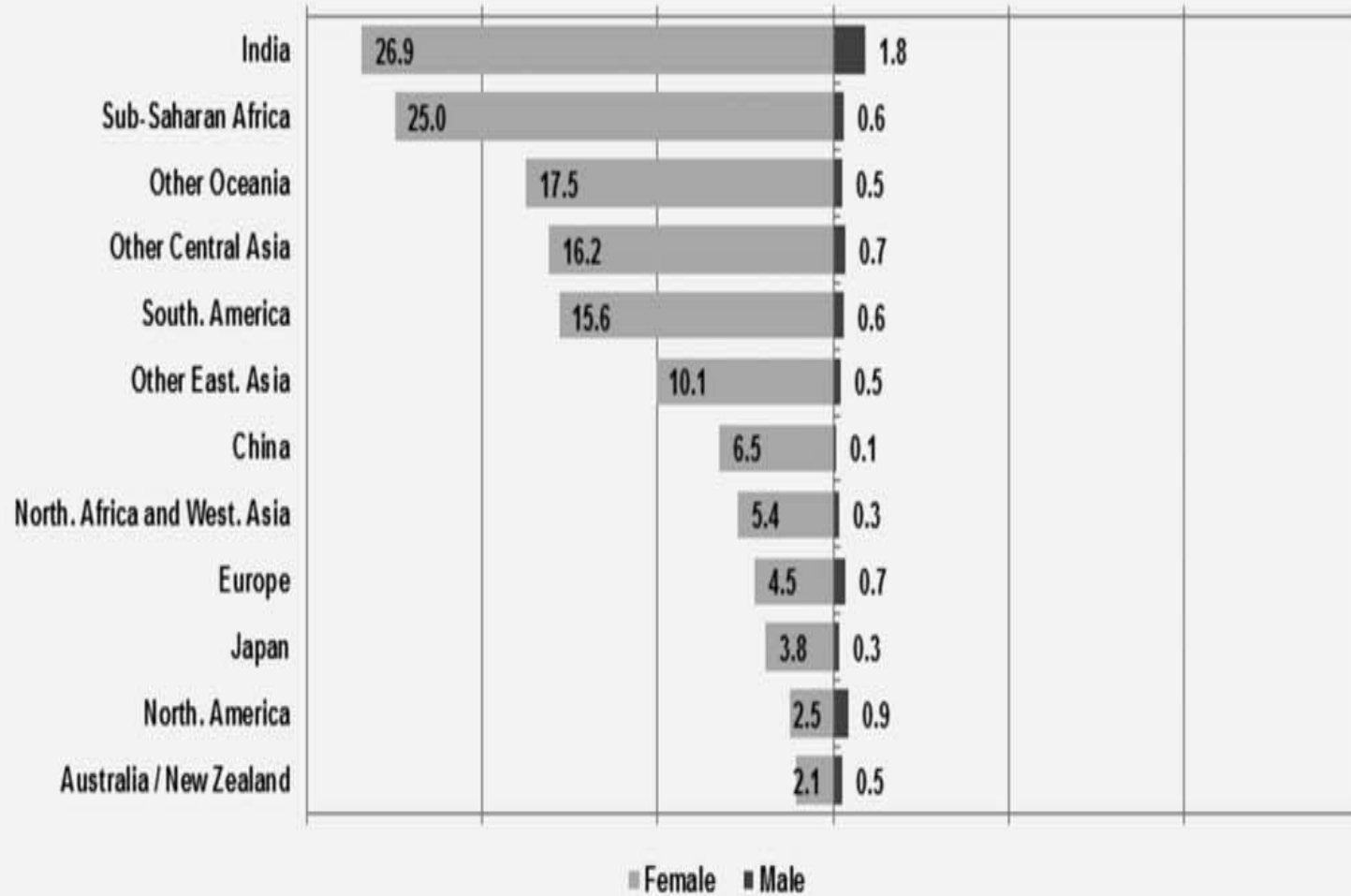
# Human papillomavirus (HPV)



- Nonenveloped double-stranded DNA virus
- Epitheliotropic, obligatory intracellular parasite
- >150 types identified
- ~ 40 anogenital types
  - Oncogenic (“High-risk”) types: **16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68**
  - Possibly oncogenic types: 26, 53, 66, 67, 70, 73, 82
  - Non-oncogenic / unknown oncogenic types include: 6, 11, 40, 42, 54, 55, 61, 62, 64, 69, 71, 72, 81, 83, 84, CP6108, IS39

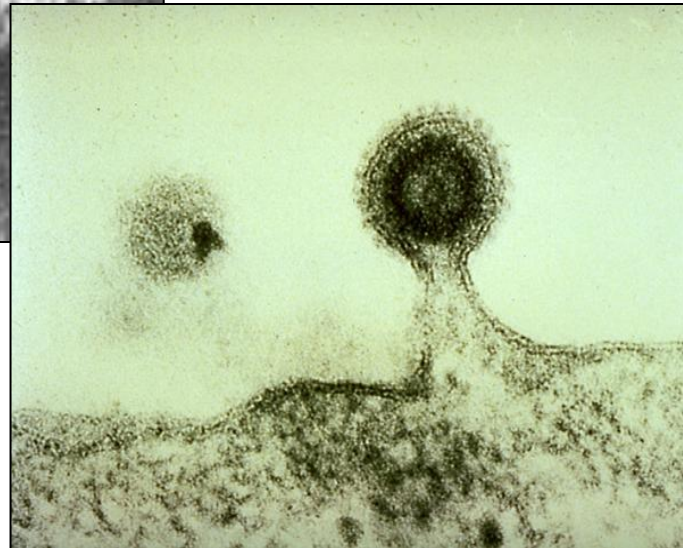
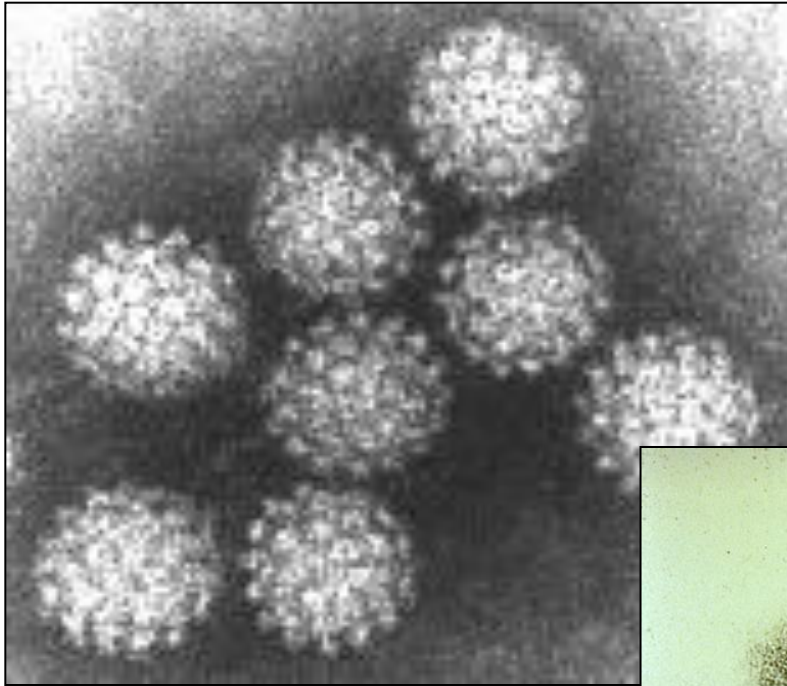
# Proportion of total cancer cases due to HPV

Giuliano et al Int J Cancer 2014



# The Benefit of teamwork?

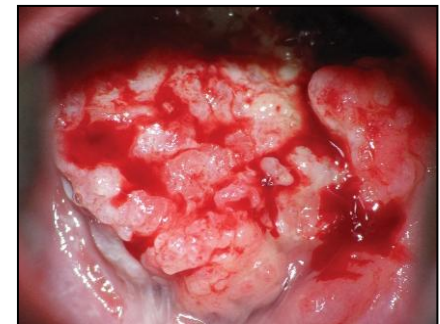
- The benefit is for the viruses –not the host



# Cervical Cancer disease course in HIV infected women in Botswana

*Dryden-Peterson et al CROI 2016 abstract 711*

- 215 women with cervical cancer were enrolled, (67.9%) HIV-infected, (27.0%) HIV-uninfected, and (5.1%) with unknown HIV status.
- Only 8 (3.7%) cancers were identified by screening and symptoms prompted diagnosis in remaining 207 (96.3%).
- HIV-infected women were younger than women without HIV— median age 41.3 and 57.6 years, respectively ( $P < 0.001$ ).
- Median CD4 count for HIV-infected women was 406 cells/ $\mu\text{L}$  (IQR 283 - 550 cells/ $\mu\text{L}$ )

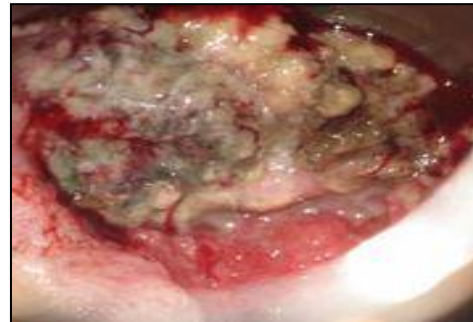




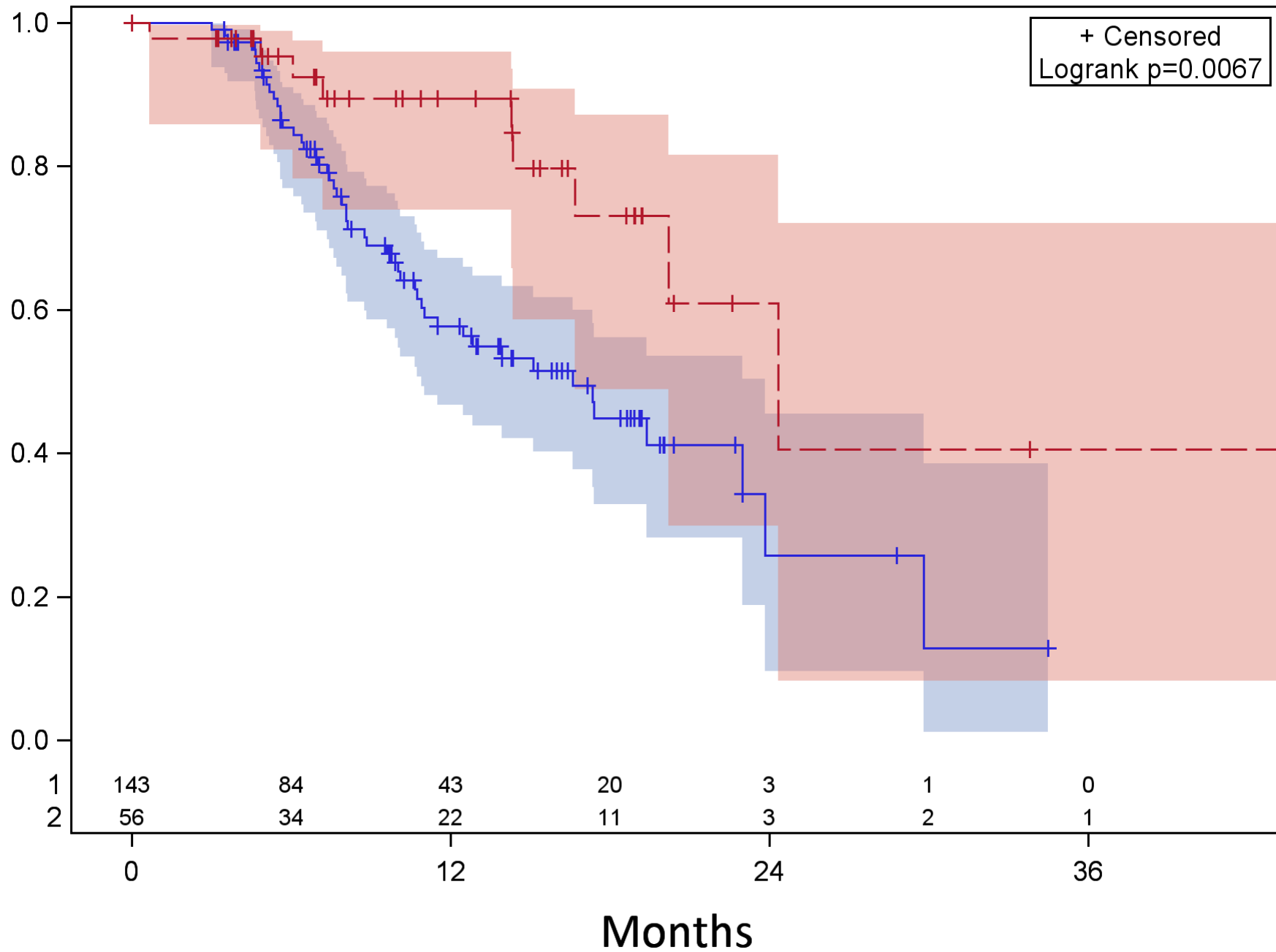
# Results Continue

*Dryden-Peterson et al CROI 2016 abstract 711*

- 86.8% were receiving ART (median duration 4.4 years).
- 35.0% HIV-infected and 16.1% HIV-uninfected women died during follow-up (most cancer related)
- Median survival for HIV-infected women was shorter 16.6 versus 24.3 months, respectively (P=0.007)
- HIV-infection associated with increased mortality (HR 2.66, 95% CI 1.3 - 5.5, P=0.008).
- Among women with HIV, CD4 cell count or ART duration was not associated with survival.



Survival Probability



Status — 1: HIV-Infected — 2: HIV-Uninfected

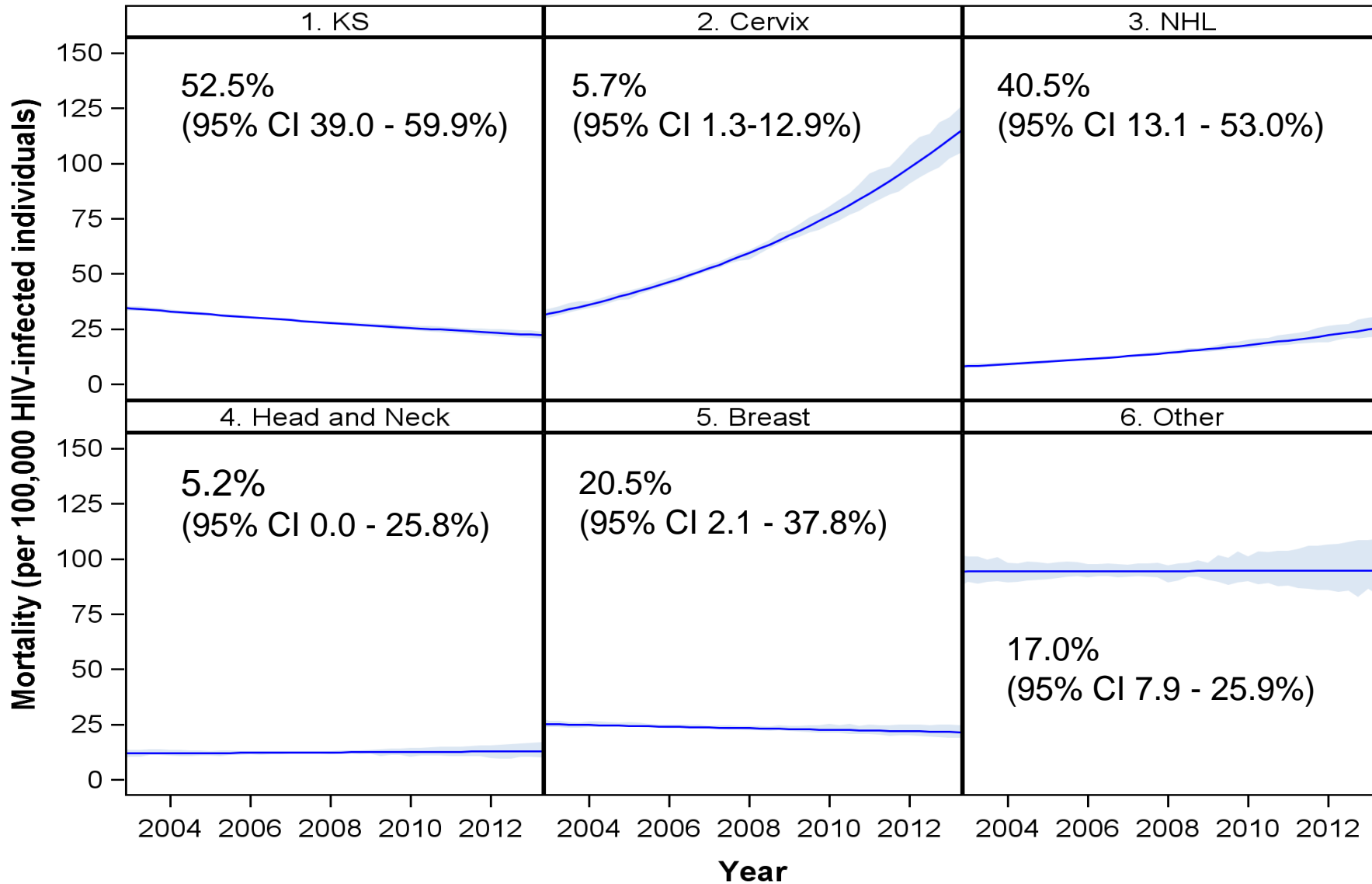
# Cancer vs TB in Botswana

*Dryden-Peterson et al CROI 2016 abstract 615*

- 8479 incident cases recorded in Botswana National Cancer Registry from 2003 to 2009 were utilized
- A total of 850 patients with HIV and cancer were followed
- ● Median 12.2 months (IQR 6.1 to 24.3 months)
- ● 1.2% loss to follow-up

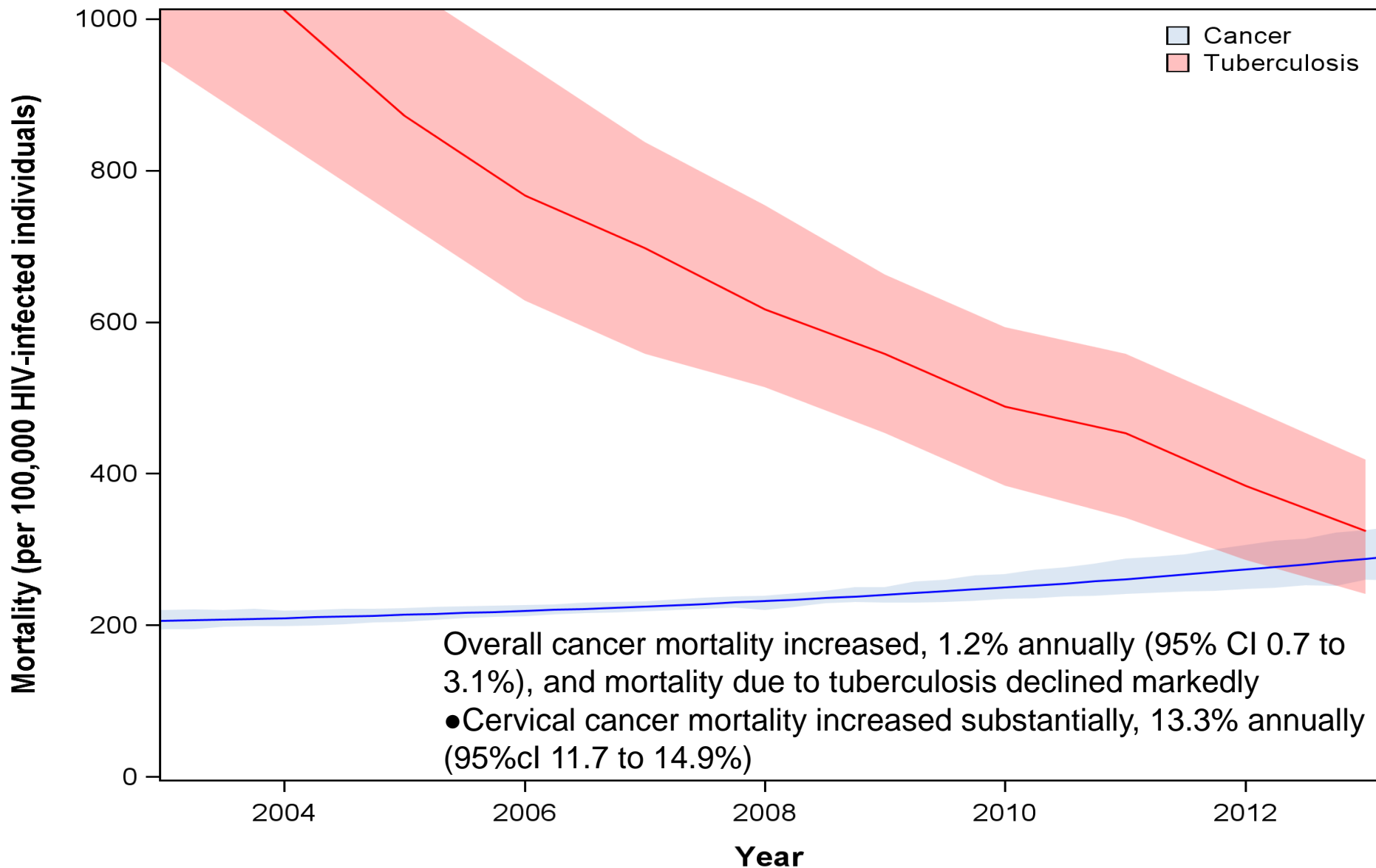


2016



# Cancer vs TB Mortality in Botswana

*Dryden-Peterson et al CROI 2016 abstract 615*



# Cervical Cancer and HIV in South Africa

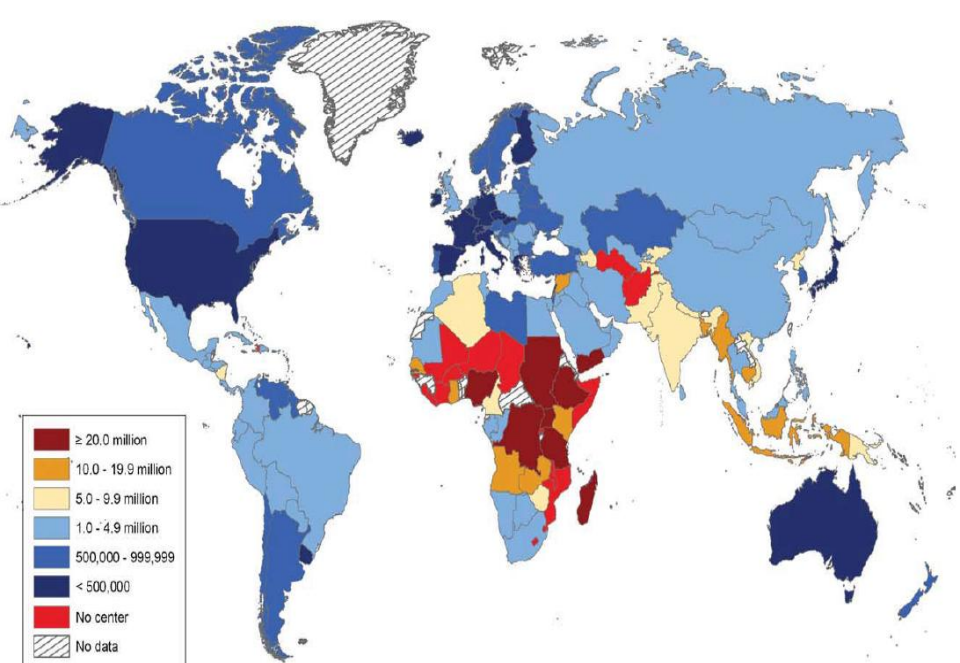
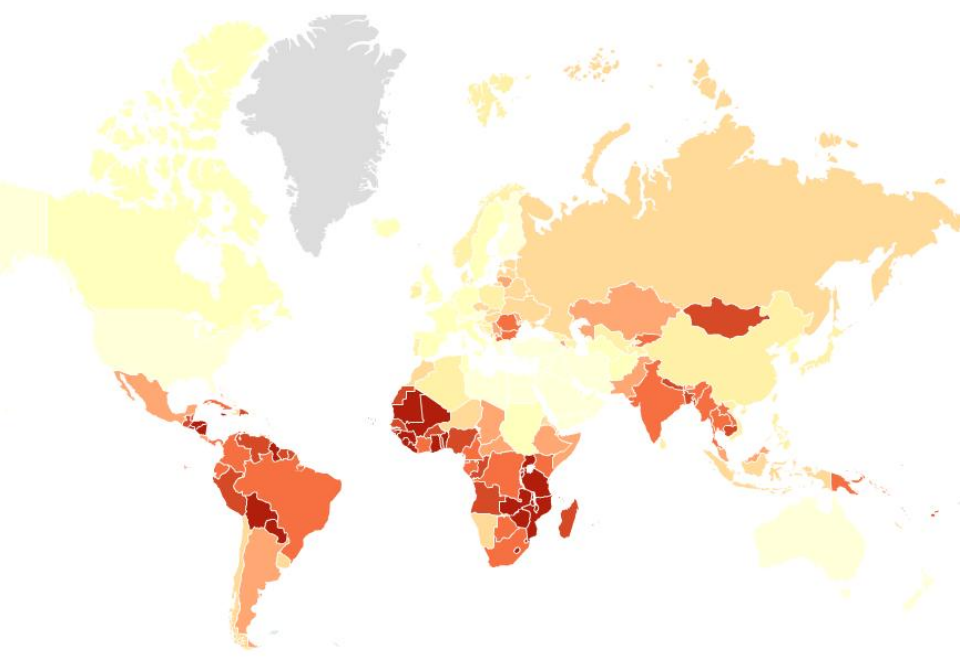
- Significantly increased risk CaCx in HIV infected women (OR 1.6 95% CI 1.2 – 2.3) (Setas et al., 2000,2007).
- In JHB, invasive cervical cancer presents almost 10 years earlier than HIV seronegative women (Lomalisa et al., 2000).
- HIV positive women are at a greater risk of lower genital tract neoplasias including vulvar and anal cancers. (Ferenczy et al.,2003).
- Our clinic seeing rates of 135/100,000 per women of Invasive cervical cancer



# HPV Vaccination

## Cervical Cancer Incidence

## Radiotherapy Centres



# Cervical Cancer and HIV

*“The doctor of the future will give no medicine, but will interest his patients in the care of the human body, in diet, and in the cause and prevention of disease.”*







Infection with HPV →



Invasive Cervical Cancer



Persistent / Recurrent HPV infection ↓



← HIV negative  
around late 40s-  
50s

HIV positive late  
20s –mid 30s

# Challenges for Screening

- Zambia – Women need permission to screen from male partner
- India – Reluctance for male health care providers to perform screening/procedures
- South Africa- myths of loss of fertility and sexual drive
- Another disease
- Infrastructure issues (electricity, water)
- Another queue
- Transportation costs, time of work and child care



# When the woman gets to the clinic

- She may not get the Pap smear due to long queues/overwhelm staff (Coverage in many clinics less than 30% or so)
- Pap smear if done- high rates of inadequacy (>50% in some clinics)
- Results sit at clinic and never placed in file
- Referred for Colposcopy /LEEP appointment in 6 to 12 months



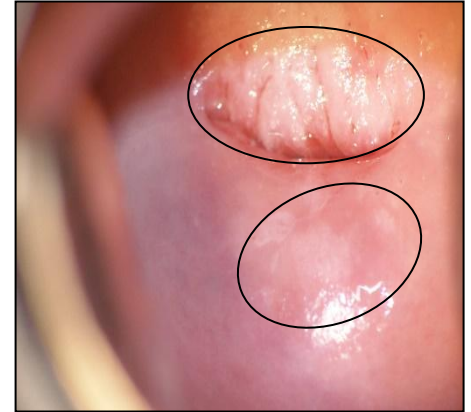
# Visual Inspection of the Cervix- VIA

## See and Treat

Place 5% acetic acid or Iodine on the cervix

White areas consider abnormal

Freeze with cryotherapy  
using N2O or CO2



# Xpert HR-HPV

1

Obtain one appropriately collected and labeled cervical specimen\*.



2

Transfer 1 mL of cervical specimen to the cartridge.



3

Insert cartridge and start assay. Results in less than 60 minutes.



Participants: 1161 HIV-positive women

➤ Xpert® HPV is a qualitative real-time PCR test for automated and rapid detection of Human Papillomaviruses (HPV).

# Xpert vs HC-2 HR-HPV

		hc-2 HR-HPV	
		pos	neg
Xpert HR-HPV	pos	655	65
	neg	56	385

- Overall agreement was **90%** between two tests.
- The agreement beyond chance (Cohen's kappa) was **0.78** (95% CI: 0.74-0.82) indicating excellent agreement.
- Discordant results were due to the influence of lower HPV DNA amounts as indicated by lower RLU in hc2 and high Ct in Xpert (P<0.0001).

# Xpert performance for CIN2/3

	CIN2/3			
	Sensitivity	Specificity	Positive predictive value	Negative predictive value
<b>hc2 positive</b>	91.5% (87.2-95.8)	51.0% (47.6-54.5)	42.1% (38.4-45.8)	93.9% (90.7-97.1)
<b>Xpert HR-HPV positive</b>	88.3% (83.6-93.0)	48.4% (44.9-51.9)	40.1% (36.5-43.8)	91.3% (87.6-95.0)
<b>P1 (HPV16)</b>	31.5% (26.3-36.7)	93.5% (91.8-95.2)	65.5% (56.7-74.2)	77.7% (74.9-80.5)
<b>P2 (HPV18/45)</b>	30.1% (25.0-35.3)	85.6% (83.2-88.0)	45.0% (38.1-51.8)	75.8% (72.8-78.9)
<b>P3 (HPV31/33/35/52/58)</b>	61.1% (55.4-66.8)	71.9% (68.8-75.0)	45.9% (41.0-50.7)	82.6% (79.4-85.8)
<b>P4 (HPV51/59)</b>	18.8% (14.5-23.2)	89.7% (87.6-91.8)	41.7% (33.5-49.9)	73.9% (70.9-76.8)
<b>P5 (HPV39/68/56/66)</b>	33.6% (28.3-38.9)	80.7% (78.0-83.5)	40.7% (34.7-46.7)	75.6% (72.4-78.8)

CIN: cervical intraepithelial neoplasia

# Relationship between the amount of DNA and the prevalence of CIN2+

- Women infected with HPV16, HPV18/45 or HPV31/33/35/52/58 were found to have significantly higher amounts of HPV DNA detected for those with CIN2+ compared to those without CIN2+,  $P < 0.0001$  for each.



*“Every woman  
has the right to  
live a life free  
from cervical  
cancer”*

# THANK YOU

- Department of Health Gauteng South Africa
- Melinda Wilson Pefpar/ USAID
- Patients at the Themba Lethu Clinic Helen Joseph Hospital
- Cervical Cancer Implementation/ Research team
- Sr Sophie William/ Maureen Siminya/ Nthombiyenkosi Rakhombe/ Sibongile Ramotshela/Patricia Kegerilwe - Right to Care
- Avril Swarts-Clinical HIV Research Unit
- Dr Tim Wilkin- Cornell University NY
- Dr Mark Faesen - Right to Care - OB/GYN
- Prof Simon Levin - Right to Care/University of Wits/ Department OB/GYN
- Dr Bridgette Goeieman MO – Right to Care
- Jennifer Smith/Lu Mao/Michael Hudgens – University of North Carolina
- Anna-Lise Williamson/Bruce Allan - University of Cape Town
- First for Women



HOLOGIC®



THE UNIVERSITY  
of NORTH CAROLINA  
at CHAPEL HILL

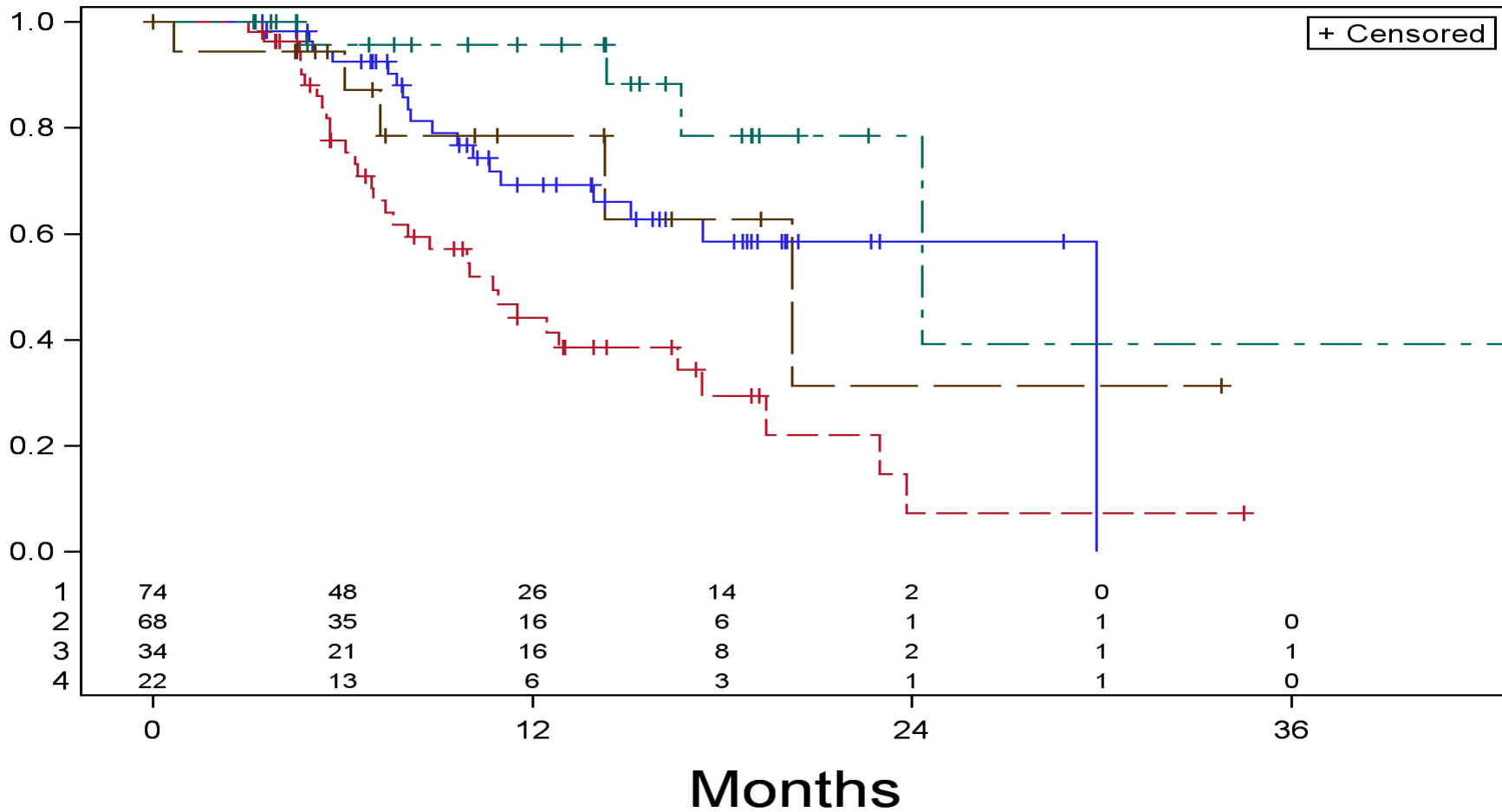


USAID  
FROM THE AMERICAN PEOPLE

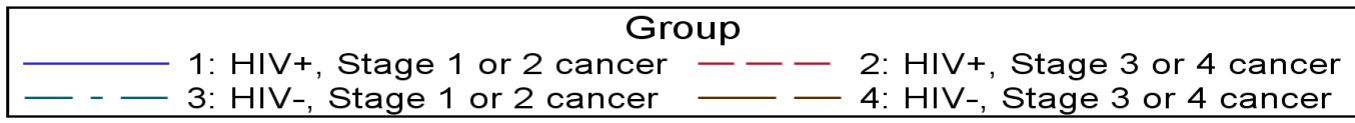


2016

Survival Probability



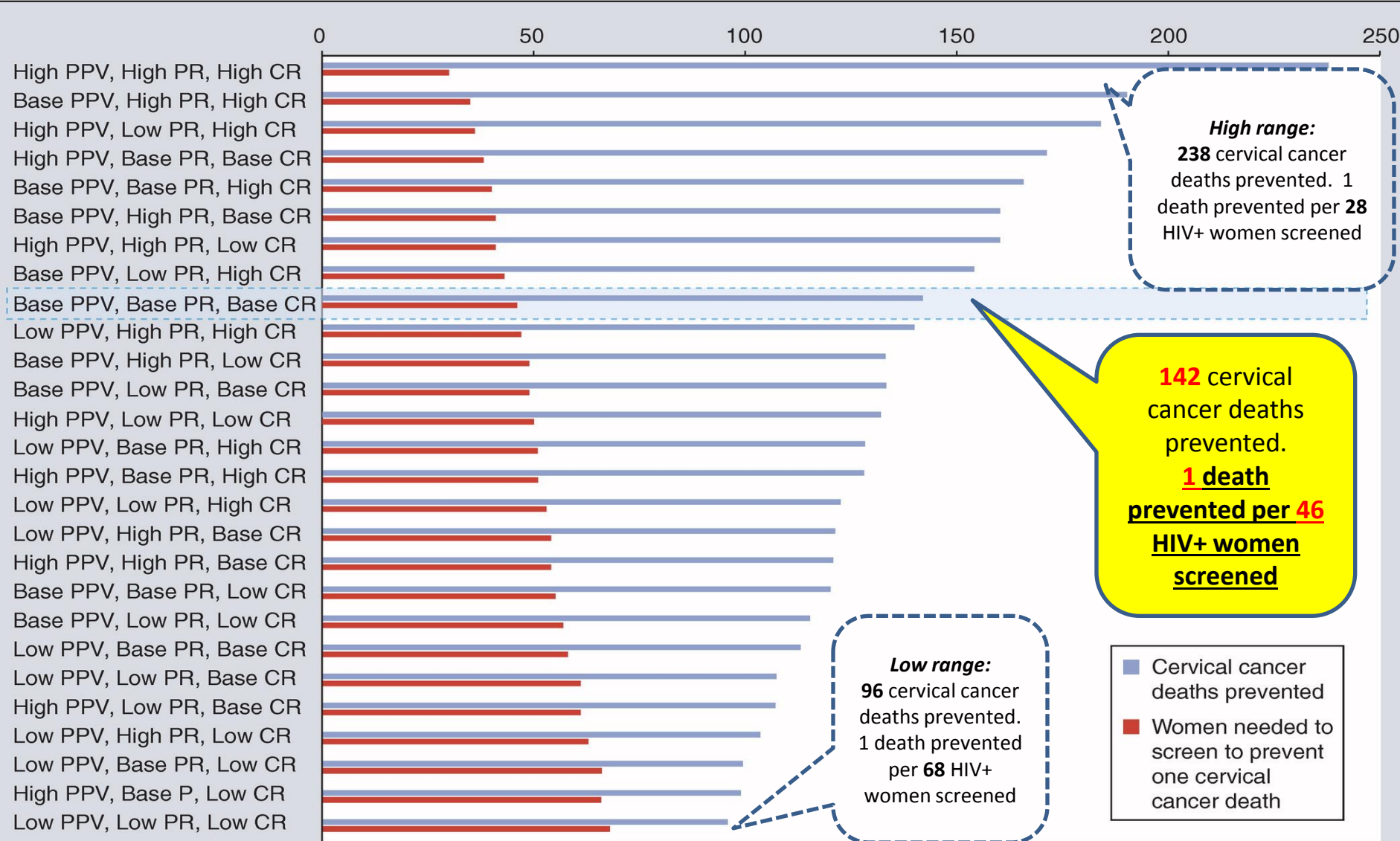
Months	Group 1	Group 2	Group 3	Group 4
0	74	74	74	74
6	48	48	48	48
12	26	26	26	26
18	14	14	14	14
24	2	2	2	2
30	0	1	1	1
36	0	0	1	0



# Sensitivity /Specificity

	CIN2+ (N=310)		CIN3+ (N=102)	
	Sensitivity 95% CI	Specificity 95% CI	Sensitivity 95% CI	Specificity 95% CI
<b>Cytology</b>	<b>75.8%</b> <b>(70.8-80.8)</b>	<b>83.4%</b> <b>(80.9-85.9)</b>	<b>94.5%</b> <b>(89.8-99.2)</b>	<b>72.7%</b> <b>(70.0-75.3)</b>
<b>VIA</b>	<b>75.5%</b> <b>(70.5-80.4)</b>	<b>68.1%</b> <b>(65.0-71.3)</b>	<b>76.2%</b> <b>(67.9-84.5)</b>	<b>58.9%</b> <b>(56.0-61.9)</b>
<b>HPV</b>	<b>91.9%</b> <b>(88.5-95.3)</b>	<b>51.4%</b> <b>(48.0-54.8)</b>	<b>97.9%</b> <b>(95.0-100 )</b>	<b>42.8%</b> <b>(39.8-45.7)</b>

# HIV-infected women undergoing cervical cancer screening in Zambia Measuring Program Effectiveness



PR: Progression rate, CR: Cure Rates, PPV: Positive Predictive Value