



Malignancy in Myanmar with focus on cervical cancer

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Aim for today

- What are the types of cancer seen in HIV?
- What characteristics do ADM share/not share?
- Which ADM and NADM are common in Myanmar?
- Distinguishing HIV related cancers from OI's
- What is the relationship between HIV and cervical cancer?
- What characteristics do cervical cancer share/not share?

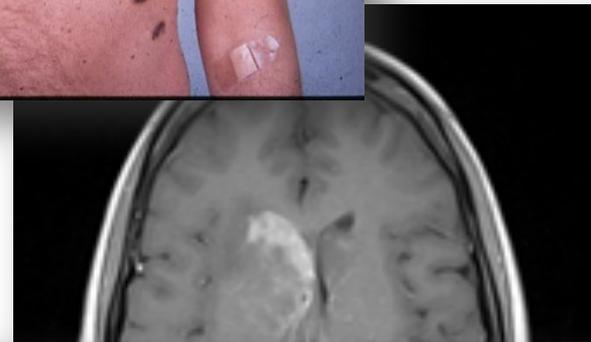




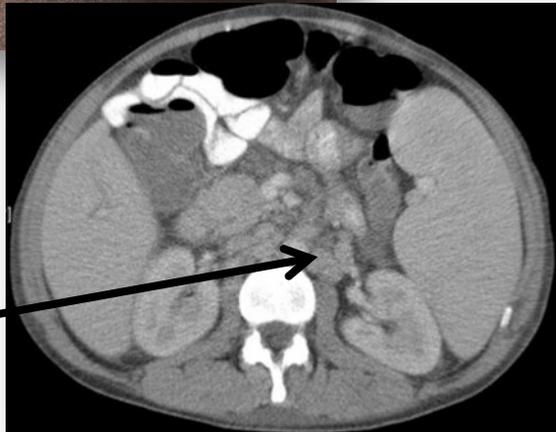
What are the types of cancers seen in HIV?

ADM and NADM

- AIDS-defining malignancies (ADM)
- Kaposi's sarcoma
- Non-Hodgkin lymphoma
- Primary CNS lymphoma
- Cervical cancer

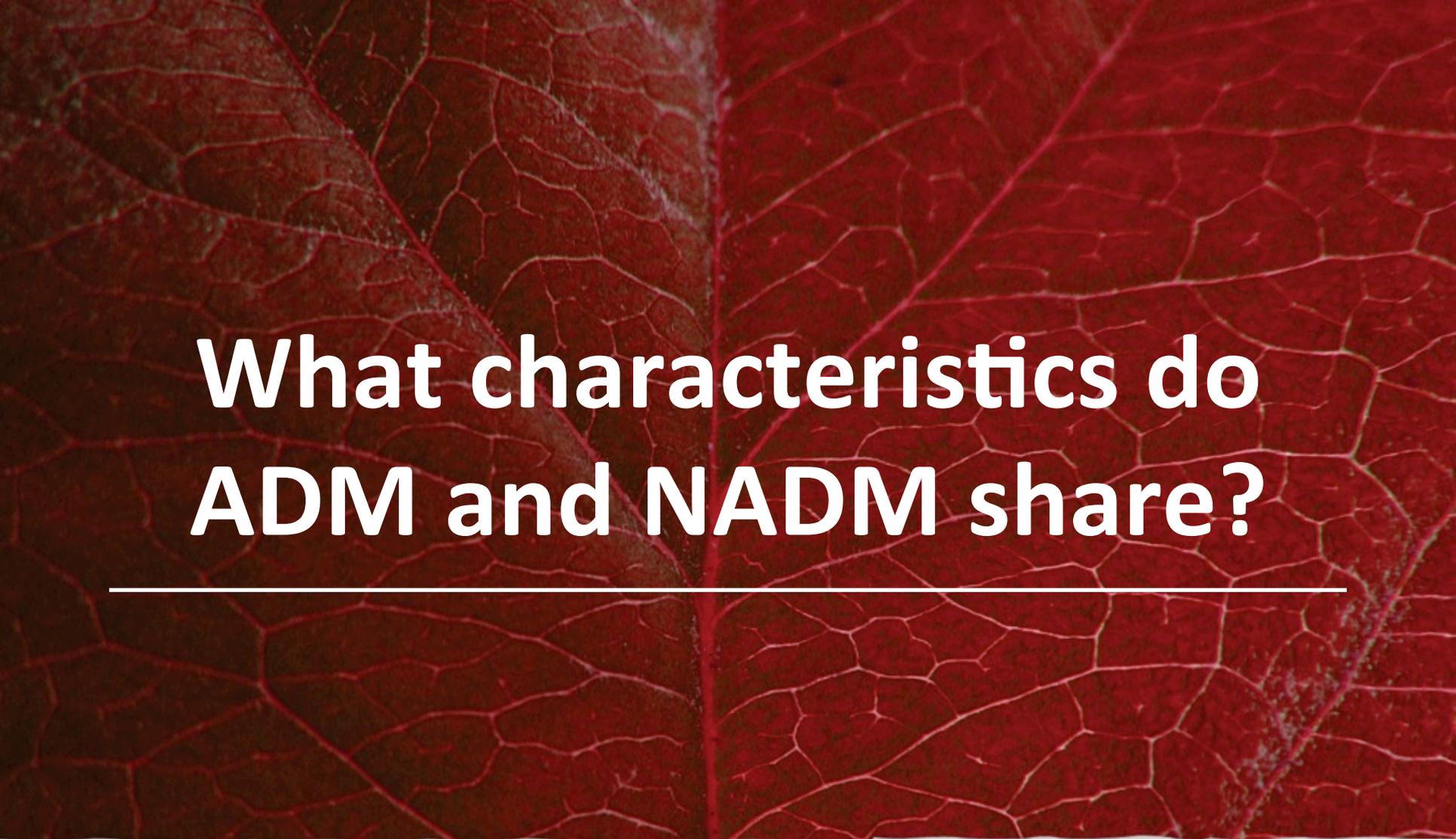


ADM and NADM



Non-AIDS defining malignancies (NADM)

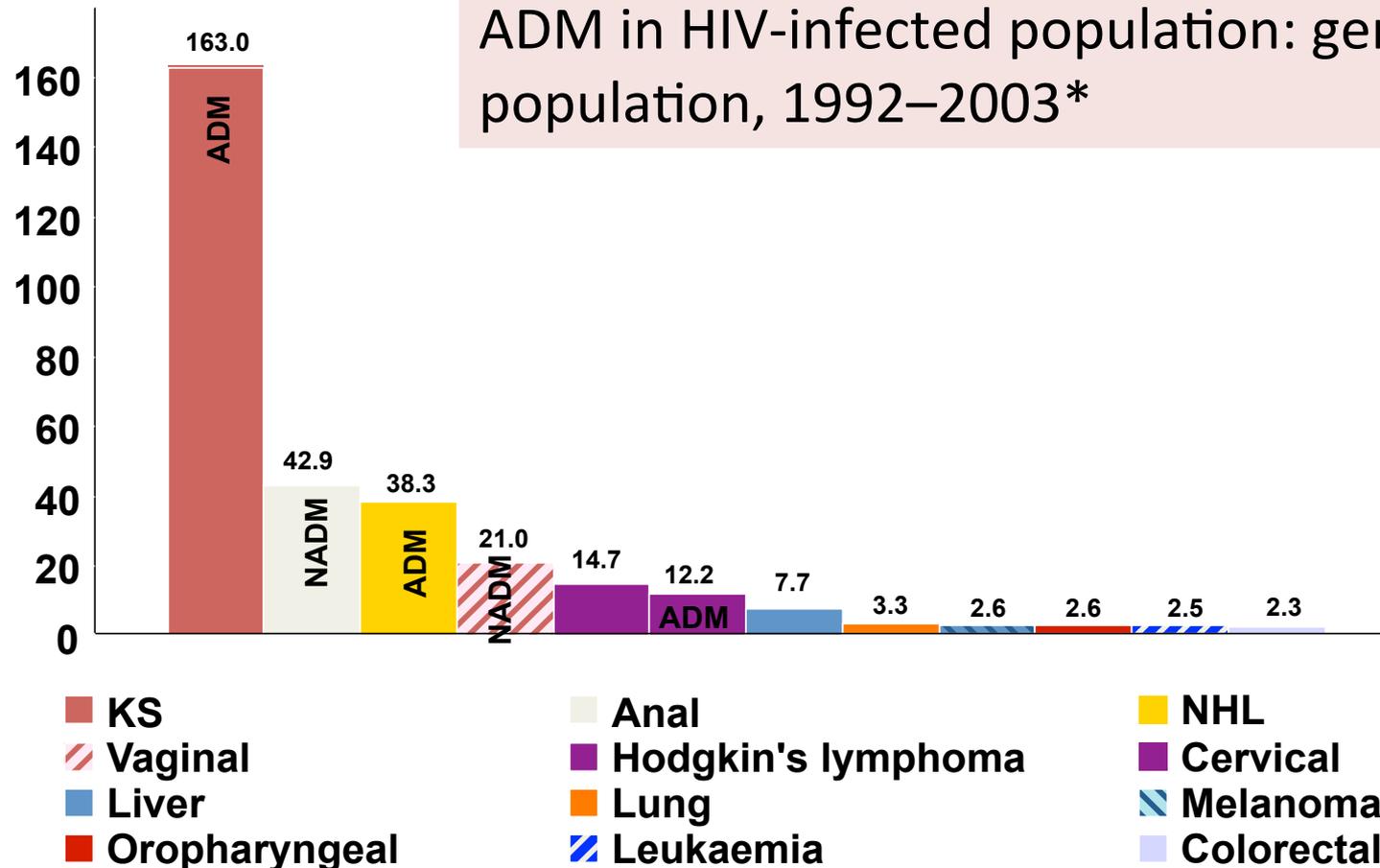
- Anal cancer
- Hodgkin disease
- Hepatoma
- Lung cancer
- Testicular cancer
- SCC conjunctiva, mucous membranes
- Many other sites..



**What characteristics do
ADM and NADM share?**

Both are more common in HIV than in non-HIV

Standardised rate ratio of ADM and non-ADM in HIV-infected population: general population, 1992–2003*



Both are associated with increasing rates with lower CD4 counts

Mortality rates by CD4 count in individuals with ADM and non-ADM

Latest CD4 count (/μL)	Person-years (py)	Non-ADM		ADM	
		Rate (/1000py) (n)	Relative risk*	Rate (/1000py) (n)	Relative risk*
<50	2335	6.0 (14)	15 (<0.001)	20.1 (47)	175 (<0.001)
50–99	2295	9.6 (22)	19 (<0.001)	4.8 (11)	41 (<0.001)
100–199	8097	6.8 (55)	10 (<0.001)	2.8 (23)	24 (<0.001)
200–349	21,048	2.0 (43)	3 (<0.001)	0.7 (14)	6 (<0.001)
350–499	24,052	1.1 (27)	2 (0.03)	0.3 (7)	3 (0.09)
500+	46,903	0.6 (27)	1 (–)	0.1 (5)	1 (–)

*Adjusted for cohort, age, gender, smoking status, weight, transmission group, ethnicity, prior non-fatal non-neoplastic AIDS, HCV and HBV status, cART exposure, and latest HIV-RNA level



Both are associated with oncogenic viruses

AIDS-Defining

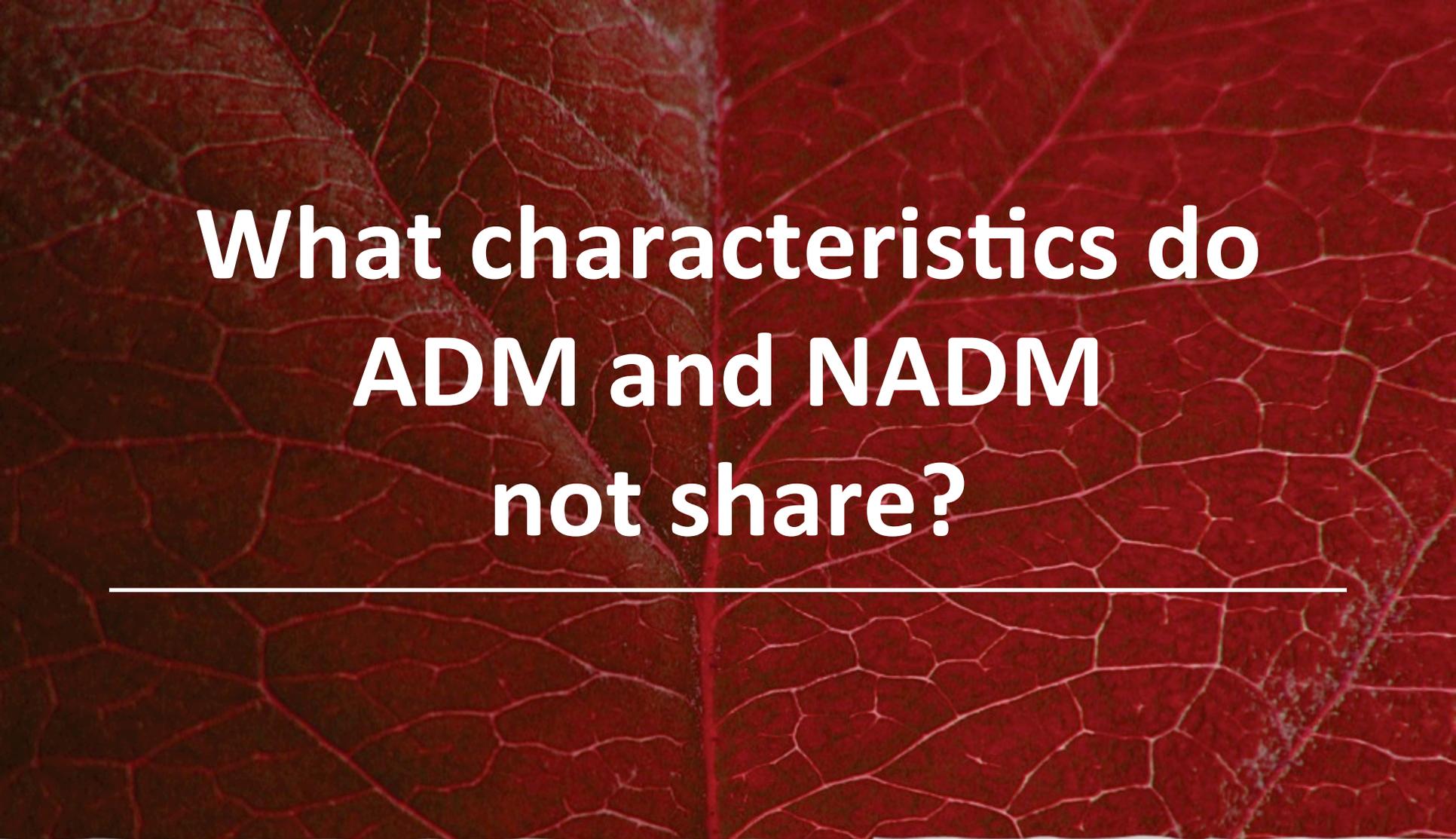
- Kaposi's Sarcoma
- Non-Hodgkin's Lymphoma
- PCNSL
- Invasive Cervical Carcinoma

Oncogenic virus

- HHV-8
- EBV, HHV-8
- EBV
- HPV

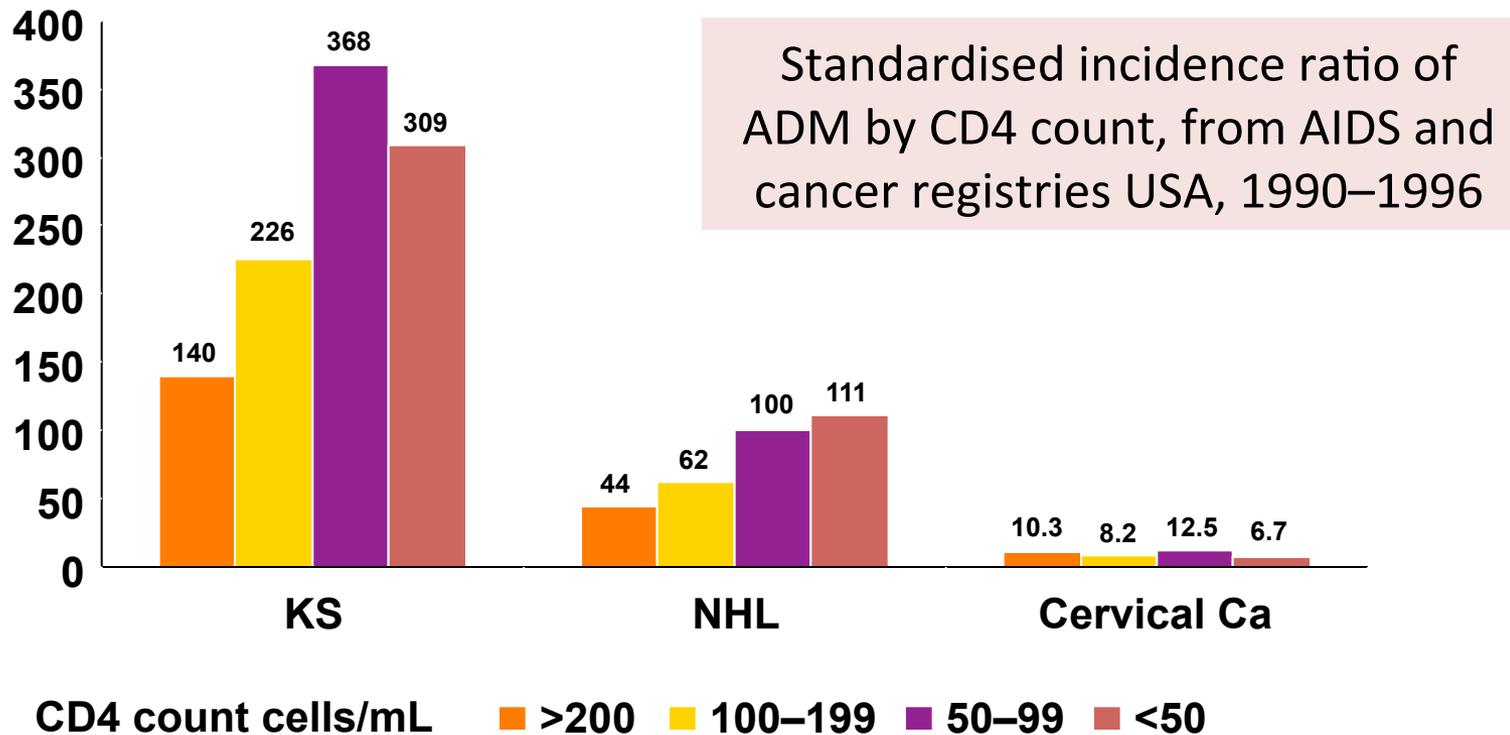
Non-AIDS Defining (e.g.)

- Anogenital cancers HPV
- Hodgkin's Disease EBV
- Leiomyosarcoma (pediatric) EBV
- Squamous Conjunctival Carcinoma HPV
- oesophagus, larynx, lip
- Hepatoma HBV, HCV

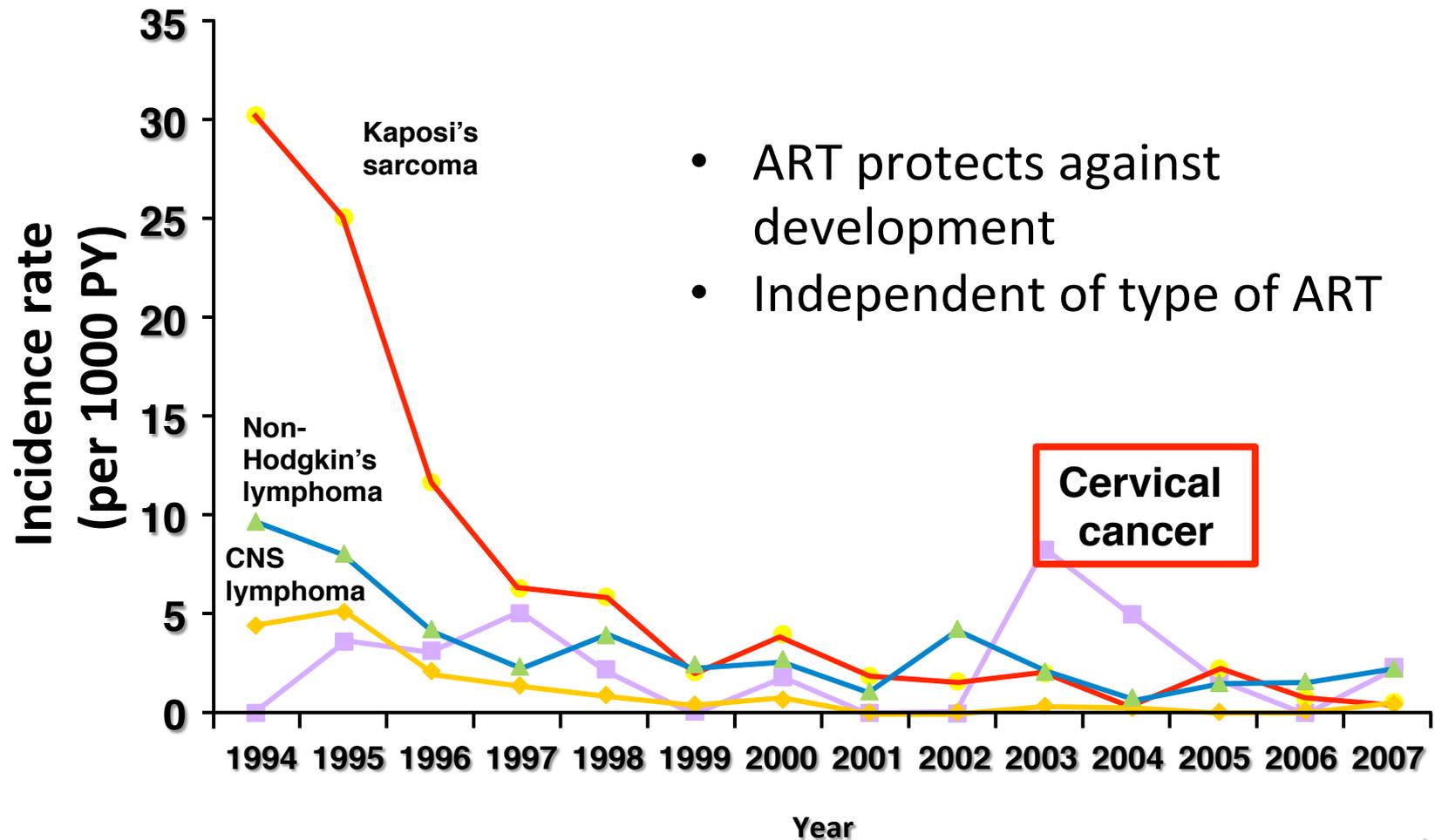


**What characteristics do
ADM and NADM
not share?**

For ADM the absolute risk is greater and varies more by type and CD4 count



ADM incidence has fallen sharply with use of ART

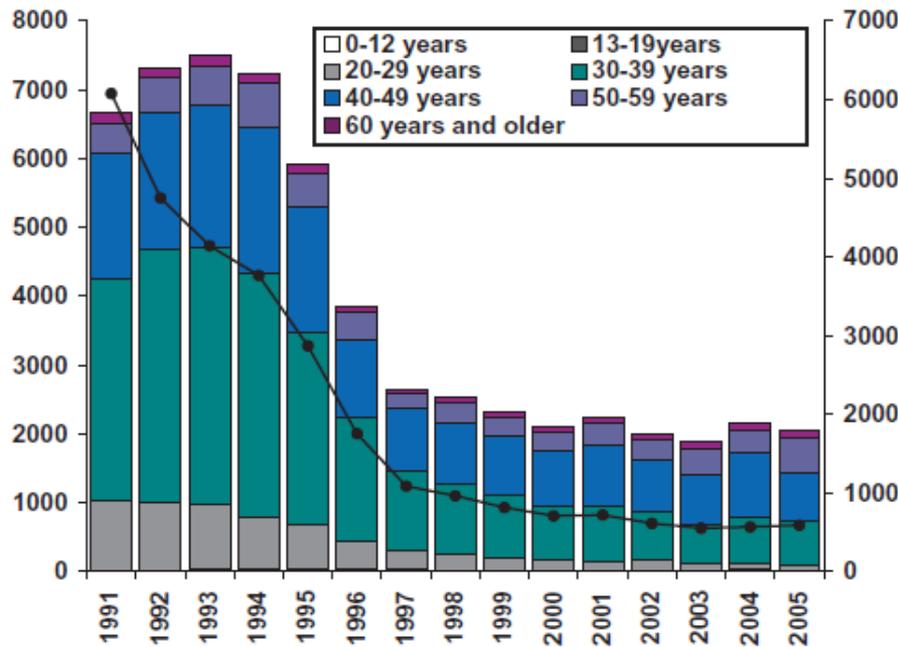


- ART protects against development
- Independent of type of ART

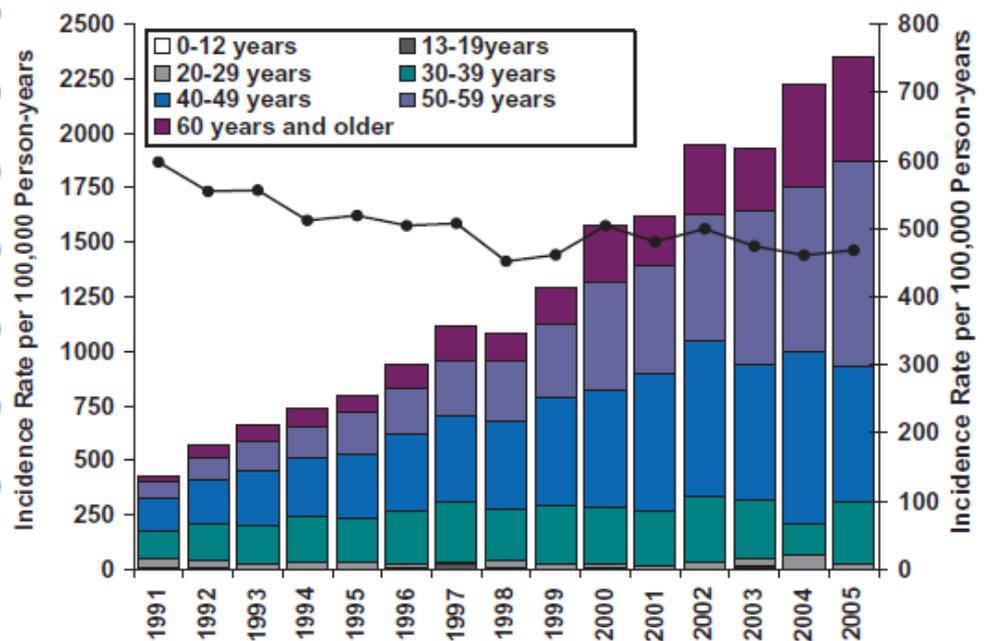
NADM incidence has increased as ADM has decreased (USA 1991-2005)

HIV-AIDS cancer match study USA

AIDS-defining malignancy



Non-AIDS-defining malignancy

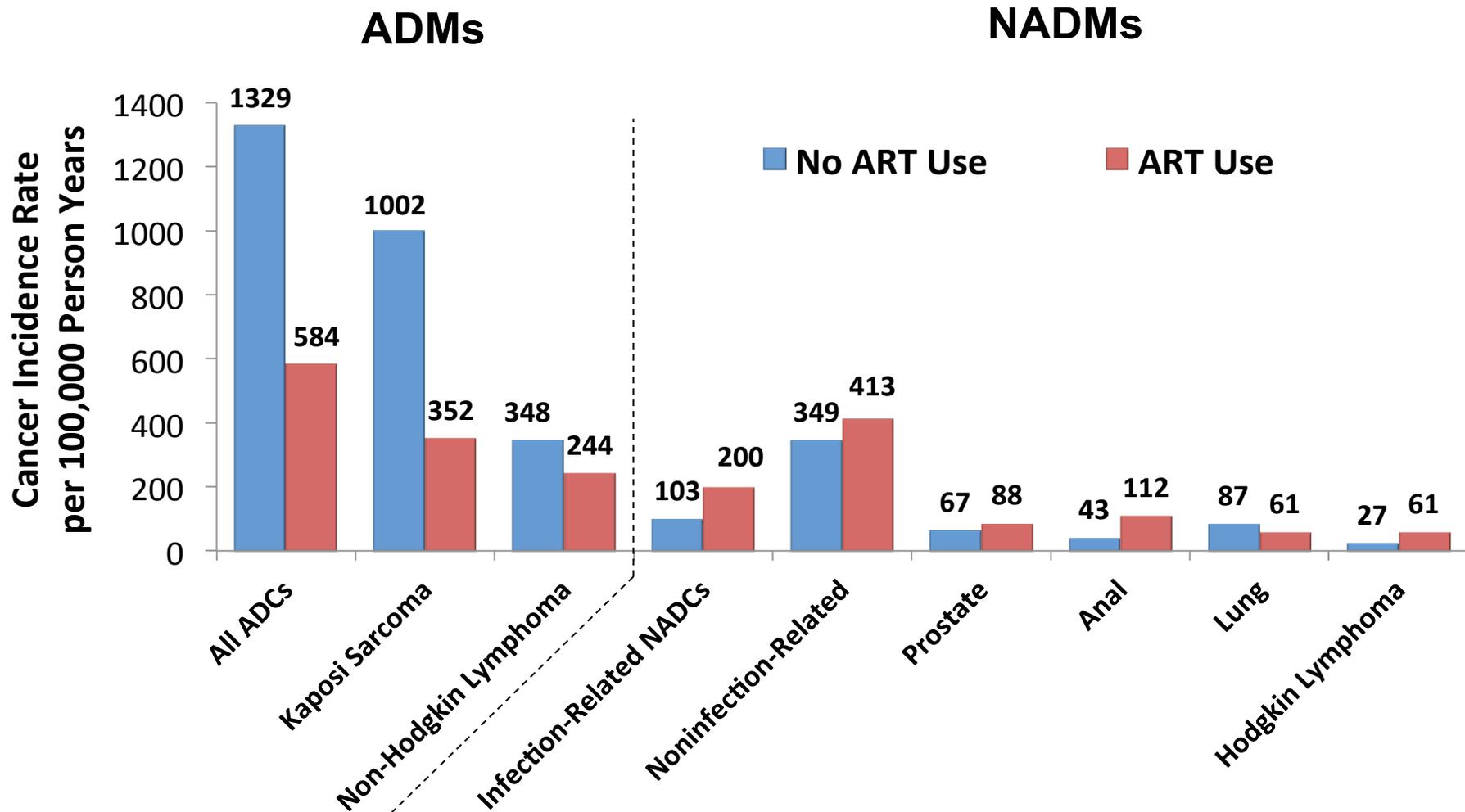


Factors Contributing to the Increase in NADM cases in HIV

- 4-fold increase in HIV/AIDS Population
- Patients living longer and not dying of OI
- Rising proportion of HIV pts > 50 yo
- Cancer incidence increases with age
- Greater and earlier start to smoking in HIV
- Increase in some CA incidence rate among HIV
 - Lung (3X), anal (29X), liver (3X), HL (13X)
 - Suggests may be additional risk from HIV



ART reduced the incidence of ADM but not NADM

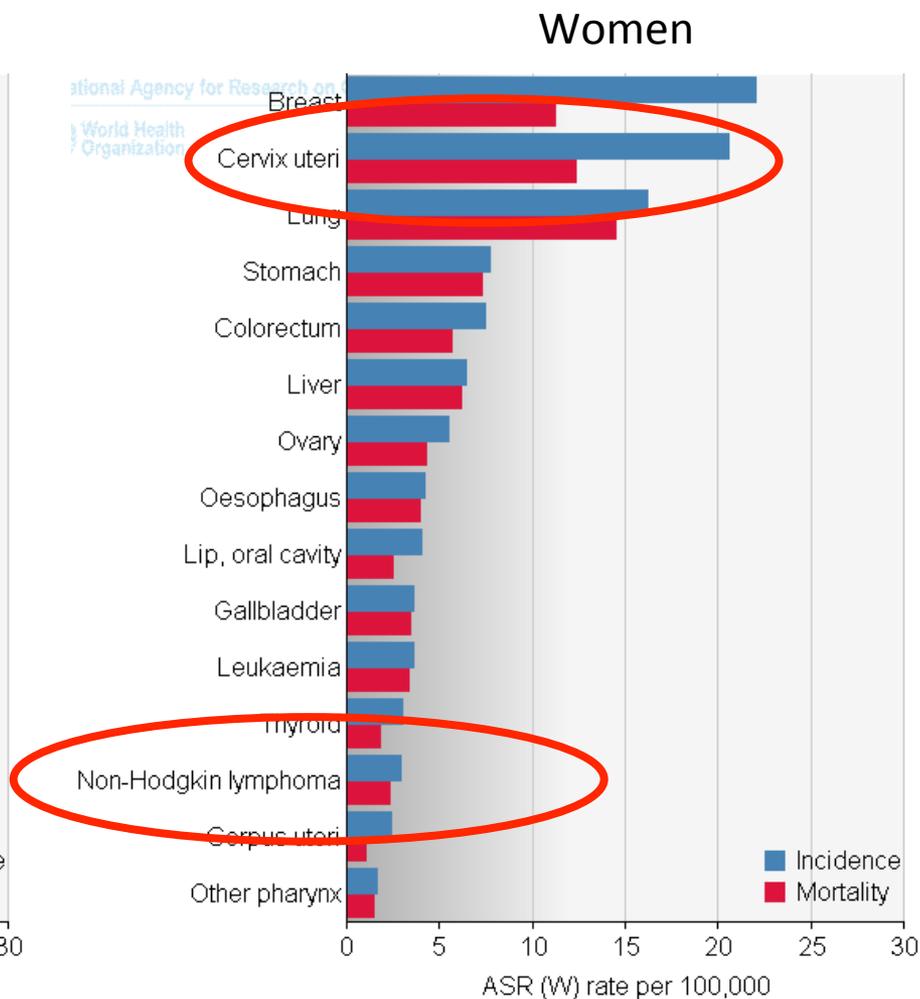
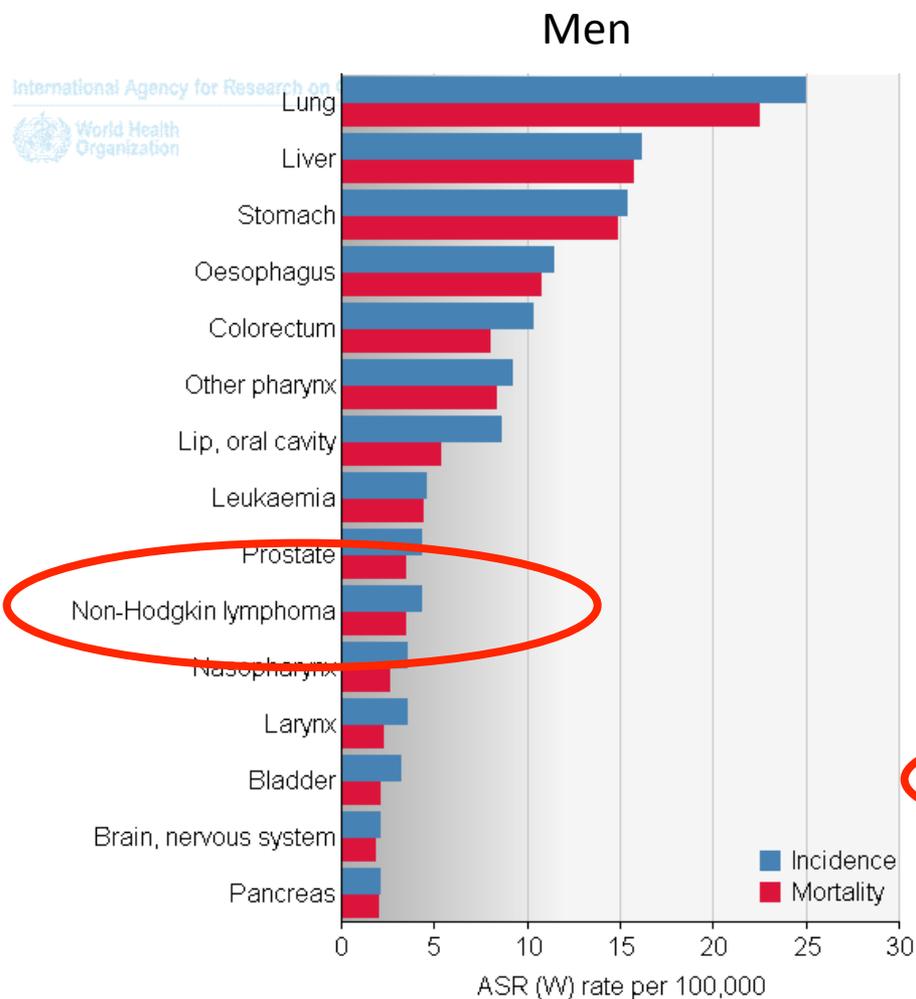


Crude Incidence Rates of Cancer Among 20,775 HIV-Positive Patients Enrolled in Kaiser Permanente California (1996-2008), by ART Use Status



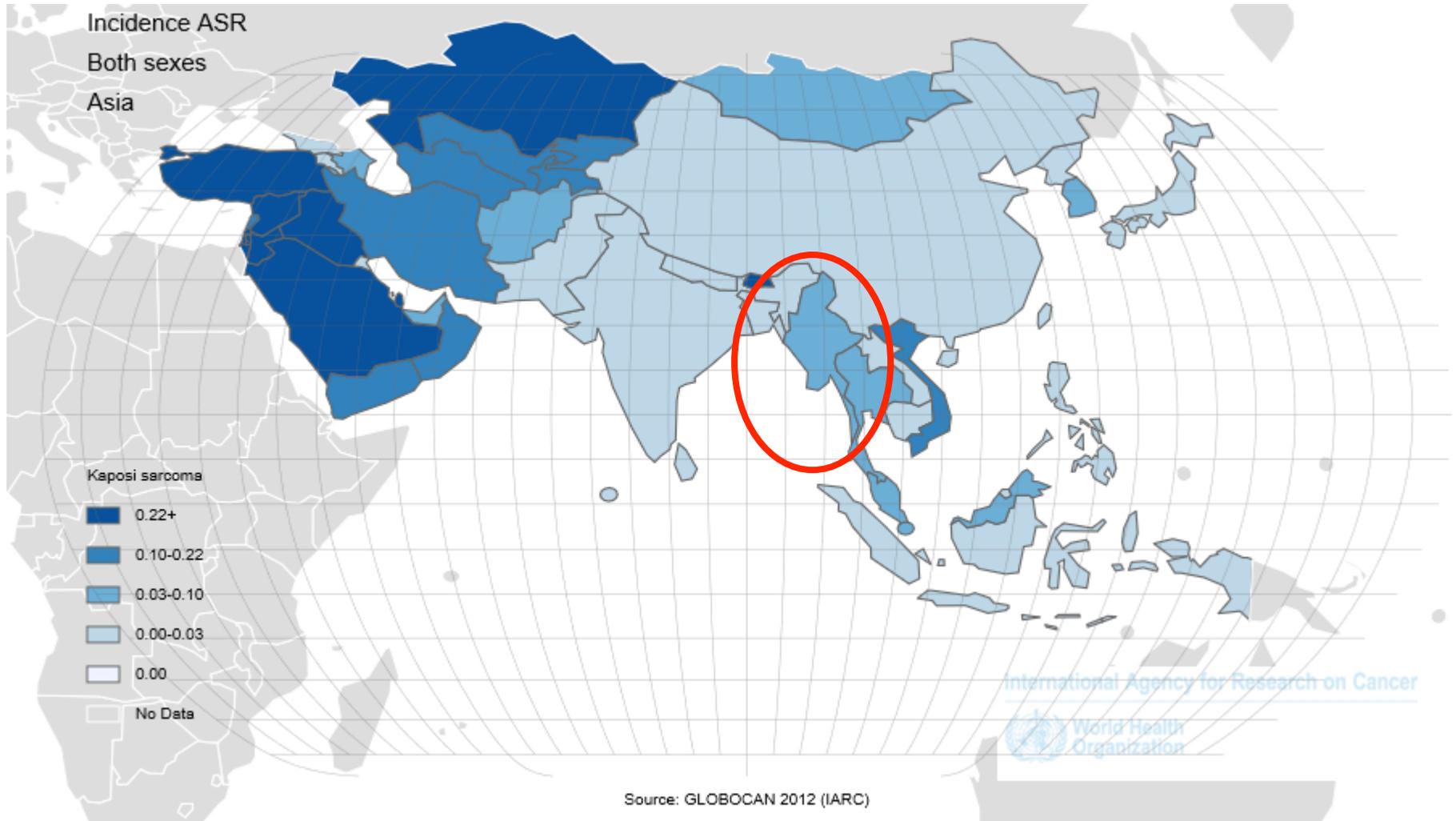
Which ADM are common in Myanmar?

Myanmar: age standard incidence cancer and mortality rates



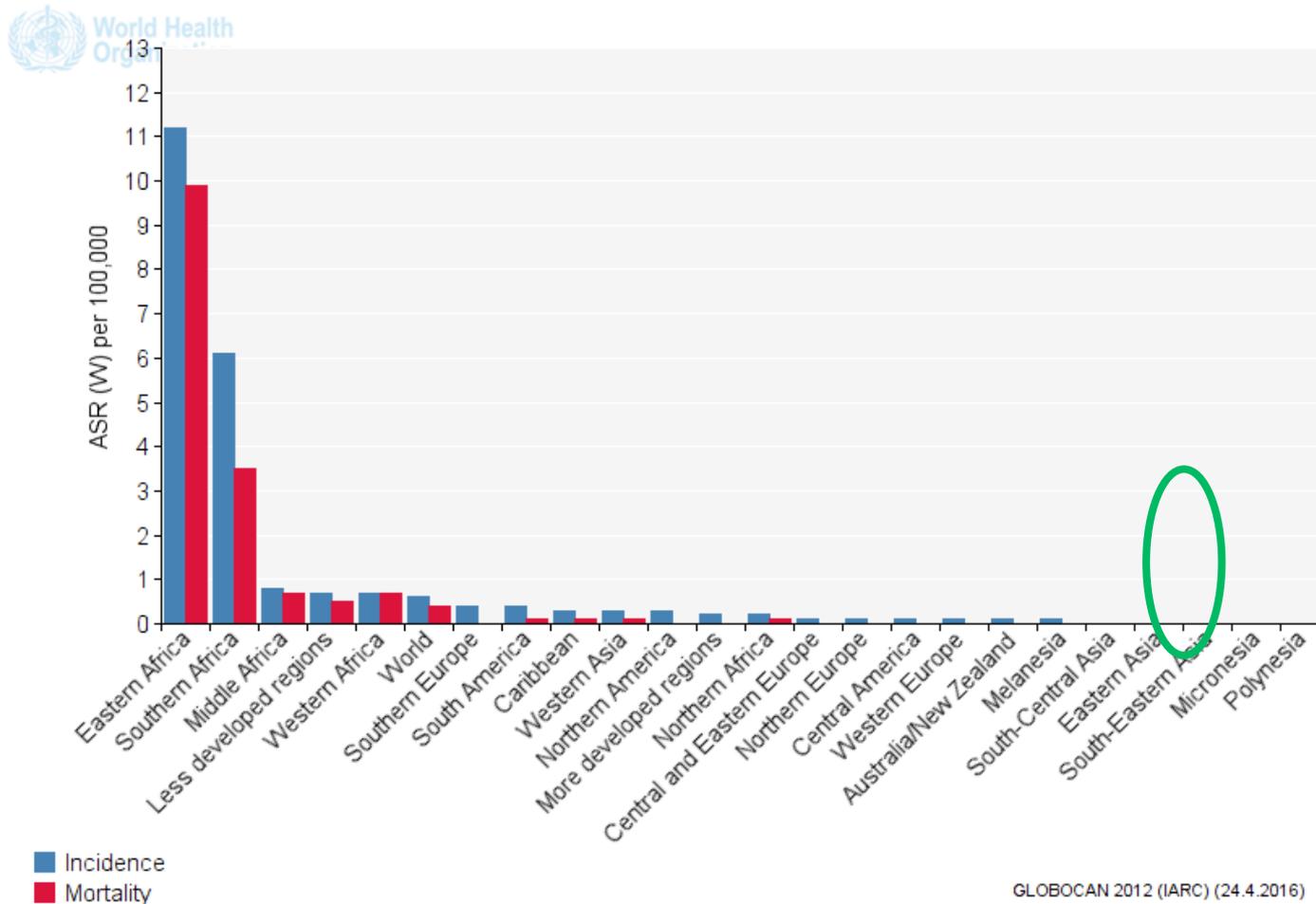
Kaposi's sarcoma: Myanmar

Age specific rate 0.03/10⁵



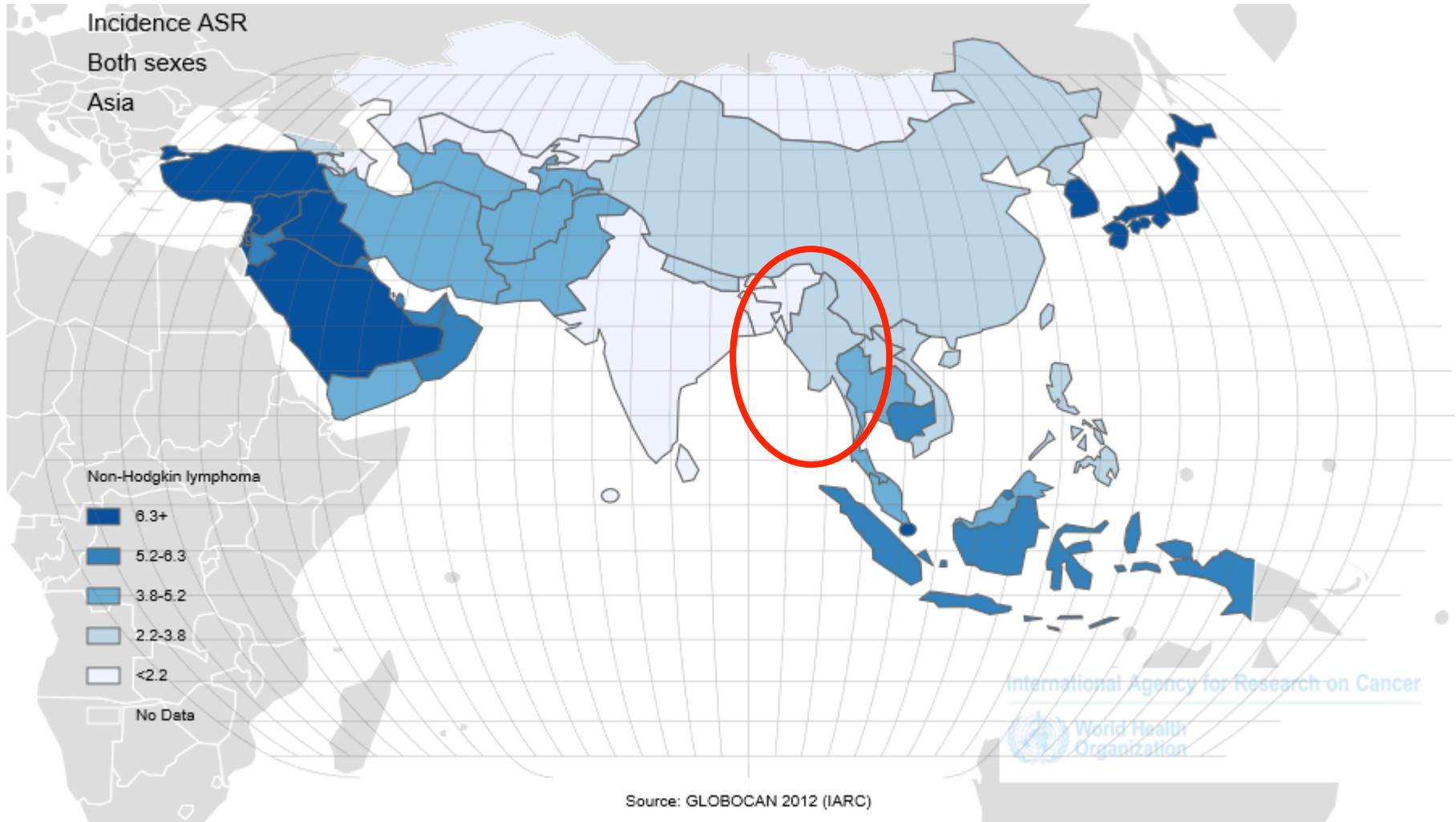
KS by region: incidence and mortality

International Agency for Research on Cancer Kaposi sarcoma: both sexes, all ages



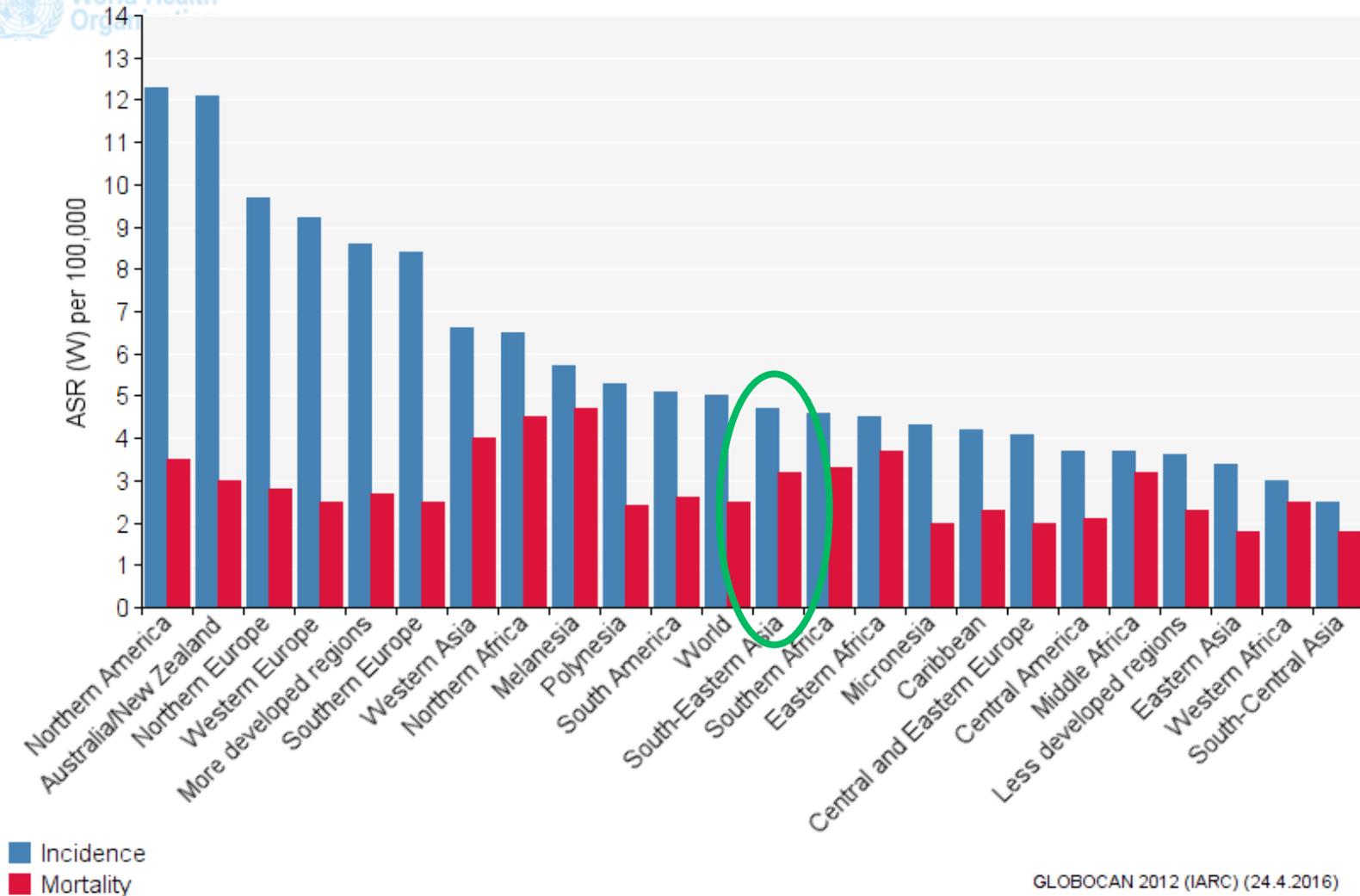
Non-Hodgkin's Lymphoma: Myanmar

Age specific rate 3.54/10⁵



NHL by region: incidence and mortality

International Agency for Research on Cancer Non-Hodgkin lymphoma: both sexes, all ages



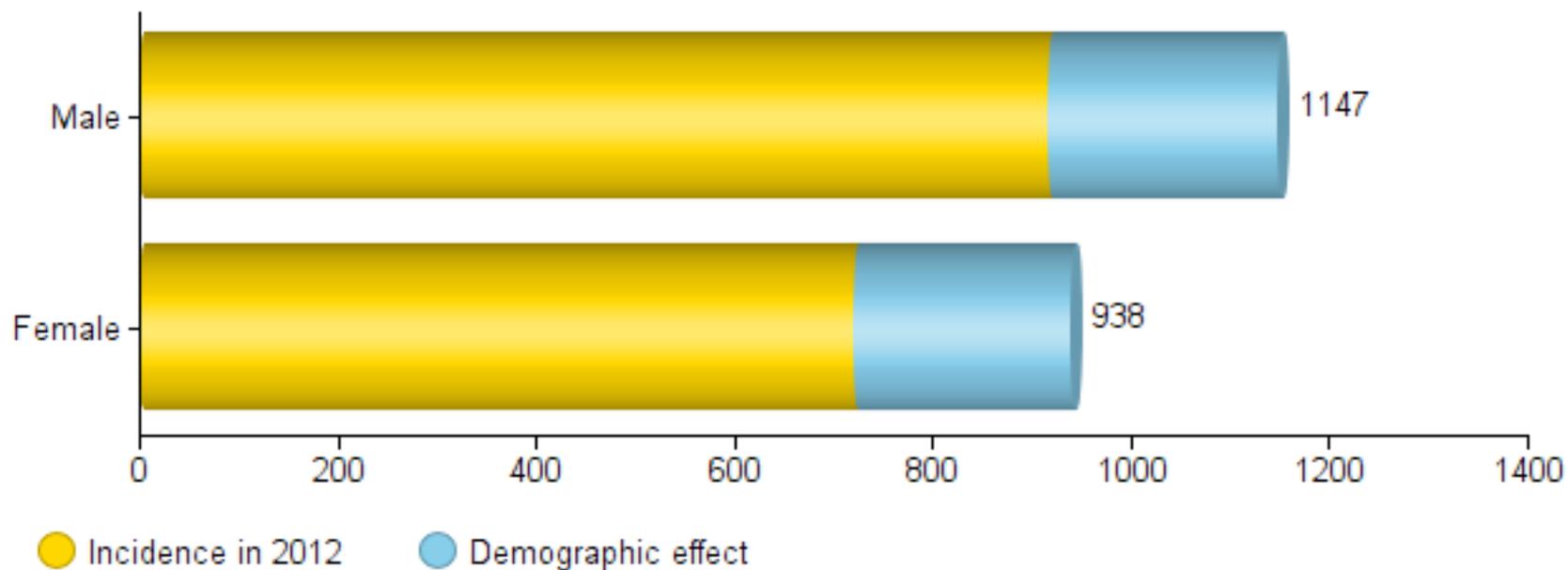
Current and predicted increase of KS and NHL

International Agency for Research on Cancer

Myanmar

Non-Hodgkin lymphoma, Kaposi sarcoma

Number of new cancers in 2020 (all ages)

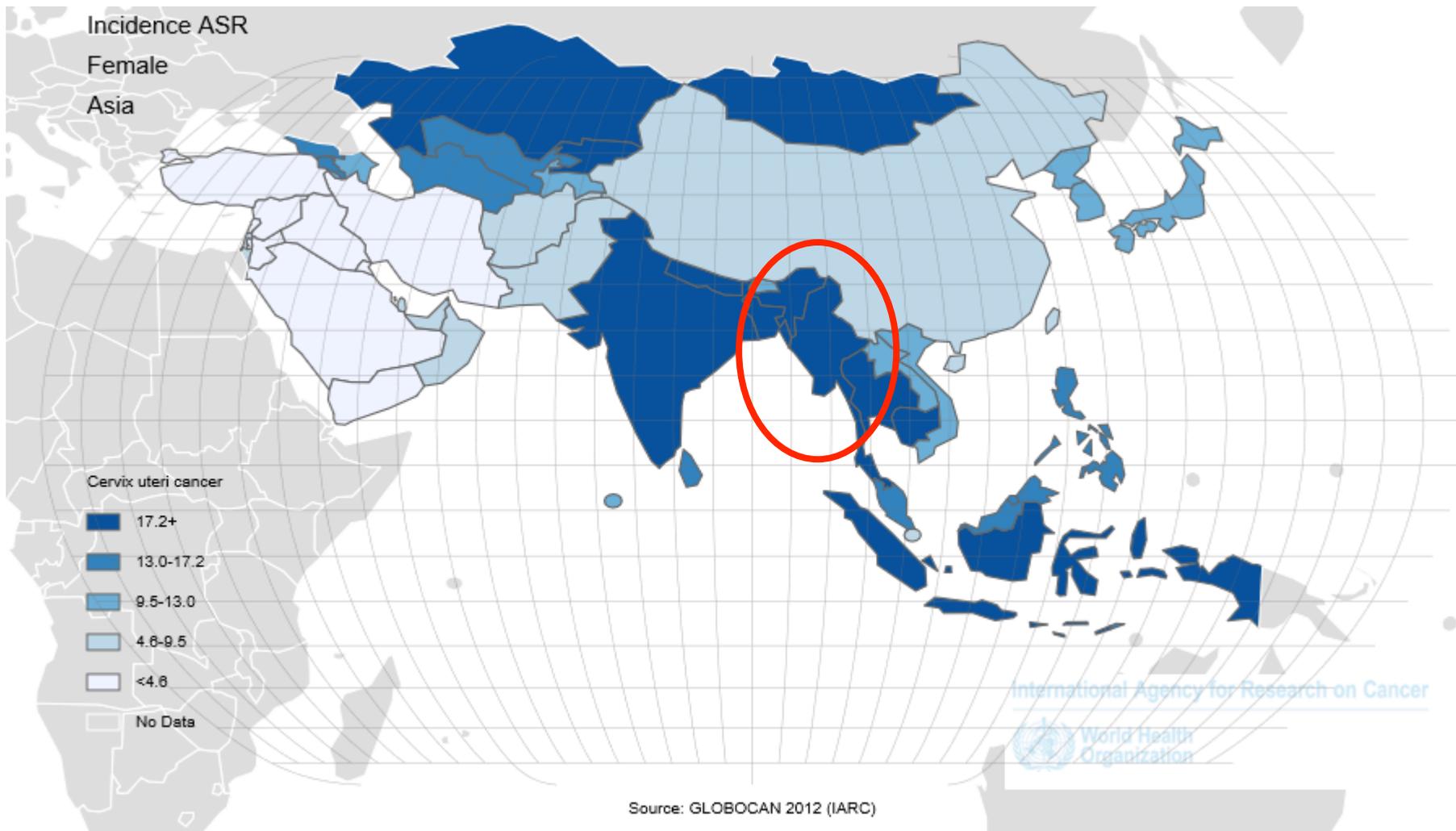


GLOBOCAN 2012 (IARC) (24.4.2016)



Cervical cancer: Myanmar

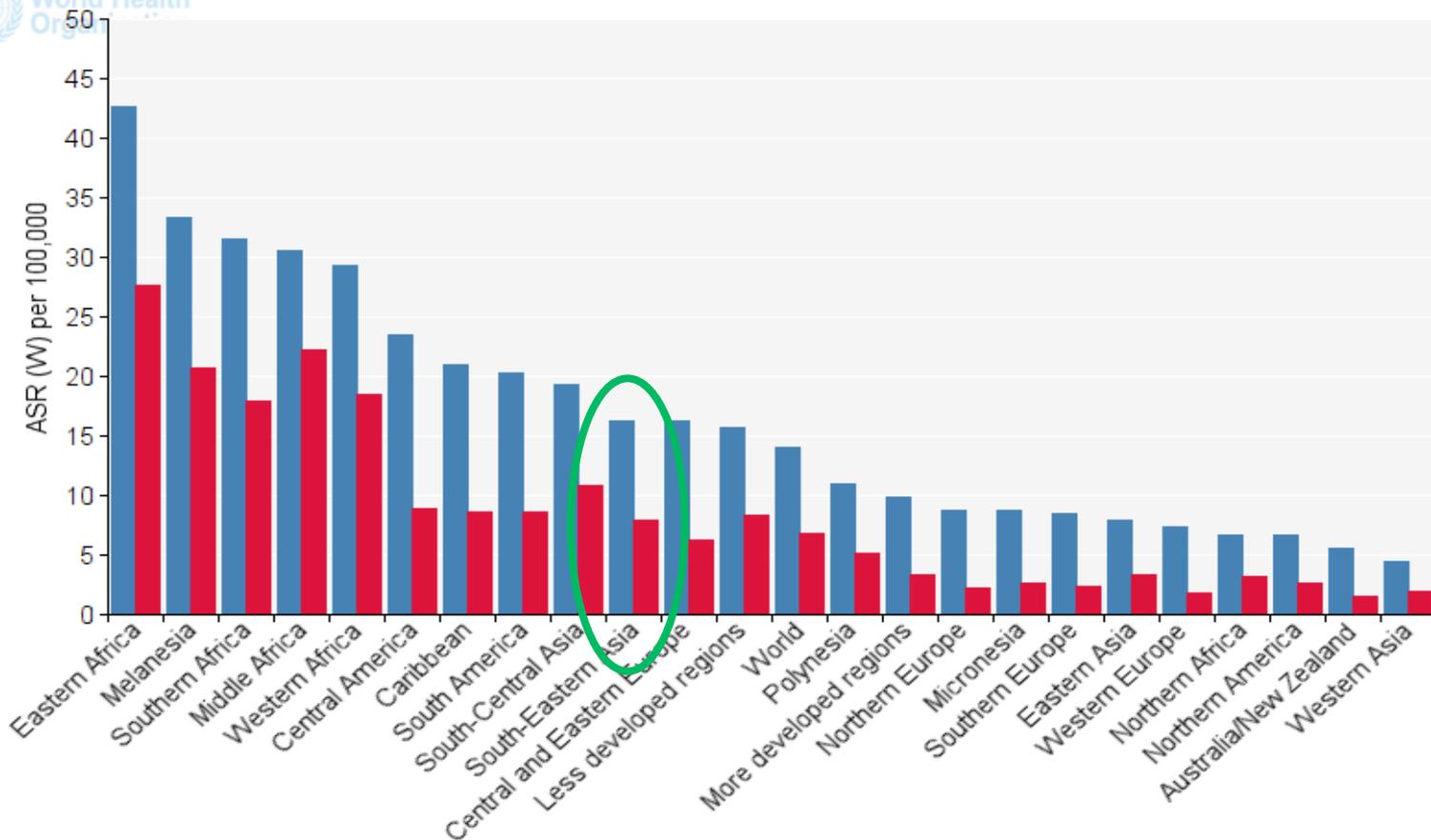
Age specific rate 20.57/10⁵



Cervical cancer: incidence and mortality

International Agency for Research on Cancer

Cervix uteri, all ages



■ Incidence
■ Mortality

Current and predicted increase of cervical cancer

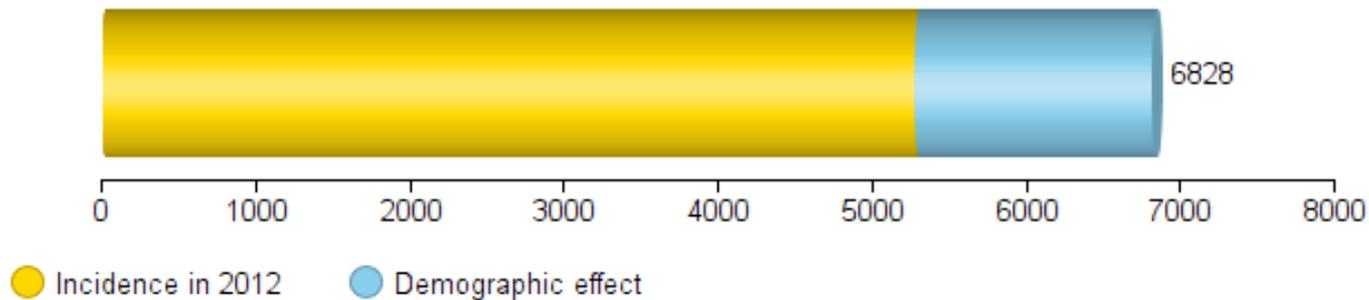
International Agency for Research on Cancer



Myanmar

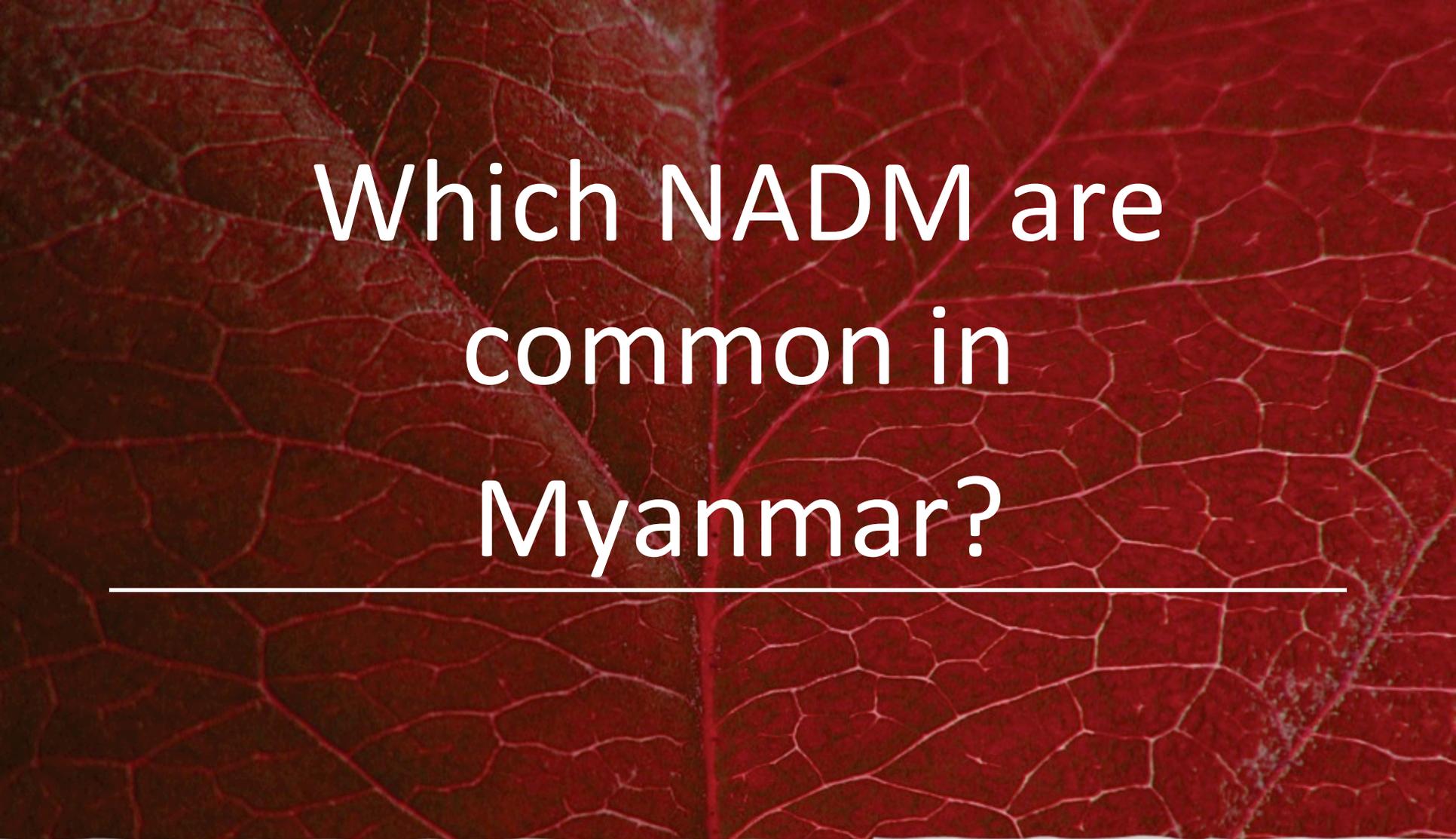
Cervix uteri

Number of new cancers in 2020 (all ages)



GLOBOCAN 2012 (IARC) (24.4.2016)

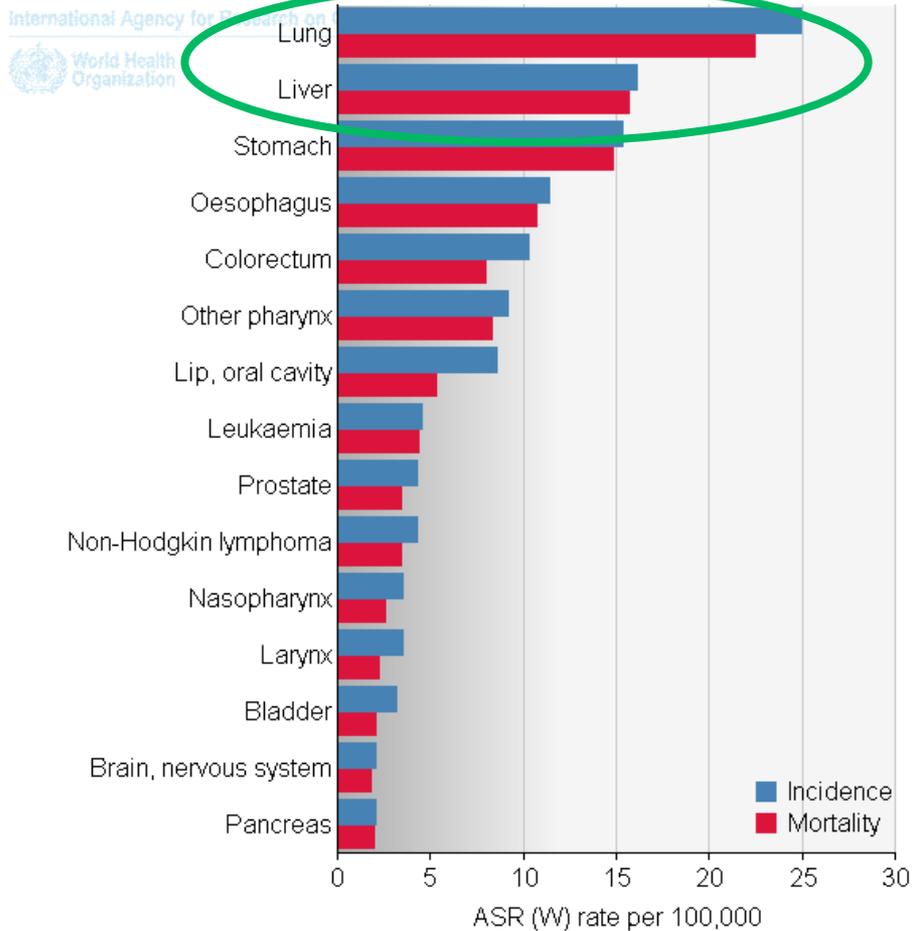




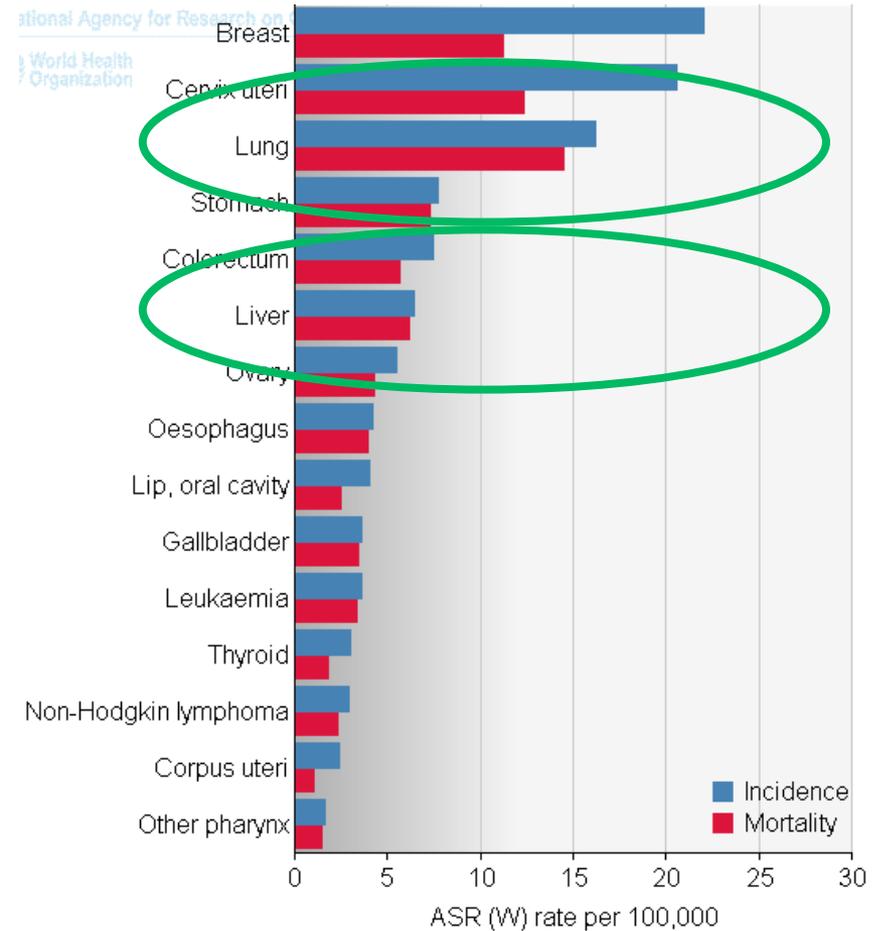
Which NADM are
common in
Myanmar?

Myanmar: age standard incidence cancer and mortality rates

Men

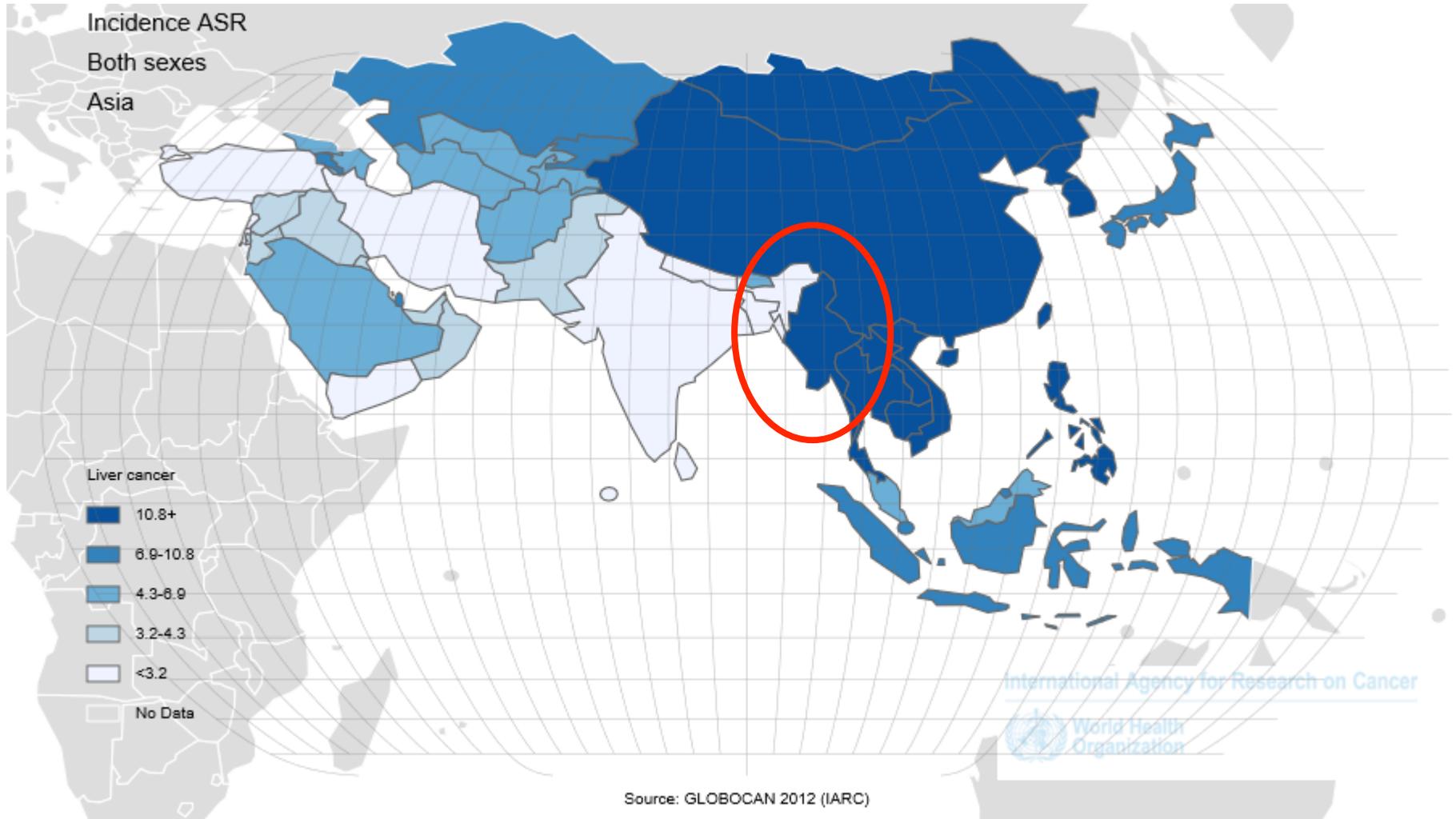


Women



Liver cancer: Myanmar

Age specific rate 6.41/10⁵



Distinguishing HIV-related cancers from OI's

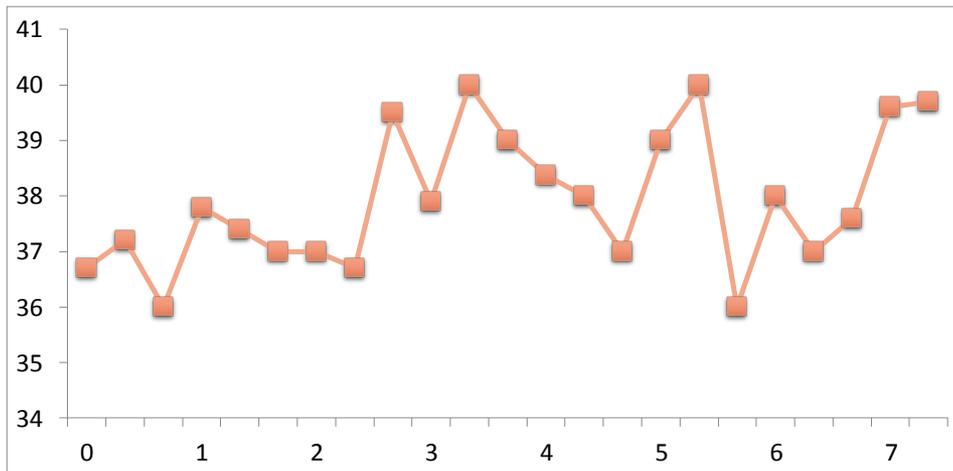
Lymphoma

Patient

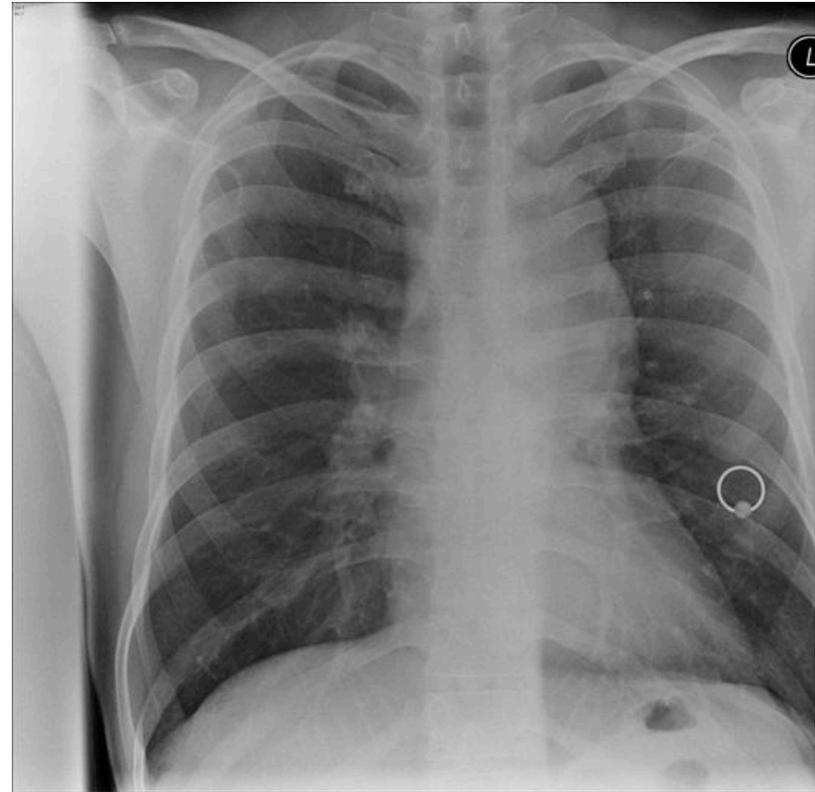
- 37y-old ex-IDU for 8y
- Travelled Asia/Europe ++
- PMH – **pulmonary TB 1998**,
HCV +ve (RNA –ve)
- Presented with 6w history of
fever, sweats, loss of weight
- HIV +ve, **CD4 280** cells/mm³,
VL 295,000 c/ml
- On methadone



Time course of symptoms



Weeks



Differential diagnosis – peripheral and mediastinal lymphadenopathy

HIV disease and malignancies

- Progressive generalised lymphadenopathy
- **Non-Hodgkin's lymphoma**
- **Hodgkin's lymphoma**
- Multicentric Castleman's disease

Opportunistic infections

- **TB**
- **MAI**
- Penicilliosis
- Histoplasmosis
- Cryptococcus

CD4 of 280..

HIV disease and malignancies

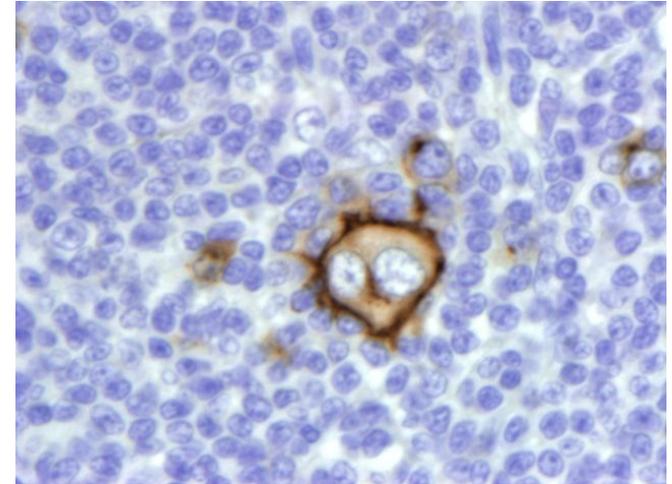
- Progressive generalised lymphadenopathy
- **Non-Hodgkin's lymphoma (BL)**
- **Hodgkin's lymphoma**
- Multicentric Castleman's disease

Opportunistic infections

- **TB**
- **MAI**
- Penicilliosis
- Histoplasmosis
- Cryptococcus

Biopsy result revealed Hodgkin's disease

- Biopsy - Reed-Sternberg cell
- CT:
 - Mediastinal mass, splenomegaly
- Bone marrow clear
- CSF cytology clear
- Type B symptoms: fever, loss of weight or night sweats
- **Stage 3b**



Lymphoma is more than one condition and not all are classical ADM

		Median CD4 range at diagnosis	Infective factor/co-factor
NHL:	Burkitt's	350–500	EBV
	Diffuse large B-cell	10–150	EBV
	PCNSL	10–50	EBV
Primary effusion lymphoma		100–200	HHV-8
Hodgkin's lymphoma		100–500	EBV
Castleman's disease		100-300	HHV-8



Few facts about Hodgkin's disease

- It is a non-AIDS defining malignancy (NADM)
- 10-20x commoner in HIV
- 90% have 'B' symptoms
- 74–92% have advanced stages of disease
- Frequent involvement of extra-nodal sites:
 - Bone marrow (40–50%); Liver (15–40%) and spleen (20%)
- HIV-HL tends to develop as an earlier manifestation of HIV
- Higher CD4 and often ART suppressed



Few facts about non-Hodgkin's lymphoma

- Second most common malignancy in HIV
- **AIDS defining (ADM) but Burkitt's lymphoma occurs at higher CD4 count**
- Several pathological types
- Prognosis improved with additional HAART and approaching that seen in HIV-negative persons
- Frequent extranodal sites involved
- HIV-related primary effusion lymphoma (PEL) is linked to HHV8 and is rare
 - Very poor prognosis



Presentation usually associated with lymphadenopathy

- Majority of patients present with:
 - Type B symptoms – fevers, sweats and weight loss
 - Lymphadenopathy which may be generalised or localised



Half have visceral/extra-nodal disease

- Extra-nodal disease is common
- Sites of extra-nodal involvement include:
 - Oral cavity
 - Liver, spleen
 - GI tract (ileum)
 - Lung
 - Skin
 - Bone-marrow

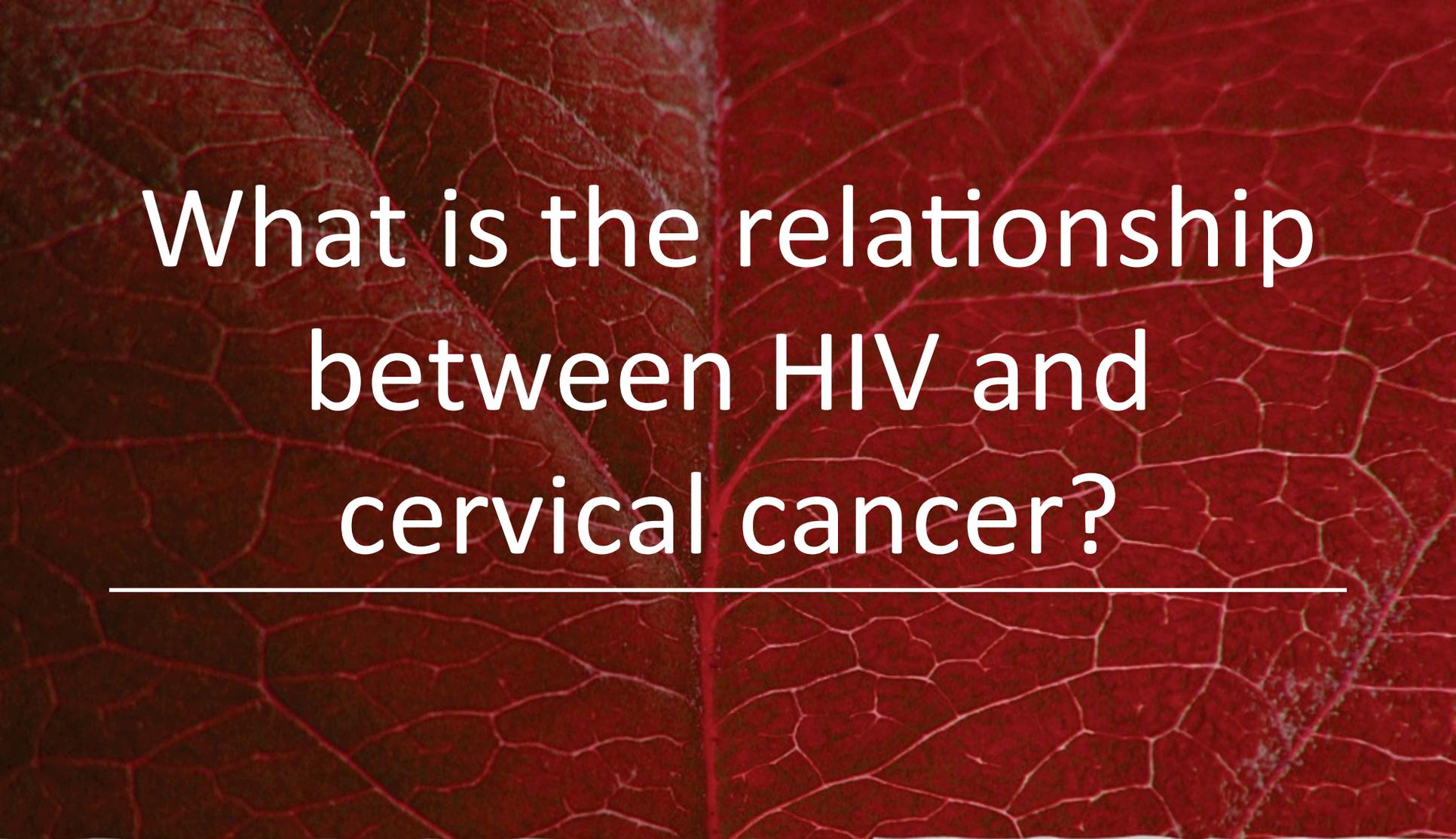


Lymphoma Treatment

HAART

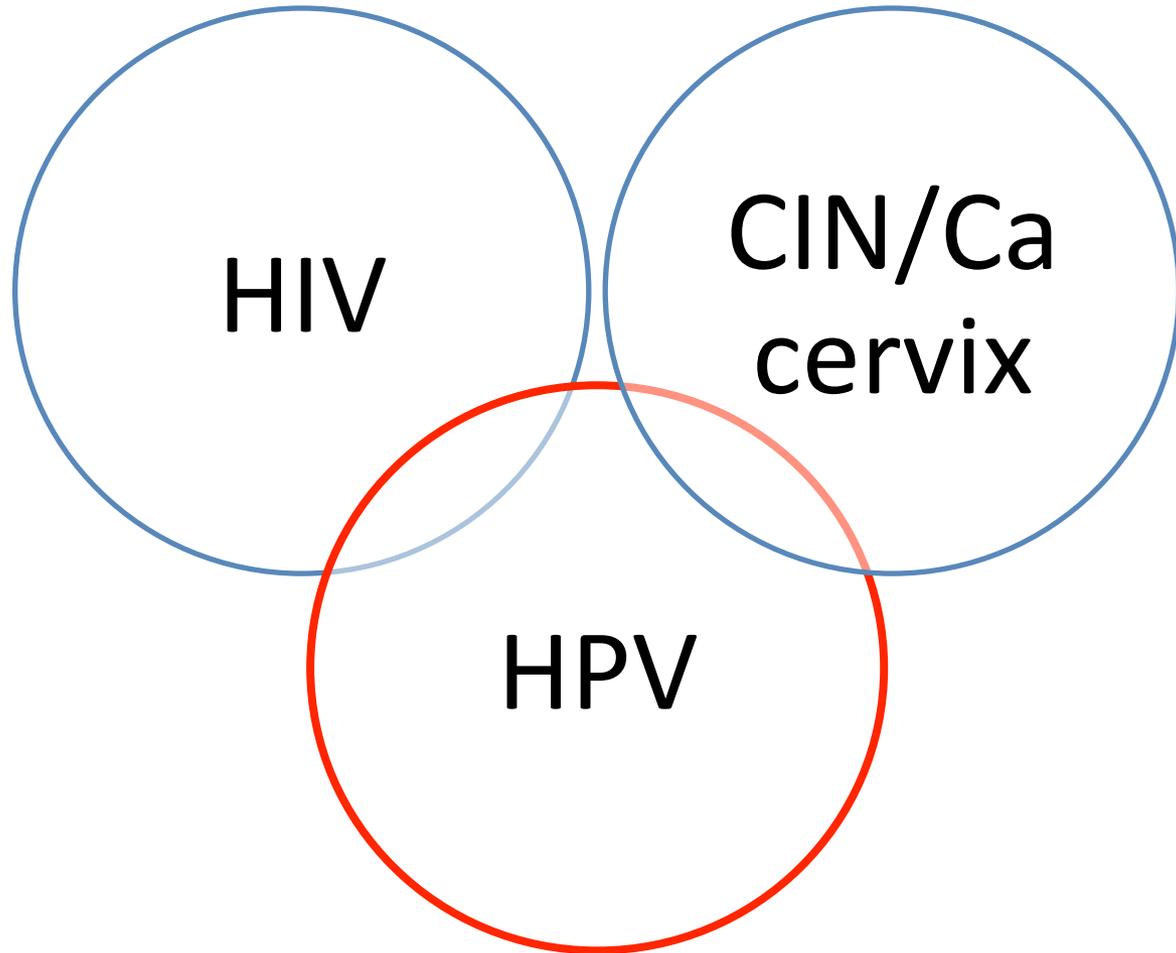
GreenShoots
FOUNDATION

Cervical cancer in HIV



What is the relationship
between HIV and
cervical cancer?

HPV/HIV link



Cervical Cancer

- Latest data on cervical cancer incidence and mortality (GLOBOCAN 2012, IARC*):
 - 4th most common cancer in women
 - Globally 528,000 cases diagnosed in 2012:
 - 86% of all cases (n=453,032) in developing world
 - Globally 274,967 deaths:
 - 88% of all deaths (n=241,818) in developing world
- Mortality to incidence ratio:
 - Developed countries: 36–43%
 - Developing countries: 54–80%

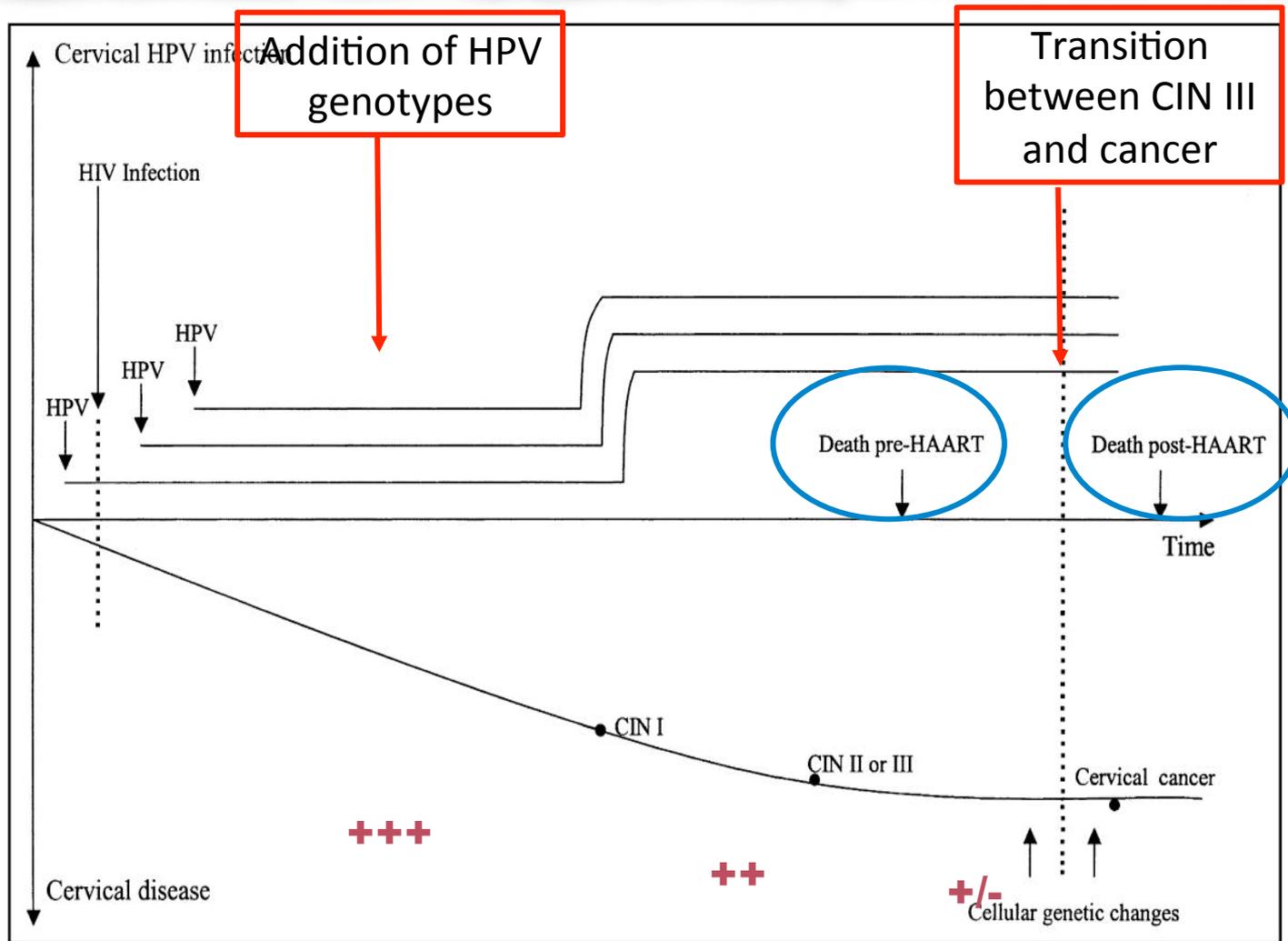
*www.iarc.fr/globocan2008

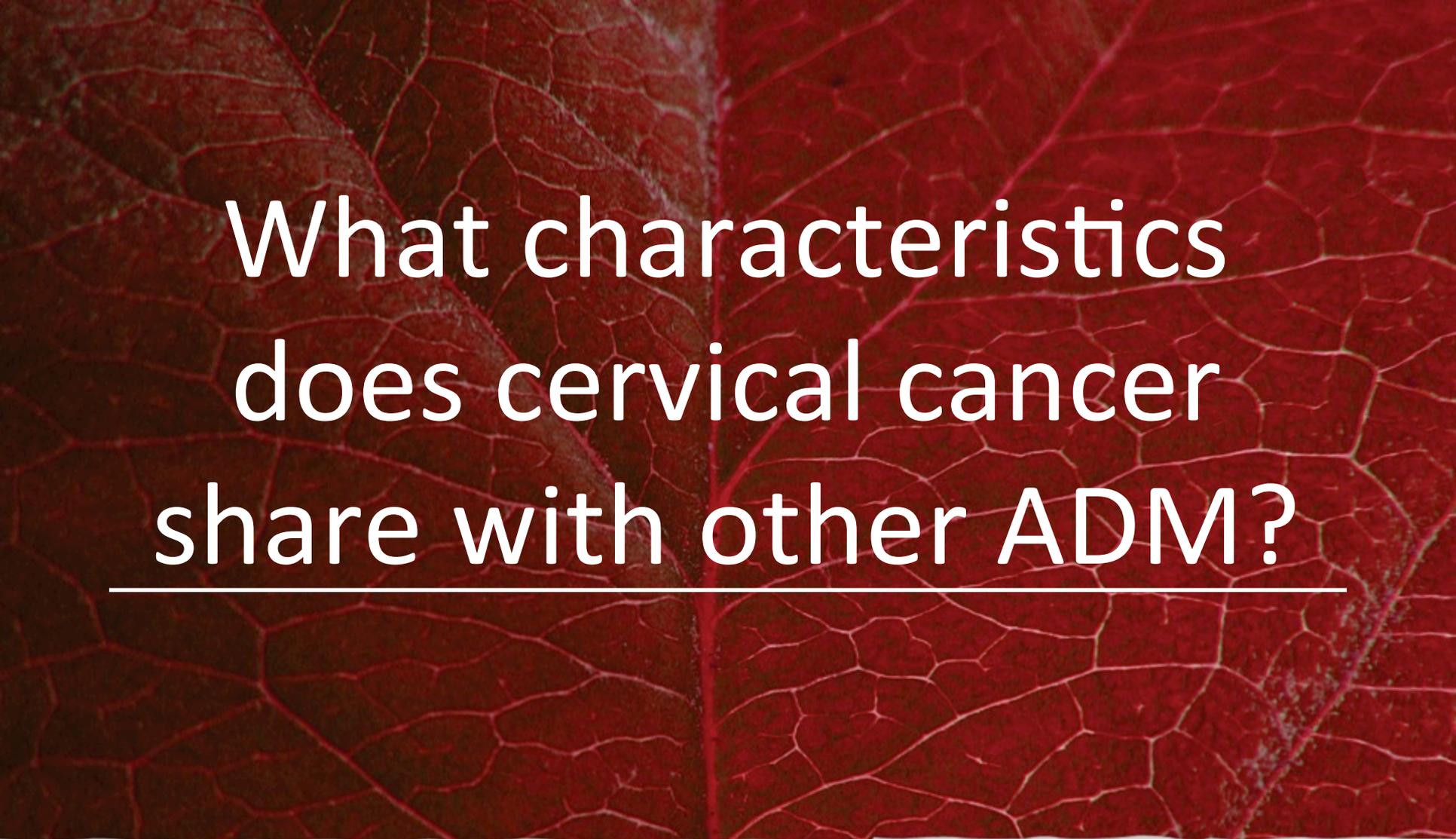
Association between HIV, CIN, and Cervical Cancer

- In HIV-positive women, there is a higher incidence of:
 - HPV infection (70-80% vs. 30%)
 - Persistent HPV with multiple and high-risk types (16/18)
 - Cervical cancer precursors (CIN)
 - Cervical cancer
- ART has minimal effect on CIN progression



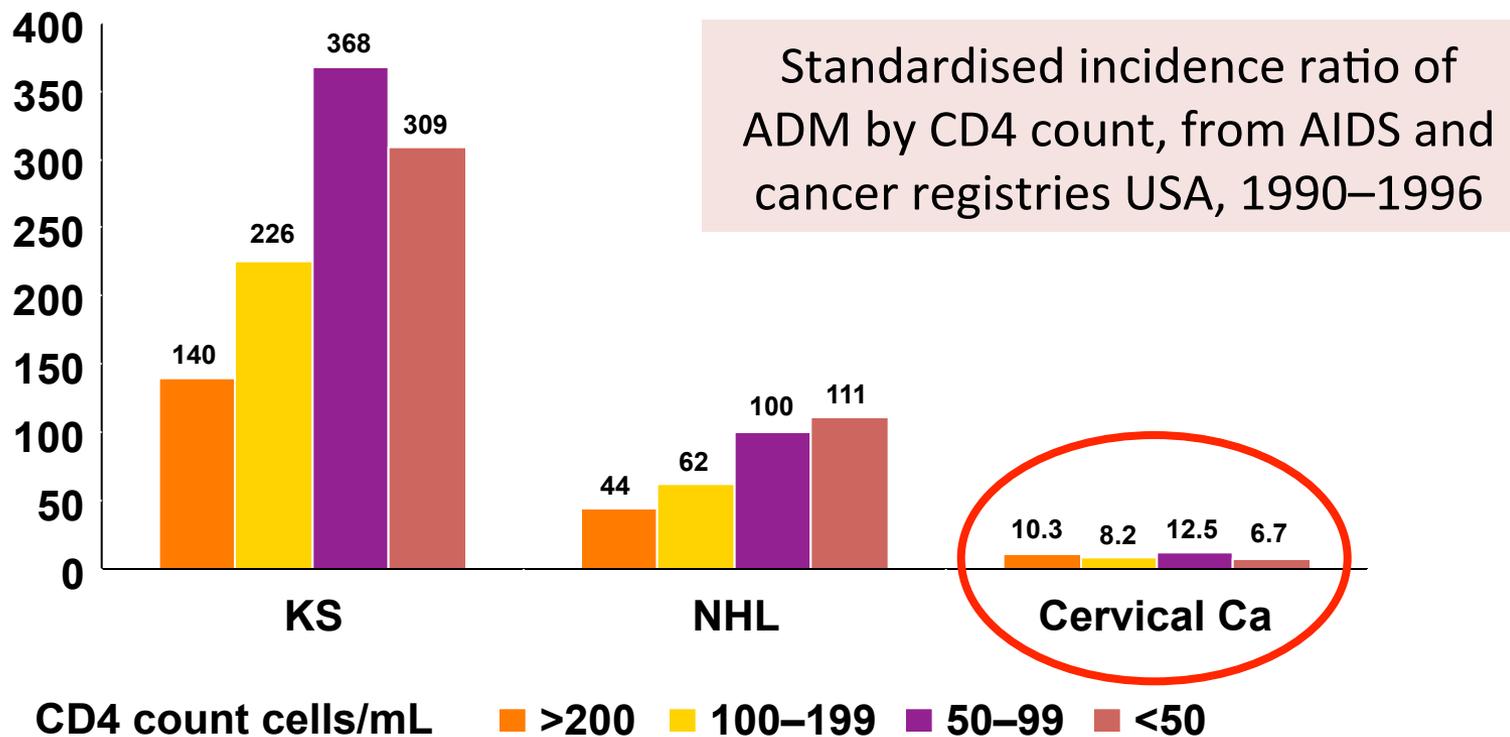
Association between HPV and HIV





What characteristics
does cervical cancer
share with other ADM?

It is more common in HIV-infected persons



Significant association between CIN and HIV and with low CD4

1. HIV Immunosuppression

a. HIV+

b. HIV+, CD4 <200

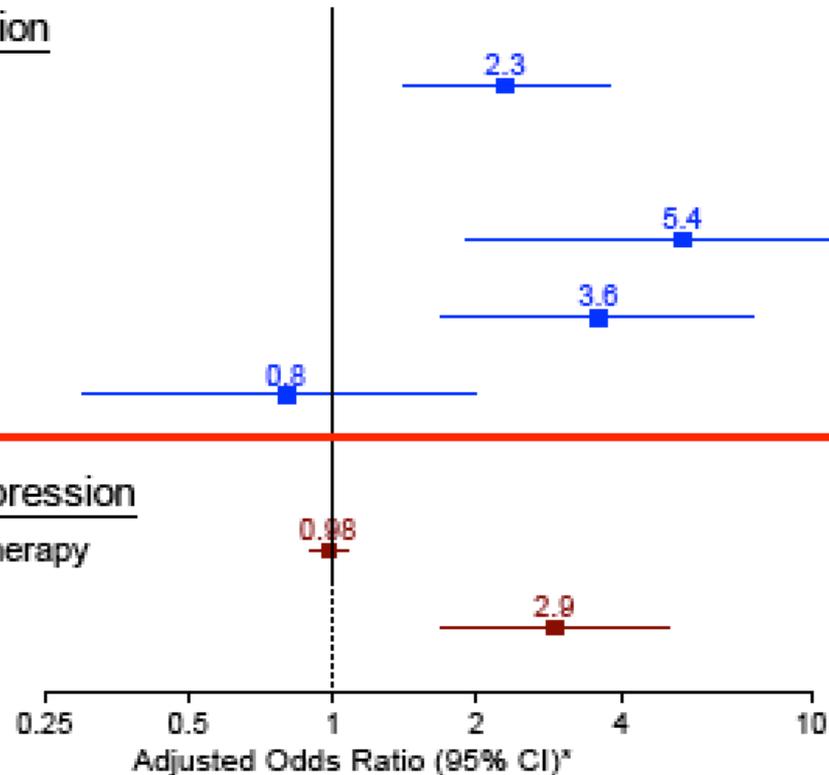
HIV+, CD4 200-499

HIV+, CD4 ≥500

2. Non-HIV Immunosuppression

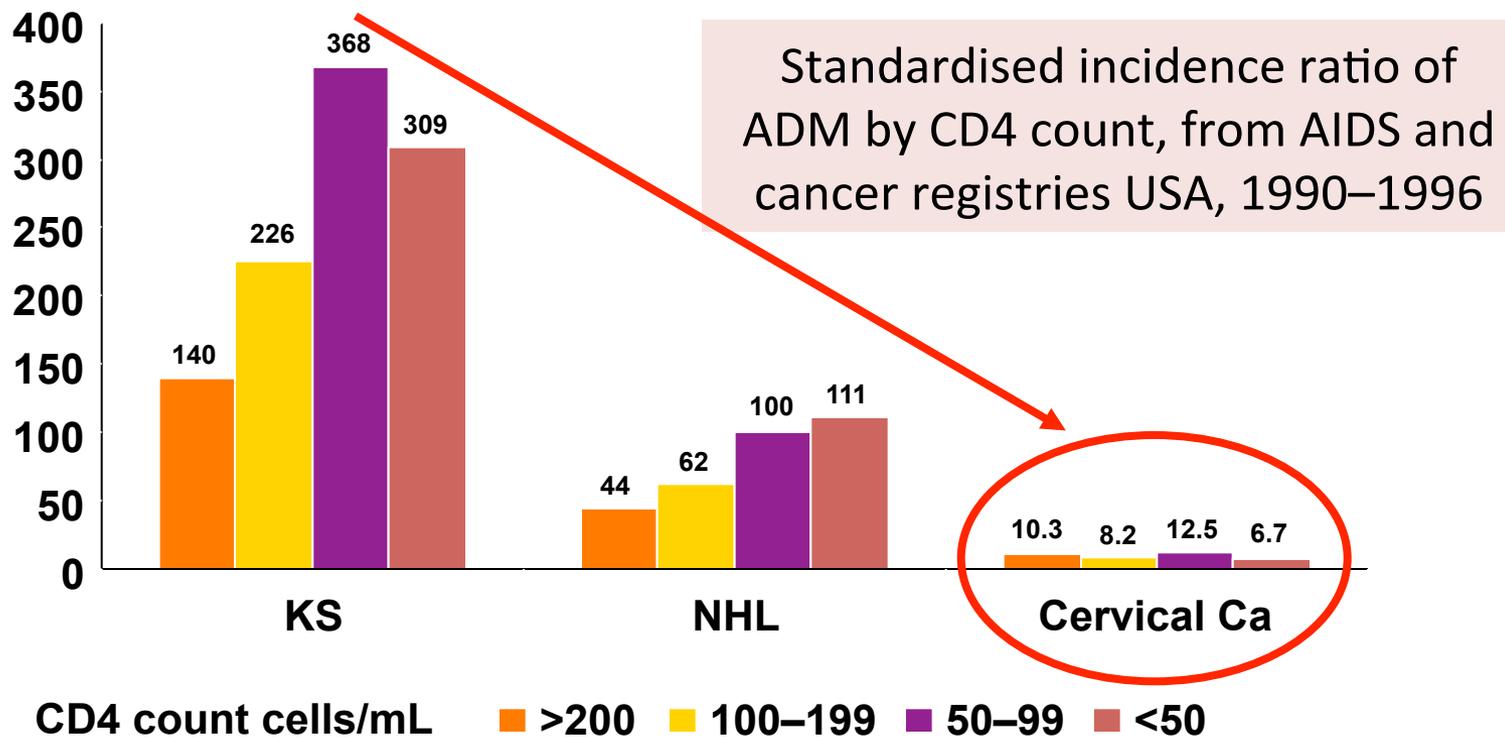
a. Immunosuppressive therapy

b. Solid organ transplant

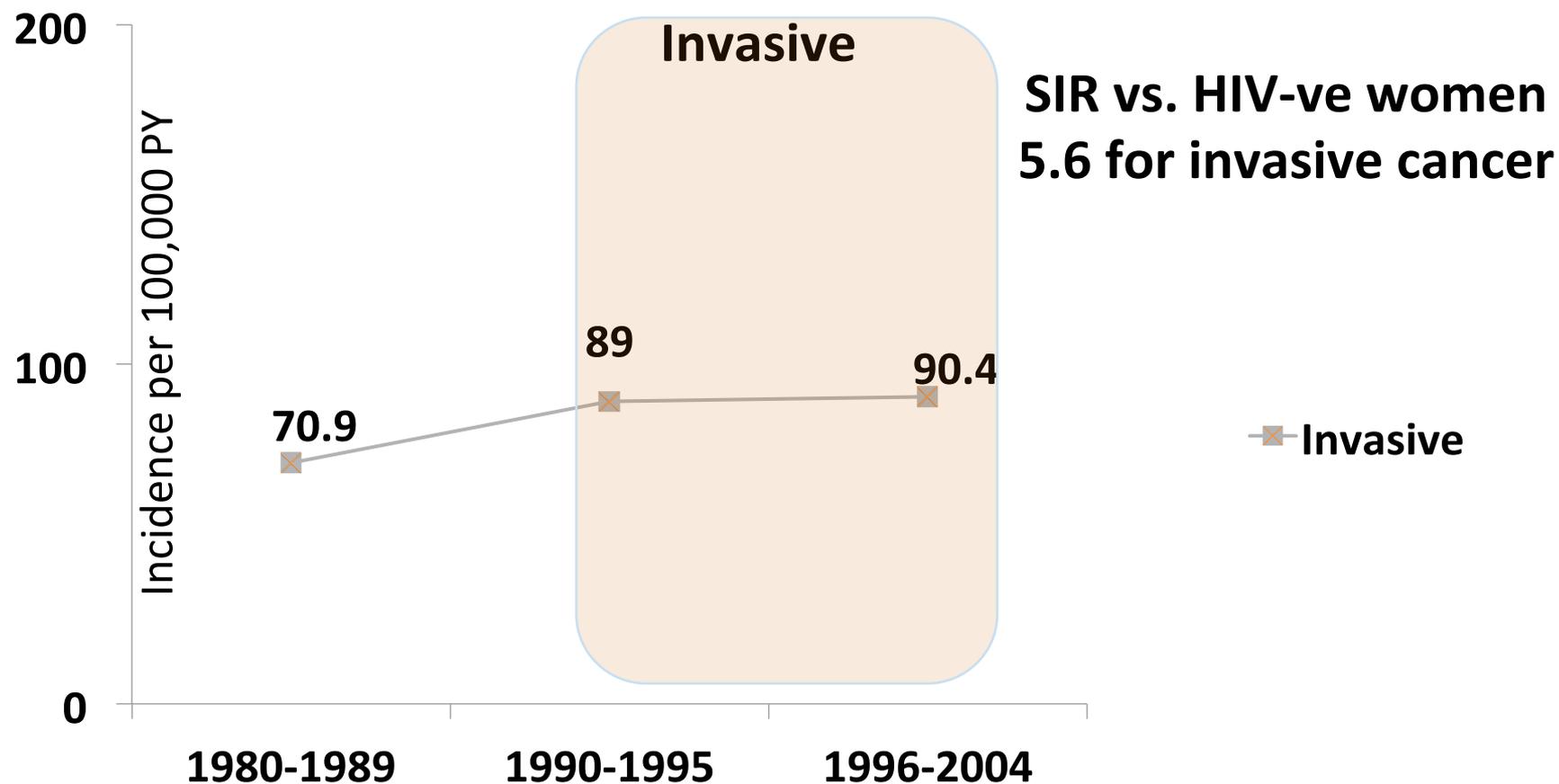


What characteristics do
cervical cancer and other
ADM not share?

Relative risk and relationship to CD4 is much less than with other ADM's



There has been little change in incidence and no impact from ART

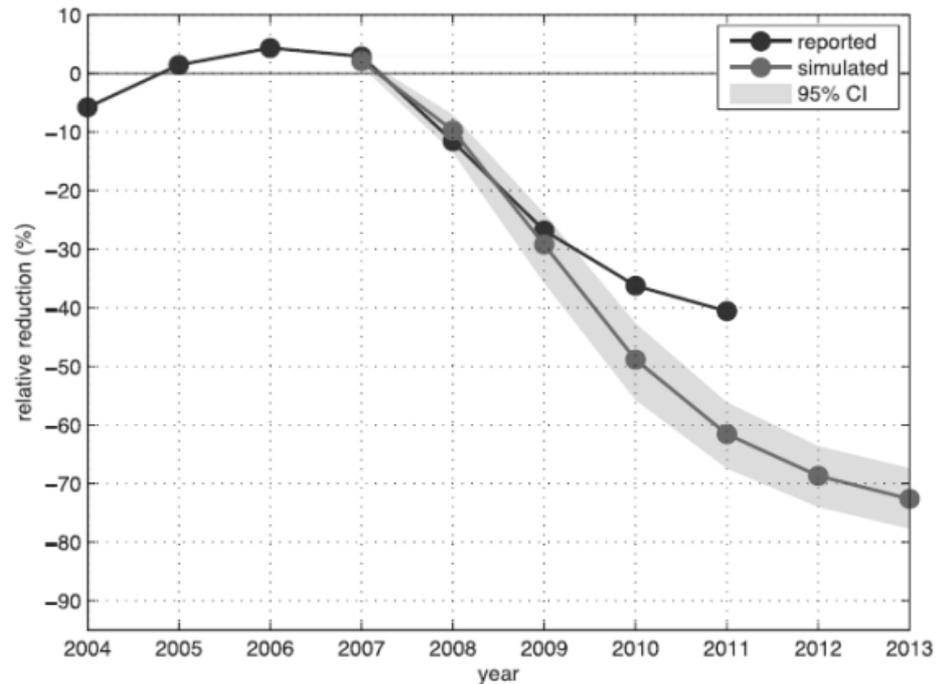
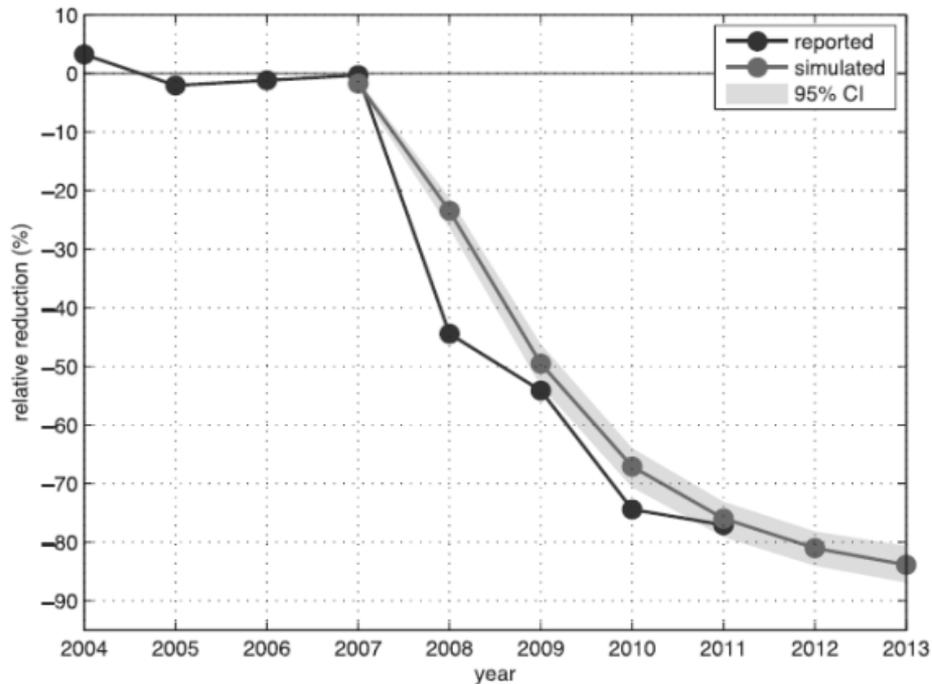


HPV vaccines are available and highly effective



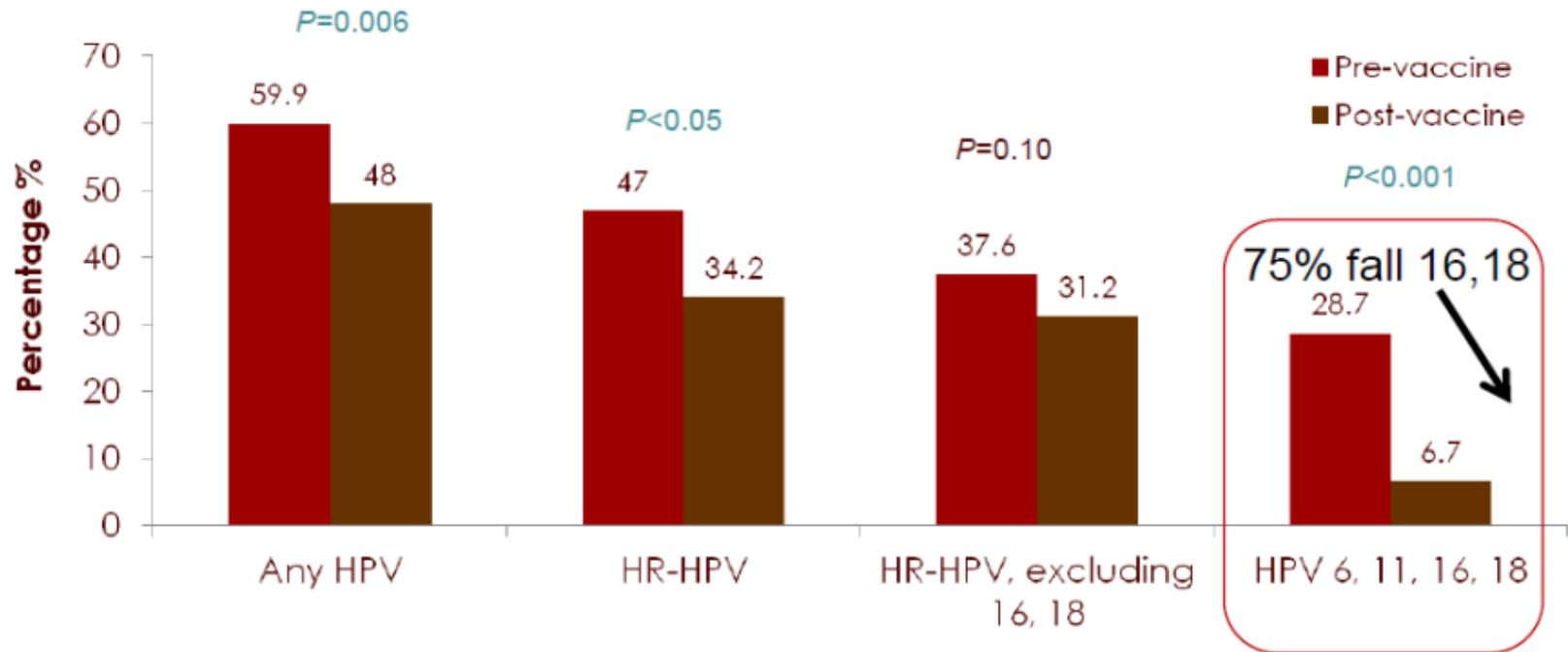
Potential to eradicate all HPV-related disease

Relative reduction of genital warts aged 16-28 with vaccination programme

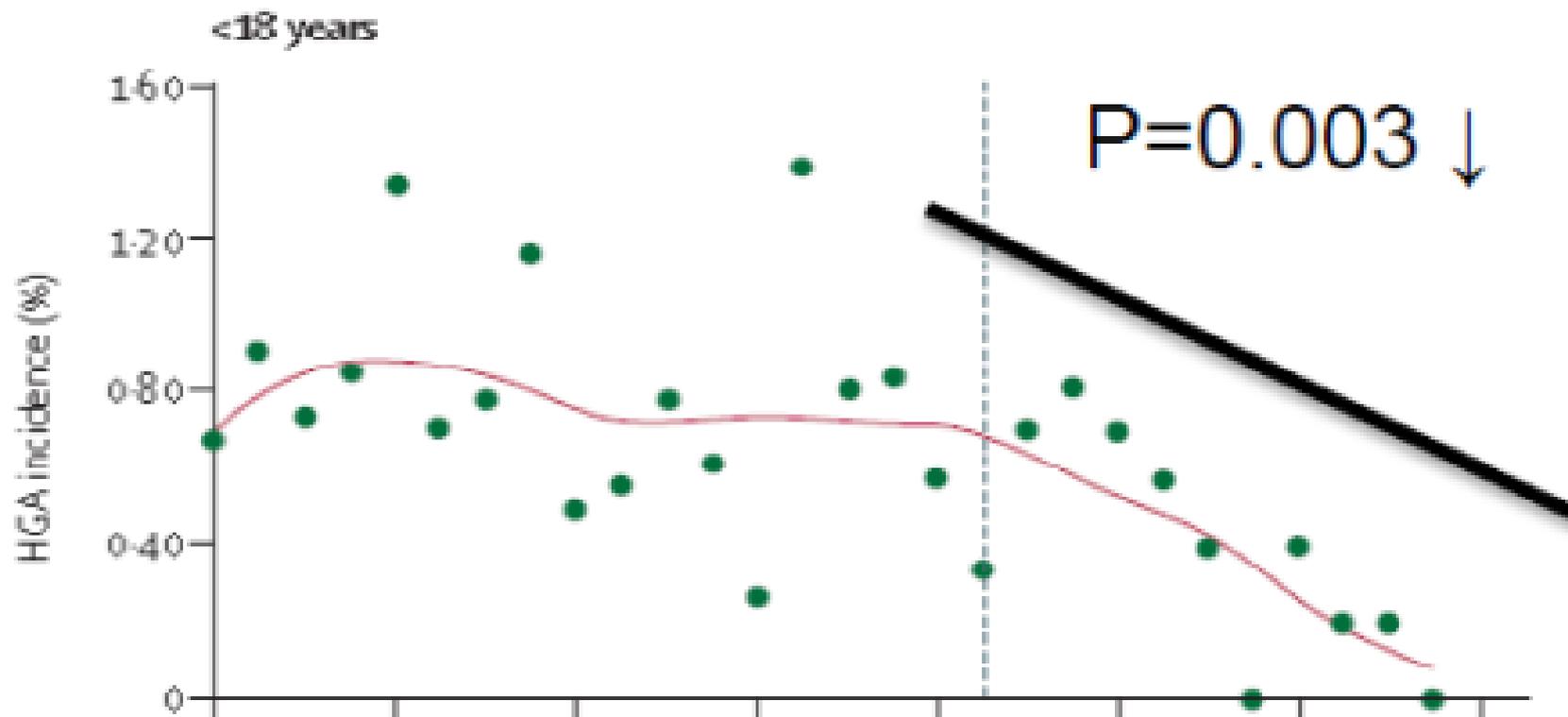


Reduction in most oncogenic strains

Differences in HPV Genoprevalence Between Pre-vaccine and Post-vaccine Female Populations in Australia



CIN III reduction in young women



Lastly, a screening programme exists which is highly effective

- Increased rate of Cervical Ca can be avoided with regular screening programmes
 - Rates before and after screening reduced 5-10 fold
 - 75% of cases of cancer can be prevented
 - Increased rate associated with HIV can be abolished with screening
- All HIV-infected women should have annual cytology
 - Same age range as for HIV-negative women (1B)



But..

Screening programs remain
difficult to implement in low and
middle-income settings

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Discussion and questions?

GreenShoots
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Malignancy in Myanmar with focus on cervical cancer