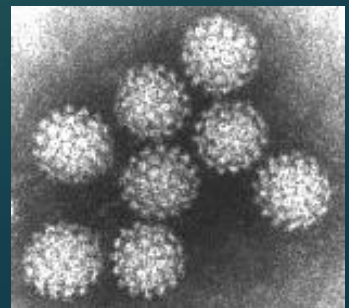


THE USE OF HUMAN PAPILLOMAVIRUS ONCOGENIC MRNA E6/E7 FOR CERVICAL CANCER SCREENING IN AN HIV INFECTED POPULATION

A DE MEYER

Human papillomavirus

- ▶ Small, non-enveloped dsDNA virus
- ▶ Commonest sexually transmitted infection
- ▶ Acquired at some time by \pm 80% of sexually active individuals
- ▶ Over 100 types described, of which:
 - ▶ \pm 40 infect the anogenital and oral epithelium
 - ▶ 90% of anogenital warts (condylomata) associated with HPV-6 & -11
 - ▶ 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 & 68 are considered high-risk for development of pre-malignant (CIN, AIN) and cancerous lesions
 - ▶ \pm 75% of cervical cancers associated with HPV-16 & -18



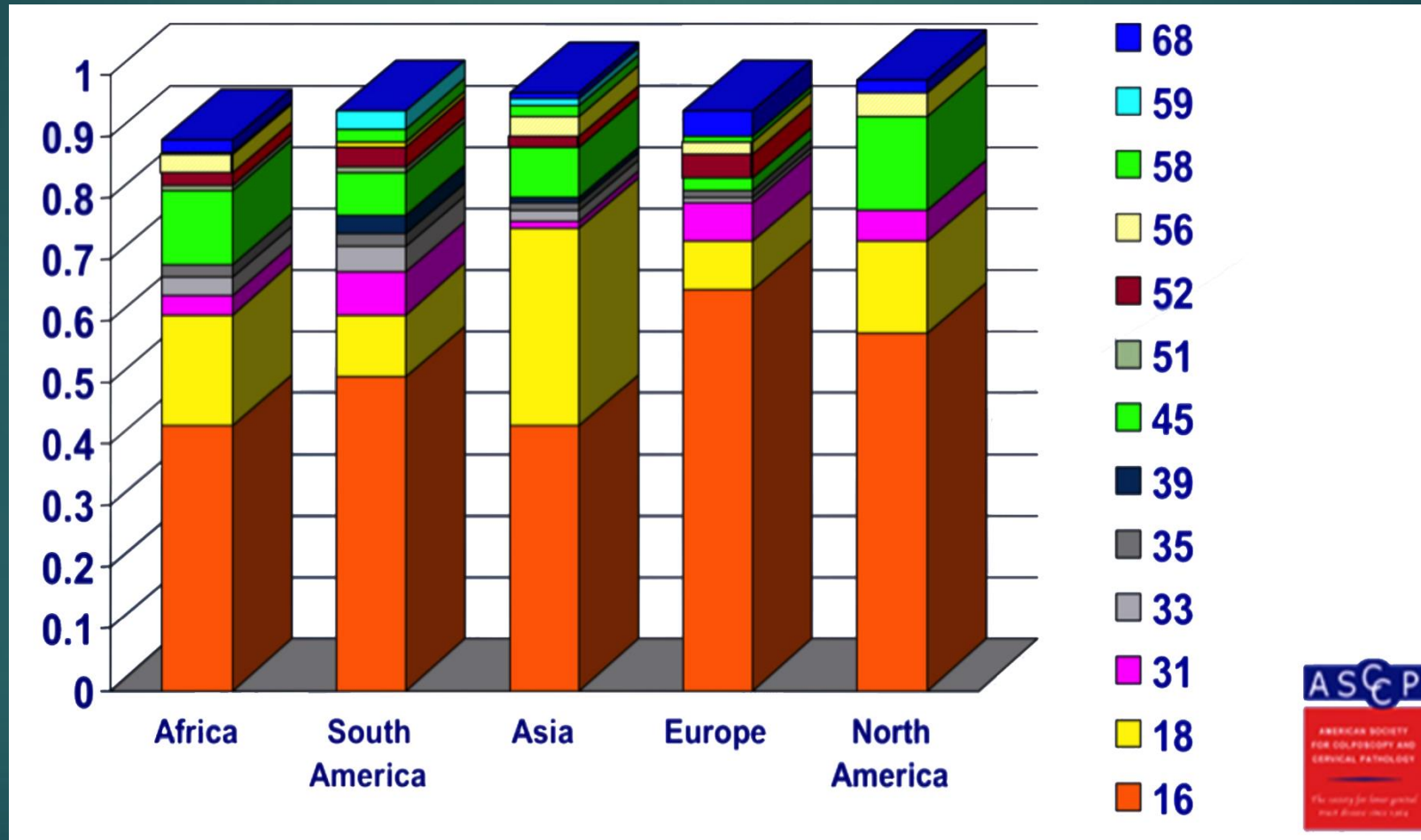
Epidemiology

- ▶ Greatest risk of acquisition 1st 5 yrs after debut
- ▶ Prevalence of HPV peaks in the mid-20's and declines after 30 years of age in heterosexual women and men
- ▶ Infection multicentric → genital and anal infection frequently co-exist
- ▶ Most HPV infections are transient → 10% will become persistent → 1% will develop clinical lesions (HSIL) that may progress to cervical cancer (average 15 – 20 years)
- ▶ Most HPV infections are transient and most people are able to clear the virus by an effective immune response.
- ▶ Infection lasts a mean of 13.5 months for high-risk HPVs and 4.8 months for low-risk types.

Epidemiology

- ▶ Cervical cancer is the 3rd most common type of cancer amongst women worldwide
- ▶ Globally > 500 000 new cases of cervical cancer and 275 000 deaths each year
 - ▶ Incidence rates: 1 – 50 / 100 000 women
- ▶ Cervical cancer incidence: USA: 7.8; sub-Saharan Africa > 40

Most Common HPV Types in Cervical Cancer

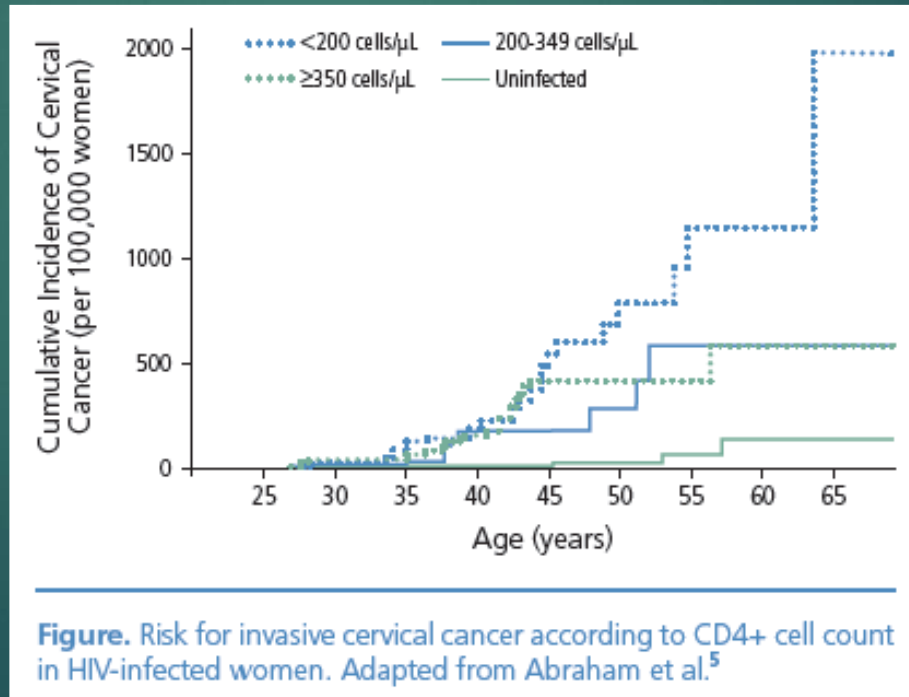


HPV in people with HIV

- ▶ Less efficient immune control
- ▶ HPV persists for longer
- ▶ Multiple HPV types often detected
- ▶ Lower rates of spontaneous regression
- ▶ Cytological abnormalities (LSIL & HSIL) more common
- ▶ Rates of progression more rapid
- ▶ Higher rates of persistent or recurrent infection following treatment

HPV in people with HIV

- ▶ Risk of detecting HPV DNA in cervical and anal cells, as well as finding cytological changes is inversely proportional to the CD4 cell count



Objectives

- ▶ Comparative evaluation of DNA L1 vs RNA E6/E7 HPV assay for screening HIV- infected individuals
- ▶ Longitudinal evaluation of mRNA clinical utility in an HIV-infected population

Design

- ▶ Western Cape Tygerberg Hospital Infectious Diseases Clinic (IDC)
- ▶ Enrolment of 300 HIV-infected women >18 years to < 60 years of age
- ▶ Half were on Antiretroviral therapy, half were not based on CD4 values
- ▶ Followed the cohort for 3 years (2010-2013)
- ▶ For molecular – ThinPrep at -20 degrees

Pathology tests

- ▶ Conventional Cytology every 6 months screened at NHLS
- ▶ ThinPrep PreservCyt liquid-based cytology specimen from initial visit, evaluated with:
 - ▶ Hologic AHPV
 - ▶ Roche Linear Array assay (DNA)
- ▶ Histology Data available for any biopsies taken

Cytology quality in Western Cape

	Polo	DGM	TAD	BRM	Univ	Grey's	IALCH	Mth	EL	PE	TBH	GSH
%Adeq	37	56.6	52.3	67.3	54.6	44.4	33.5	57.1	48.4	64.3	79.3	74.9
%U/s	1.6	0	0.5	1.7	6.1	3	2.2	1.5	0.7	2.2	1.5	2.6

2005-2013

Results DNA & RNA

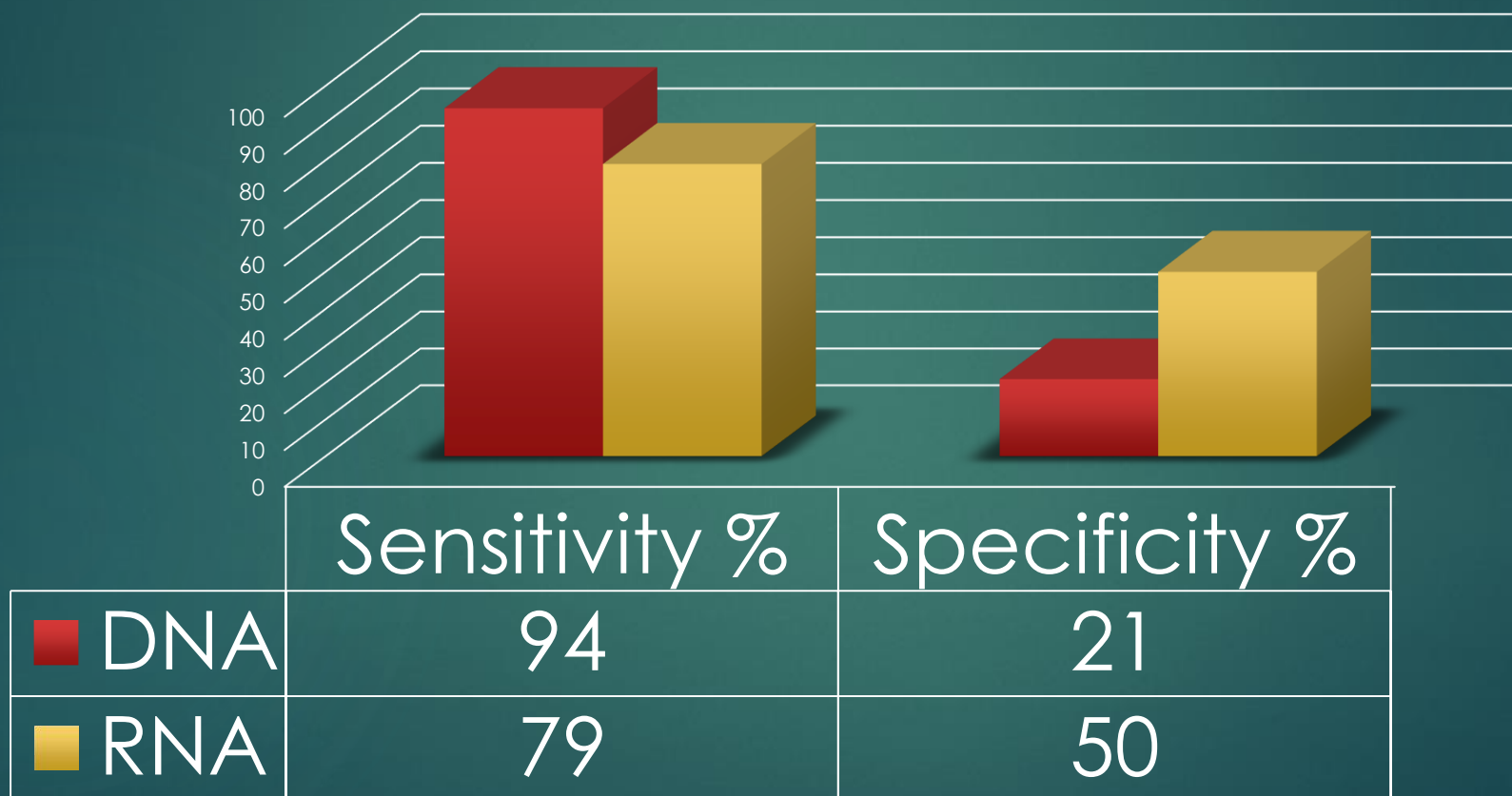
1st vist	AGUS	ASCUS	LSIL	Normal	HSIL	Total 1st visits
DNA postive	0	14	117	81	52	264
DNA Negative	1	0	11	22	0	34
						298

Prevalence HPV DNA pos: 89%

1st vist	AGUS	ASCUS	LSIL	Normal	HSIL	Total 1st visits
RNA positive		6	90	48	54	198
RNA negative		5	32	48	2	87
						285

Prevalence HPV RNA pos: 69%

Results DNA vs RNA



Cut-off : NILM vs non-NILM

Conclusion

- These results support the use of HPV mRNA as an effective solution for cancer screening of women that are HIV- infected.
- HPV mRNA showed a good sensitivity for high grade lesions positive by cytology combined with a much better specificity.
- The extremely high prevalence of DNA positivity makes DNA testing a clinically non-realistic option in this population.

Next Steps

- ▶ STI analysis :Chlamydia Trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis
- ▶ HIV Viral load in cervix compartment
- ▶ Analysis of the cohort and linkage with real clinical outcome will be performed.
- ▶ Longitudinal analysis of cohort

Thank You

