

Cervical cancer and HPV Associated disease in HIV positive women

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HIV and Cervical Cancer

- Studies have shown that among HIV positive women consistently higher incidence of*:
 - HPV infection
 - Persistent HPV infection with high risk types
 - Infection with multiple types HPV
 - Cervical cancer precursors (CIN or SIL)
 - Greater failure rate of treatment
 - Cervical cancer
- Invasive cancer of the cervix proclaimed an AIDS-defining illness in 1993 (CDC)

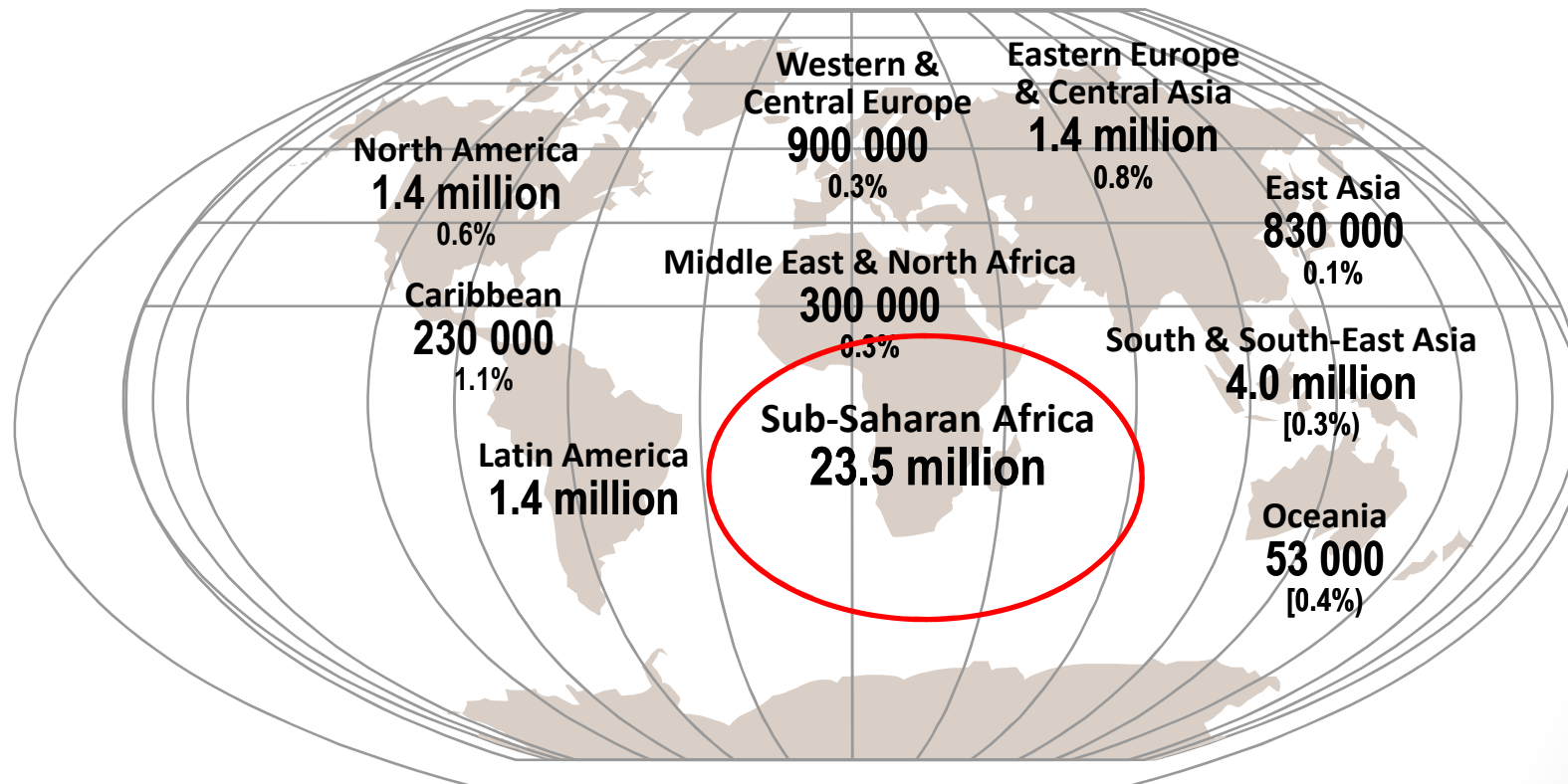
*Smith-McCune, K.K. et al. PLoS One, 2010. **5**(4): p. e10094, Averbach, S.H. et al. AIDS, 2010. **24**(7): p. 1035-42.
Low, A.J. et al. BMC Infect Dis. **11**: 20 – 26, Veldhuijzen, N.J. et al. AIDS, 2010. **24**(14): p. 2289-92,
Avert, B. et al. Infect Dis Obstet Gynecol, 2011: p. 692012

Global Estimates of HIV for Adults and Children 2009 and New Infections and Deaths in 2011*

- People living with HIV 33.3 million
 - Adults 30.8 million
 - **Women 15.9 million**
 - Children < 15 years 2.5 million
- New HIV infections 2011 2.6 million
- Deaths due to AIDS 2011 1.8 million

* Source: www.unaids.org UNAIDS Report on the Global AIDS Epidemic, 2010

Adults and children estimated to be living with HIV, 2011*



Total: 34 million (31.4 – 35.9 million)



*UNAIDS Global Report 2012

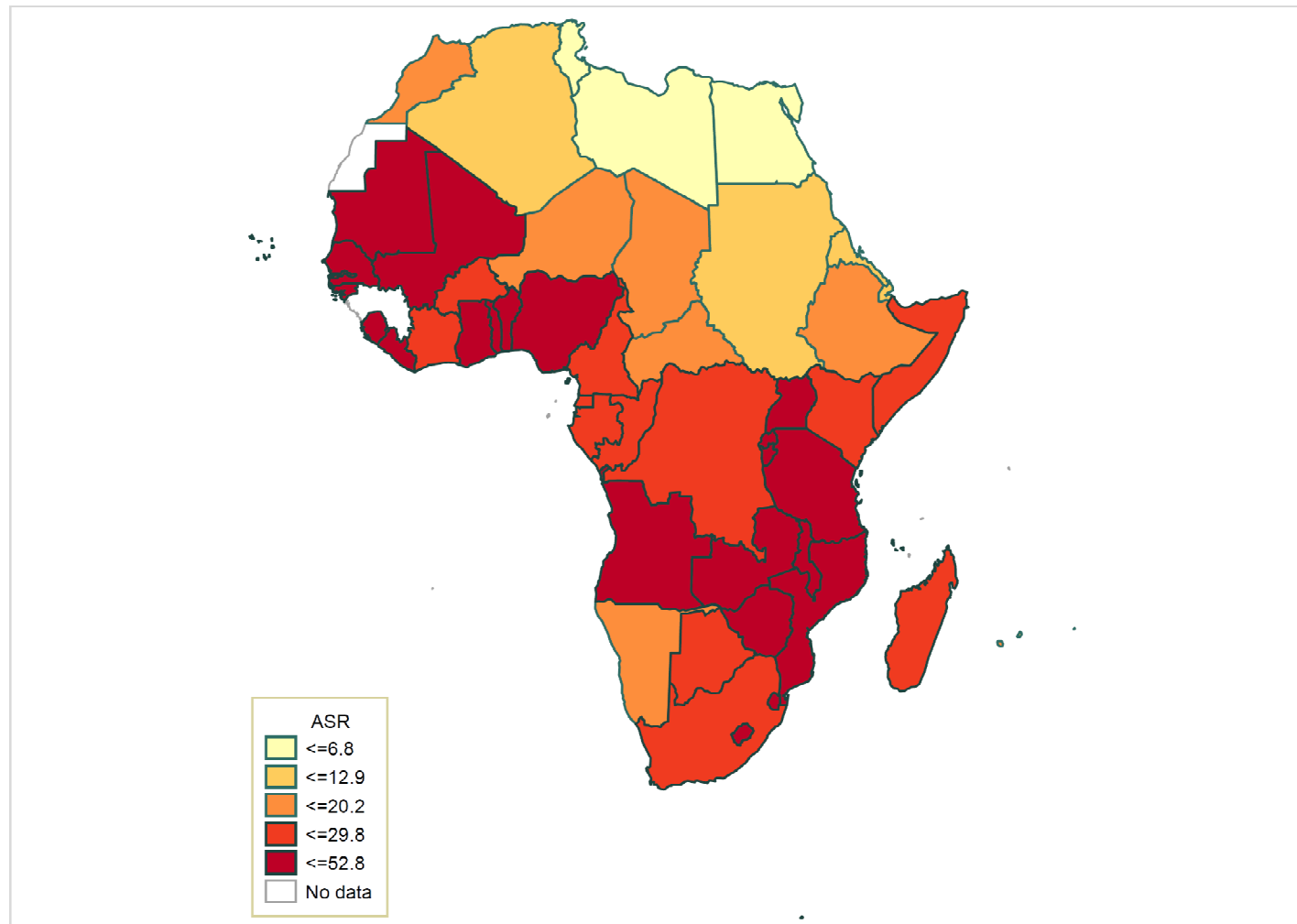
Sub-Saharan Africa AIDS statistics

- Epidemic in SSA varies considerably with Southern Africa the most severely affected
- Southern Africa in **2009**
 - 11.3 million people living with HIV
 - 34% of people living with HIV resided in the 10 countries of Southern Africa
 - 31% of new infections and 34% of AIDS-related deaths documented
 - 40% of all adult women living with HIV live in Southern Africa
- 5.6 m people living with HIV live in South Africa – largest proportion in the world

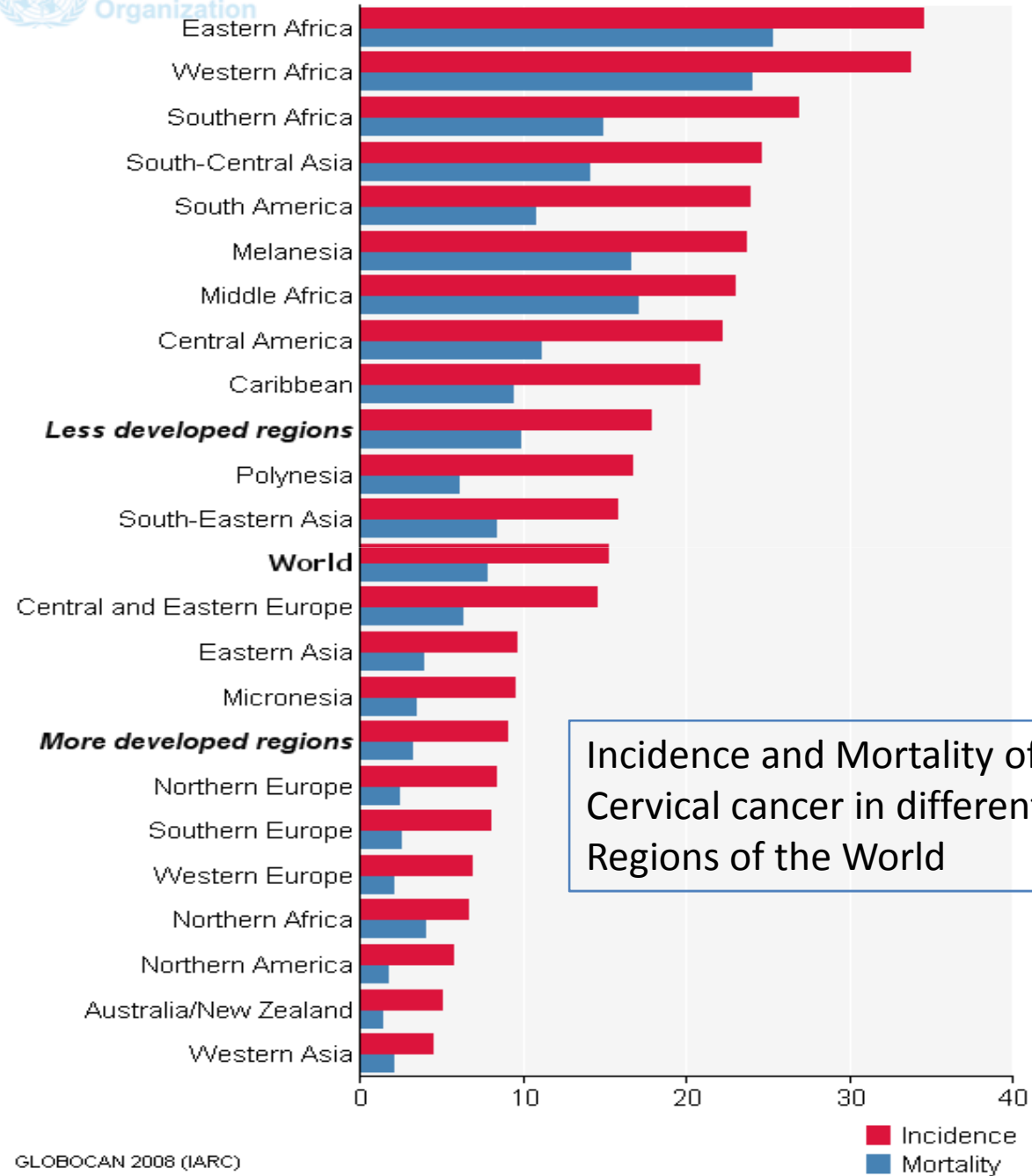
Cervical Cancer

- Worldwide per year
 - 2.3 million prevalent cases
 - 500 000 new cases
 - 250 000 deaths
- 80% of new cases and deaths
- Less than 5% of global cancer resources
- Disease of *inequity of access* to health care

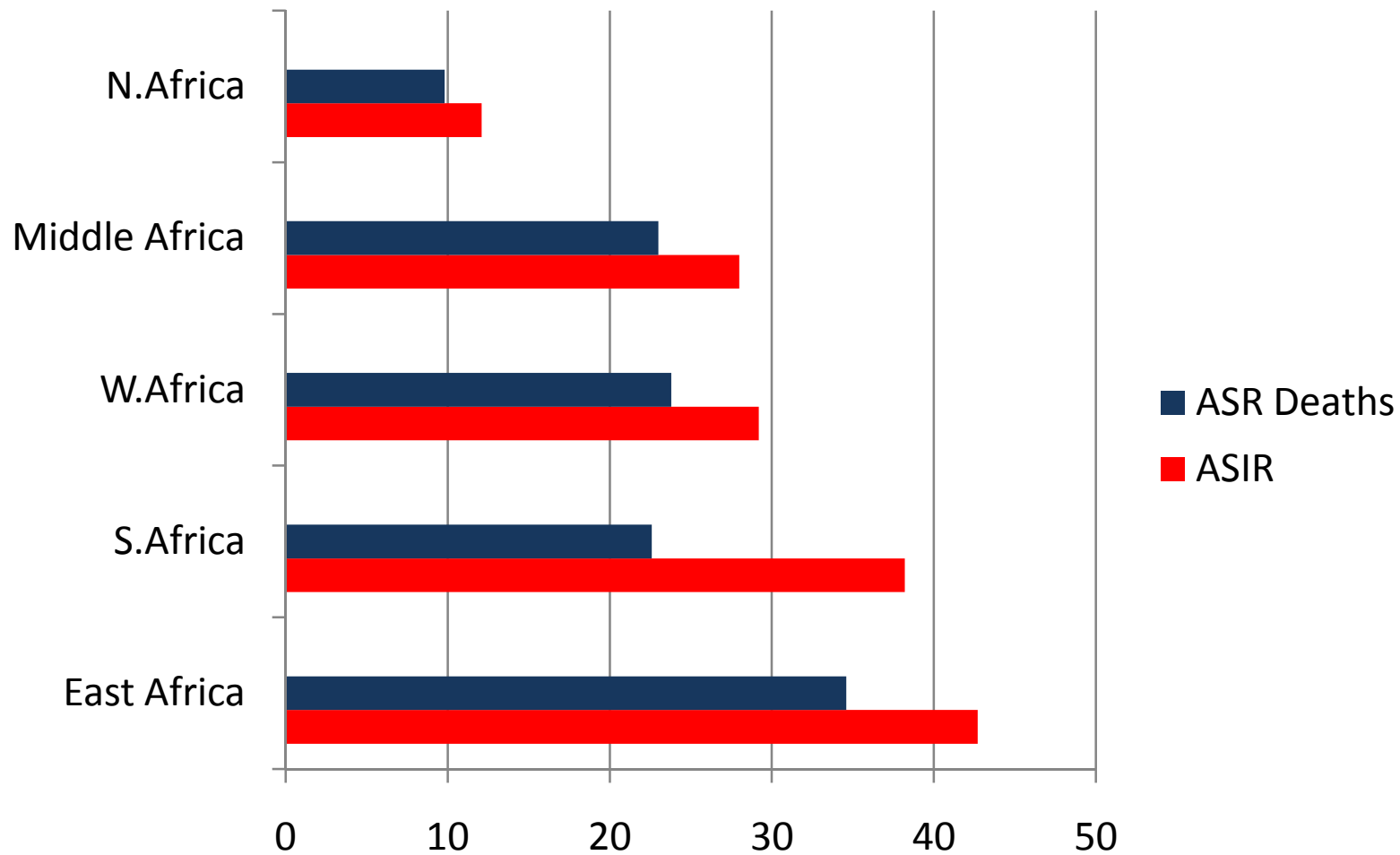
ASIR of cervical cancer in Africa*



*Globocan 2008



ASIR and ASR of Deaths from Cervical cancer per 100 000 in different regions of Africa



Cervical cancer in HIV positive women

Source	No. women with HIV/cervical cancer	RR, OR or SIR
Frisch et al (2000)* USA	355 cases cervix cancer	RR 5.4 (95% CI 3.9 – 7.2) Match cancer and AIDS registers
Tanon et al (2012)^ Benin/Cote d'Ivoire	152 cases of cervical cancer	OR 7.9 (95% CI:3.8 – 16.7) multivariate analysis
Odida et al (2011)+ Uganda	55 women with ICC and 54 controls	OR 1.6 (95% CI:1.0 – 2.6) (adjusted for age and CD4 count)
Adjorlolo-Johnson et al (2010) Cote d'Ivoire#	132 with ICC/ 120 controls	OR 3.4 (95% CI:1.1 – 10.8) Logistic regression and in women positive for hr-HPV infection
Kahesa et al (2008)@ Tanzania	138 cases ICC/138 controls	OR 2.9 (95% CI: 1.4 – 5.9) Logistic regression analysis

*Frisch et al, J Natl Cancer Institute, 2000;92 (18):1500 -10; ^ Tanon et al PLOS one2012;7(10)e48108
+ Odida et al Infectious Agents and Cancer 2011;6:8-13; # Adjorlolo- Johnson et al BMC Infectious diseases 2010;10:242
@Kahesa et al. BMC Pubic Health 2008;8:262

Prevalence and incidence of HPV infection

- Meta-analysis* of 157 879 women with normal cytology (78 studies) who underwent HPV DNA testing and the prevalence of HPV estimated:

• Globally	10.4%
• Africa	22.1%
• Central America and Mexico	20.4%
• Northern America	11.3%
• Europe	8.1%
• Asia	8.0%

*Sanjose et al. Lancet Infect Dis 2007;7:453- 59

HPV Prevalence In HIV positive Women with Normal cytology*

Region	Number of Women	HPV prevalence (%)
Africa	489	56.6
Asia	238	31.1
Europe	340	32.4
North America	2039	31.4
South/Central America	124	57.3
All regions	3230	36.3

*Clifford et al AIDS 2006;20:2337- 44

HPV type distribution in SCC in women in Africa

	SCC n = 570 (%)*	SCC N = 2402 (%) ^	SCC N = 544 (%)+	SCC N = 410 (%) #
HPV 16	51.2	53.1	48.0	49.0
HPV 18	15.0	19.8	23.0	23.0
HPV 45	7.1	11	10.0	13.0
HPV 35	8.7	4.1	5.0	5.0

*Schmidt et al IPV Sept 2011 Abstract P32, ^ Guan et al. Int J Cancer 2012
+ de Sanjose et al. Lancet Oncol 2010 # Muwonge et al IPV 2010

HIV and Cervical Cancer Precursors

- Cytological diagnosis at baseline in 400 HIV positive women followed over 36 months in Cape Town*
 - LSIL 35%
 - HSIL 13%
 - ASC-US 7%
 - Normal 45%

Denny et al Obstet Gynecol 2008;111(6):1380 - 87

HPV Genotypes (Roche Reverse Line Blot Assay)

- Baseline HPV types (n = 397)
 - **HPV 16** **60 (15%)**
 - HPV 52 60 (15%)
 - HPV 53 59 (15%)
 - HPV 35 57 (14%)
 - **HPV 18** **44 (11%)**
- Number of HPV types:
 - One 27%
 - **Two** **21%**
 - **Three** **12%**
 - **Four** **10%**
 - Five and eight 8%

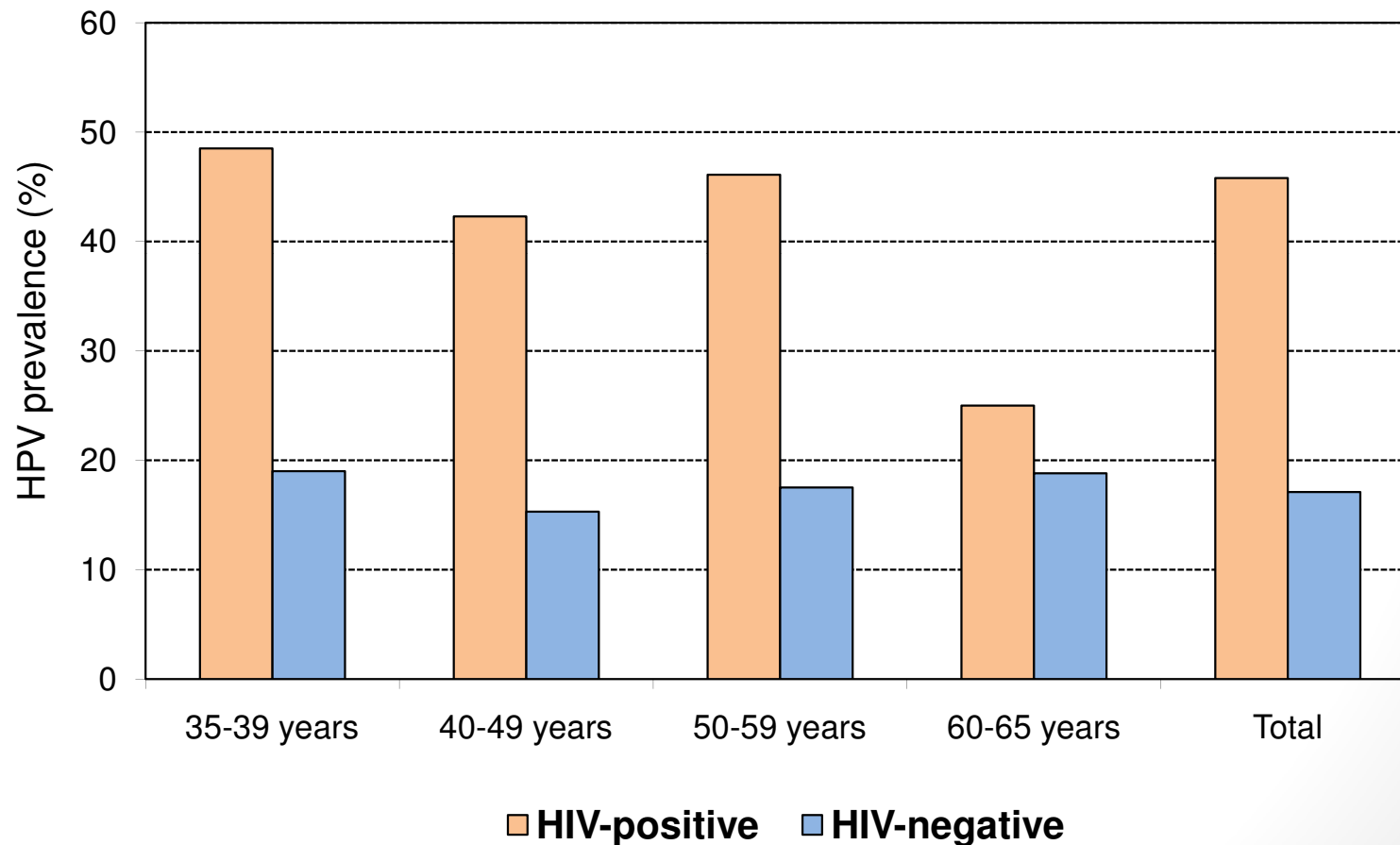
Strongly associated with Low CD4 count and high viral loads (p < 0.001)

Cape Town Screen and Treat Study

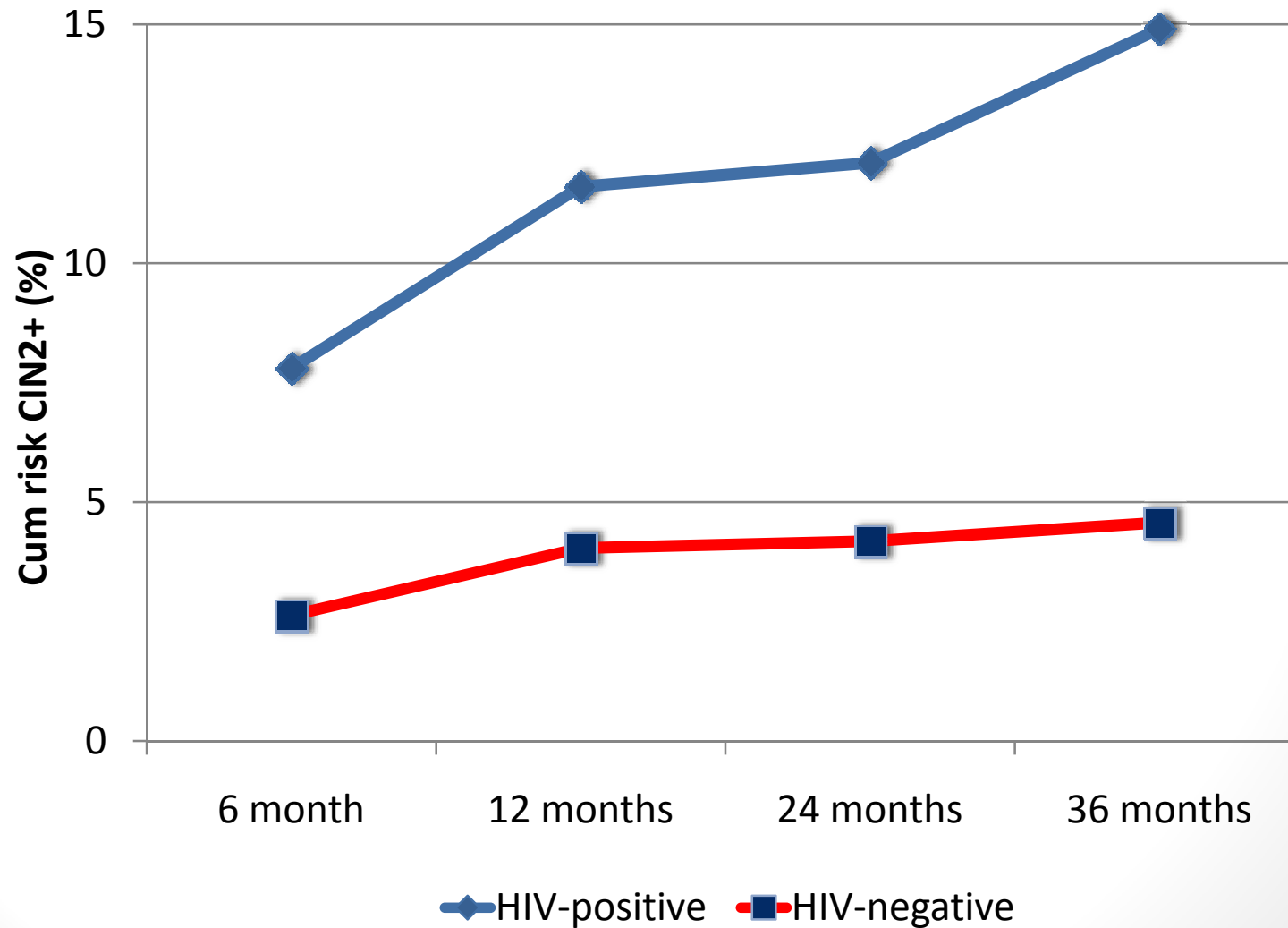
- Randomized clinical trial
- 6553 unscreened women 35-65 years in Cape Town, South Africa*
- 14% HIV-positive at baseline
- Comparison of HPV prevalence and CIN
 - 956 HIV-positive vs. 5596 negative women +

*Denny et al JAMA 2010

HR-HPV prevalence In HIV-positive and HIV-negative women



Risk of CIN2+ in HIV-positive And HIV-negative women



HPV infection attributable cancer in 2008 in Women and Men*

Site	No. of new cases 2008	Attributable to HPV (%)	No. attributable to HPV	Less Developed regions	More Developed regions
Cervix	530 000	100%	530 000	470 000	180 000
Vulva	27 000	43%	12 000	4 100	7 500
Vagina	13 000	70%	9 000	5 700	3 400
Anus	27 000	88%	24 000	12 000	12 000
Naso-pharynx	84 000	86%	72 000	66 000	5 900
Oro-pharynx	85 000	26%	22 000	6 400	15 000
Total			669 000	564 200	223 800

*de Martel et al. Lancet Oncol 2012, May 9th, 1 - 9

Ano-genital Cancers

- Proportion of anal cancers associated with HPV 16 or 18 is as high as the proportion associated with cervical cancer¹
- Incidence of anal cancer increasing by 2% per year among men and women in general population²
- Incidence highest in MSM and in HIV positive women/men³
- 7 fold increase in Penile cancer in HIV infected men⁴
- 60 fold increase in anal cancer in HIV infected men⁵
- High rates of genital warts in both men and women, often resistant to conventional therapies^{5,6}

¹Hoots BE, et al. Int J Cancer 2009;124:2375-83, ²Scholefield JH, et al Br J Surg 2005;92:1133- 36, Johnson et al, Cancer 2004;101:281 – 8, ³ Palefsky J, Curr Opin HIV AIDS 2009;4:52-6, ⁴Frisch M et al J Natl Cancer Instit 200;92:1500 – 10; ⁵Dolev et al AIDS 2008; 22:1213 – 19; ⁶De Panfilis et al Sex Trans Dis 2002; 29:121-25

Prevention of cervical cancer in HIV positive women

- Primary prevention
 - HPV Vaccination
 - Published studies on quadrivalent vaccine in three groups
 - Children 7 – 12 years old
 - Women older than 16 years
 - Men over age 18
 - Show vaccine is safe with no impact on HIV status in terms of CD4 cell count and HIV viral load
 - Immunogenic, although may be need for booster doses
 - Longer term follow up and efficacy data awaited

Prevention of cervical cancer in HIV positive women

- Secondary prevention
 - Cytology, HPV DNA testing and VIA
 - Followed by colposcopy
 - Infrastructure for secondary prevention not available in most SSA settings
 - Currently, due to PEPFAR funding ART available free in many countries but NOT cervical cancer screening
 - Linkage between the two not structurally integrated and women cannot afford to pay for screening and 'ecosystem' around screening e.g treatment, histology, follow up
 - As women live longer due to ART, scenario of increasing incidence of cervical cancer if no screening and linkage between the two virally-associated diseases not made

Conclusions

- HIV and cervix cancer worlds need to work together
- Ideal method of preventing cervical cancer in HIV positive women not fully defined
- Screen and treat or even prophylactic ablation of the transformation zone in HIV positive women likely to be effective however, more long term data required
- **Cervical cancer screening and prevention should be an integral part of chronic care package for HIV positive women**