Beyond HIV
Takin HIV to another level
CLUSTER 2.0
Beyond Comorbidities

The New Phenomenology of Cancer in Persons Living with HIV

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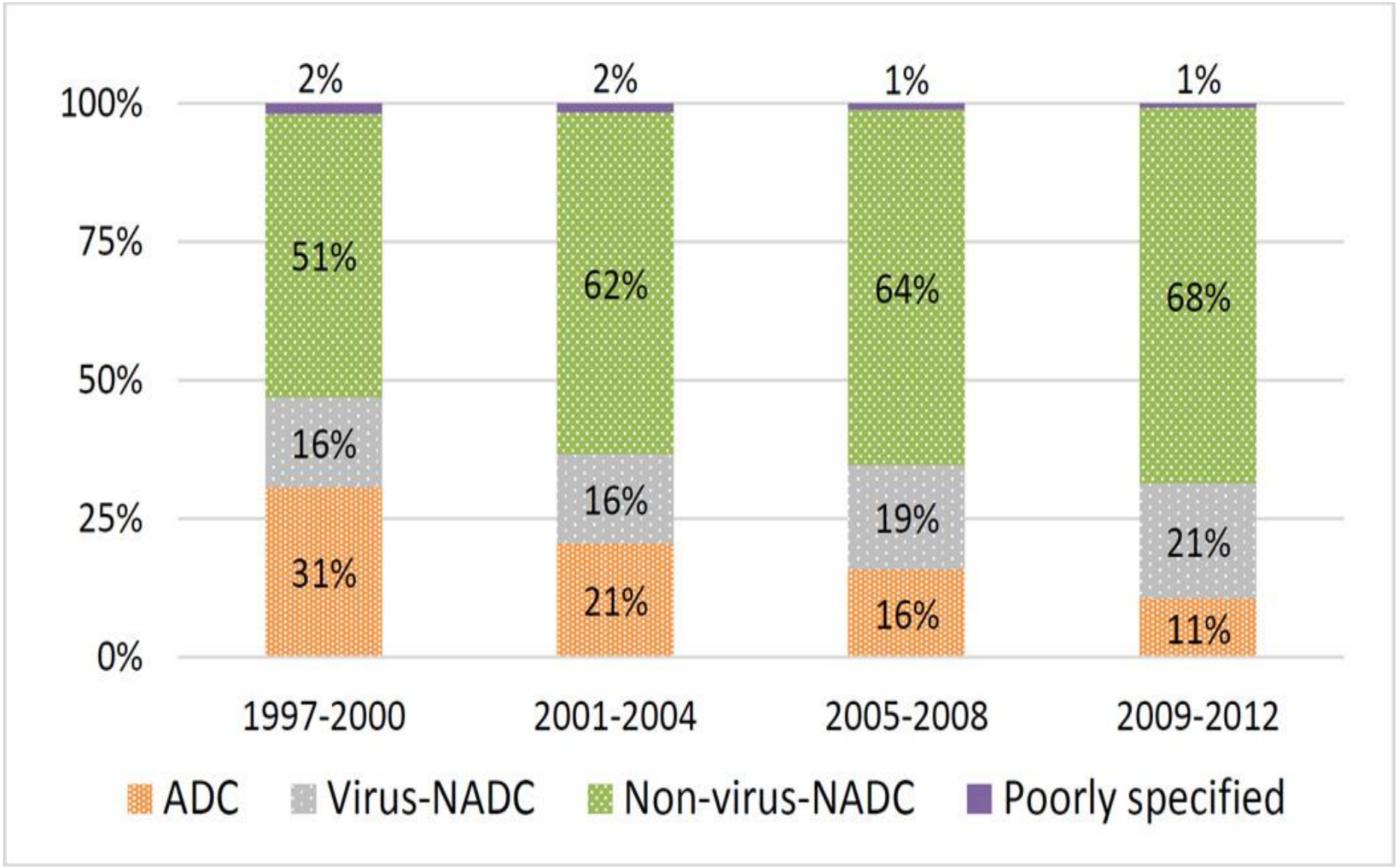
HIV-related Cancers

Background

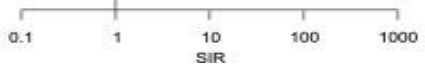
- The epidemiology of HIVdisease has evolved in the cART era
- The incidence and morbidity of AIDS-defining cancers has decreased, whereas morbidity and mortality of NADCs has increased
- People living with HIV (PLWH) have a markedly increased risk of anal, liver, lung cancer and of other HPV-associated malignancies including Head-Neck cancers
- Understanding the changing patterns of HIV-related malignancies will direct screening and treatment strategies to ensure optimal outcomes for PLWH

Proportion of Cancer Cases among HIV-infected Patients by Cancer Group in each Calendar Period (VA System 1997-2012)



Meta-analysis of Standardized Incidence Ratio (SIR) for non-AIDS-defining Cancers among People Living with HIV(PLWH) (1992-2022)

Type of Cancer	SIR (95%CI)	Number of studies	Number of effect sizes	Number of observed cancers	Heterogenity I^2(%)
A. Infection related cancers					
Anus and anal canal	28.33 (20.30-38.96)	27	82		
Vulva and vagina	14.13 (7.58-26.36)	14	26		
Hodgkin lymphoma	10.93 (9.05-13.20)	32	81		
Eye and adnexa	8.97 (2.95-27.28)	9	20		
Penis	7.60 (3.68-15.70)	11	17		
Liver	5.54 (4.39-7.00)	34	69		
Skin nonmelanoma	4.41 (2.80-6.92)	22	36		
Nasal cavity, middle ear, and accessory sinuses	3.29 (1.55-6.98)	7	10		
Lip, oral cavity and pharynx	3.15 (2.25-4.41)	26	112		
Lip	2.85 (1.47-5.54)	6	16		
Salivary glands	3.32 (0.28-39.12)	4	5		
Nasopharynx	3.06 (1.88-4.97)	13	13		
Tongue	2.44 (1.84-3.22)	8	12		
Tonsil	2.32 (1.74-3.09)	3	3		
Oropharynx	2.23 (0.25-20.18)	3	5		
Uterus	2.61 (1.05-6.52)	12	18		
Head and neck	2.06 (1.32-3.22)	12	23		
Larynx	2.21 (1.50-3.24)	15	29		
Esophagus	2.16 (1.35-3.46)	17	27		
Stomach	1.86 (1.36-2.54)	24	52		
B. Non-infection related cancers					
Mesothelial and soft tissue	3.50 (2.10-5.81)	14	36		
Multiple myeloma	3.41 (2.44-4.77)	18	42		
Biliary tract	3.19 (0.78-13.02)	5	7		
Bone and joints	2.94 (1.53-5.64)	12	18		
Trachea, bronchus, and lung	2.48 (1.94-3.16)	38	99		
Leukaemia	2.81 (2.18-3.62)	22	77		
Brain and central nervous system	2.80 (1.80-4.37)	23	50		
Small intestine	2.53 (1.15-5.54)	8	12		
Ovary	2.40 (1.53-3.77)	15	24		
Thymus, heart, mediastinum, and pleura	2.17 (0.90-5.21)	7	9		
Testis	2.10 (1.43-3.11)	18	47		
Pancreas	1.99 (1.32-3.01)	19	35		
Kidney and renal pelvis	1.47 (0.98-2.21)	20	40		
Gallbladder	1.39 (1.01-1.90)	3	3		
Melanoma of skin	1.19 (0.89-1.61)	25	55		
Bladder	1.18 (0.82-1.68)	25	48		
Colon and rectum	1.09 (0.79-1.51)	25	75		
Thyroid	0.98 (0.60-1.59)	20	33		
Breast	0.91 (0.68-1.20)	29	56		
Prostate	0.81 (0.63-1.05)	28	61		



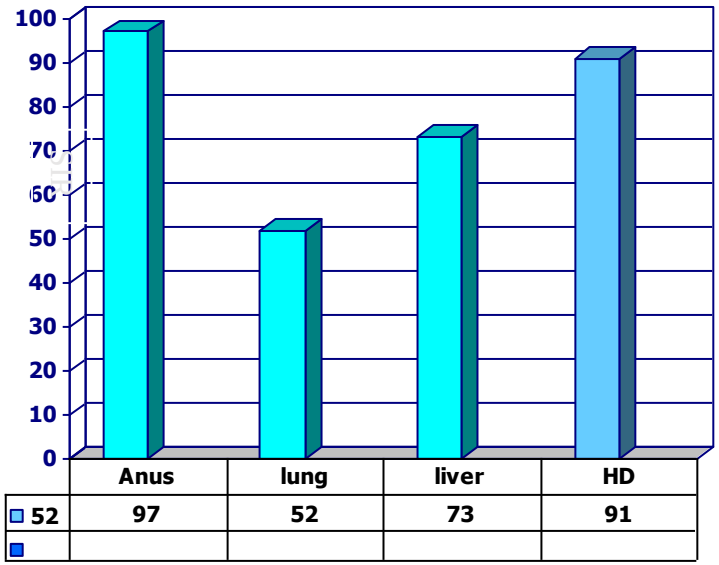
Virus-related Cancer	SIR (95%CI)
Anus	**28 (**20.3-38.9)
Vulva-Vagina	**14 (**7.6-26.4)
Penis	**7.6** (3.4-15.7)
Hodgkin L.	**10.8** (8.9-13.7)
Eye and Adnexa	**8.9** (2.9-27.3)
Liver	**5.5** (4.4-7.2)
Skin nonmelanoma	**4.4** (2.8-6.9)
Lung	**2.48** (1.94-3.16)
Oropharynx	**2.23** (0.25-20.1)
Larynx	**2.21** (1.50-3.2)

Yuan T et al Thelancet.com 2022

Excess Cancers Among 859.522 people living with HIV in the United States (2010)

NADCs

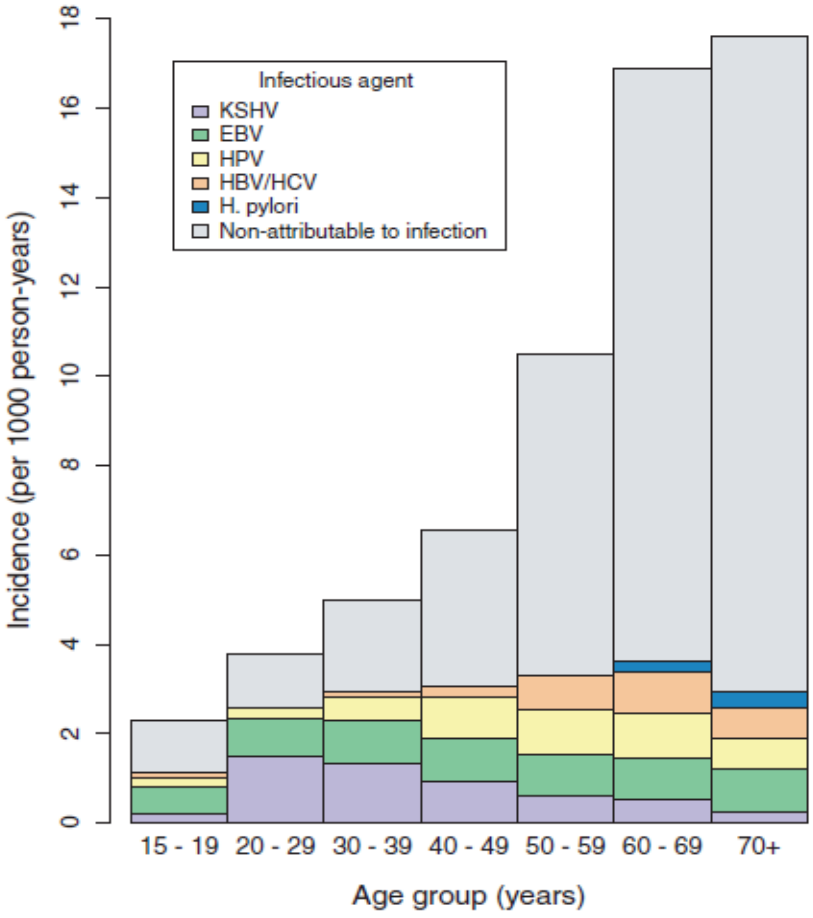
Excess of Non-AIDS-Defining Cancers %



NADCs	DEFICIT %	(95% CI)
Breast	- 42	(-42 to -14)
Prostate	- 41	(-53 to -26)

Robbins H. Br J Nat Cancer Inst 2015

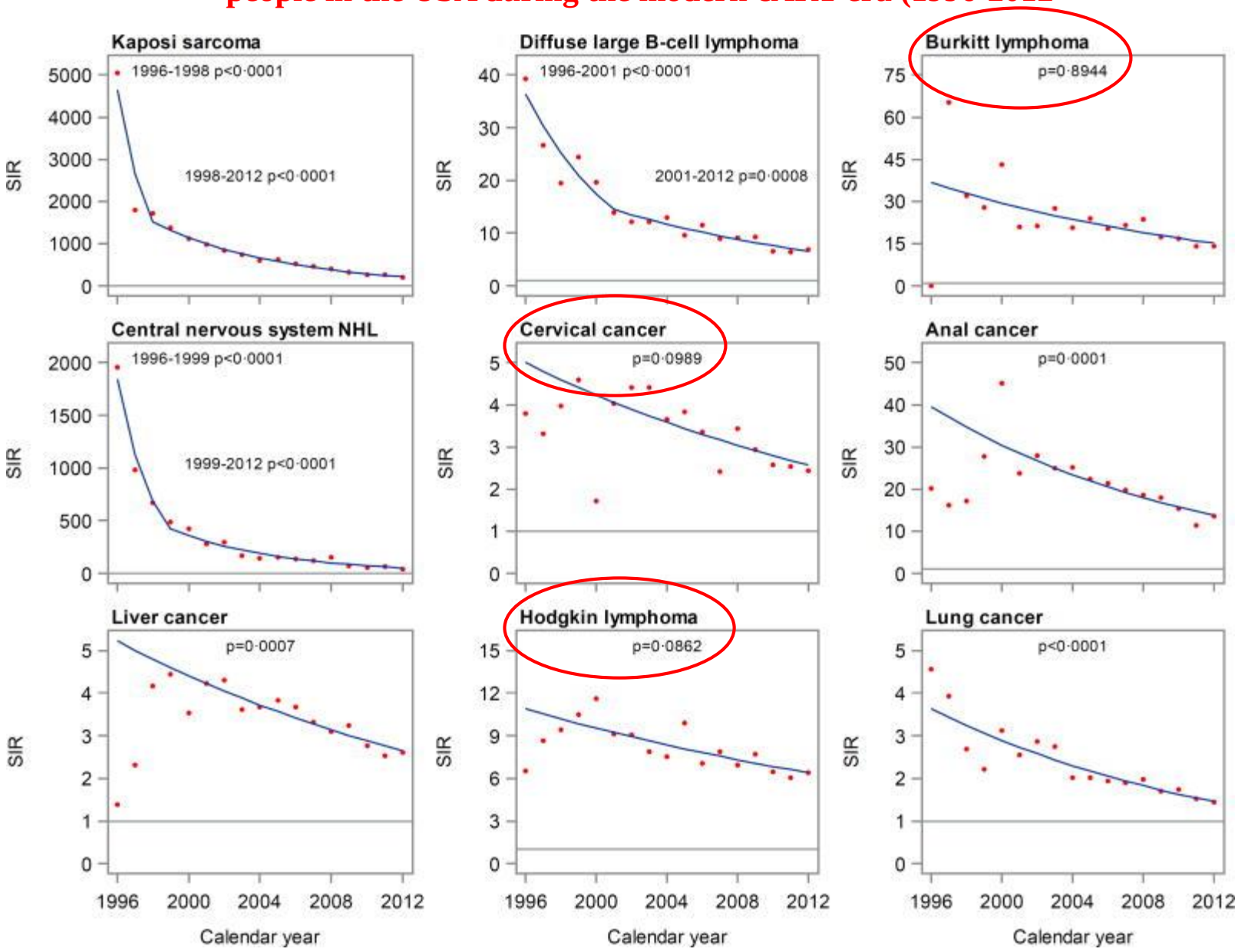
Cancers attributable and non-attributable to infections among adults with HIV in the United States (2008)



The incidence rate of cancer non-attributable to infection, including breast and prostate cancers steeply increased with age,.

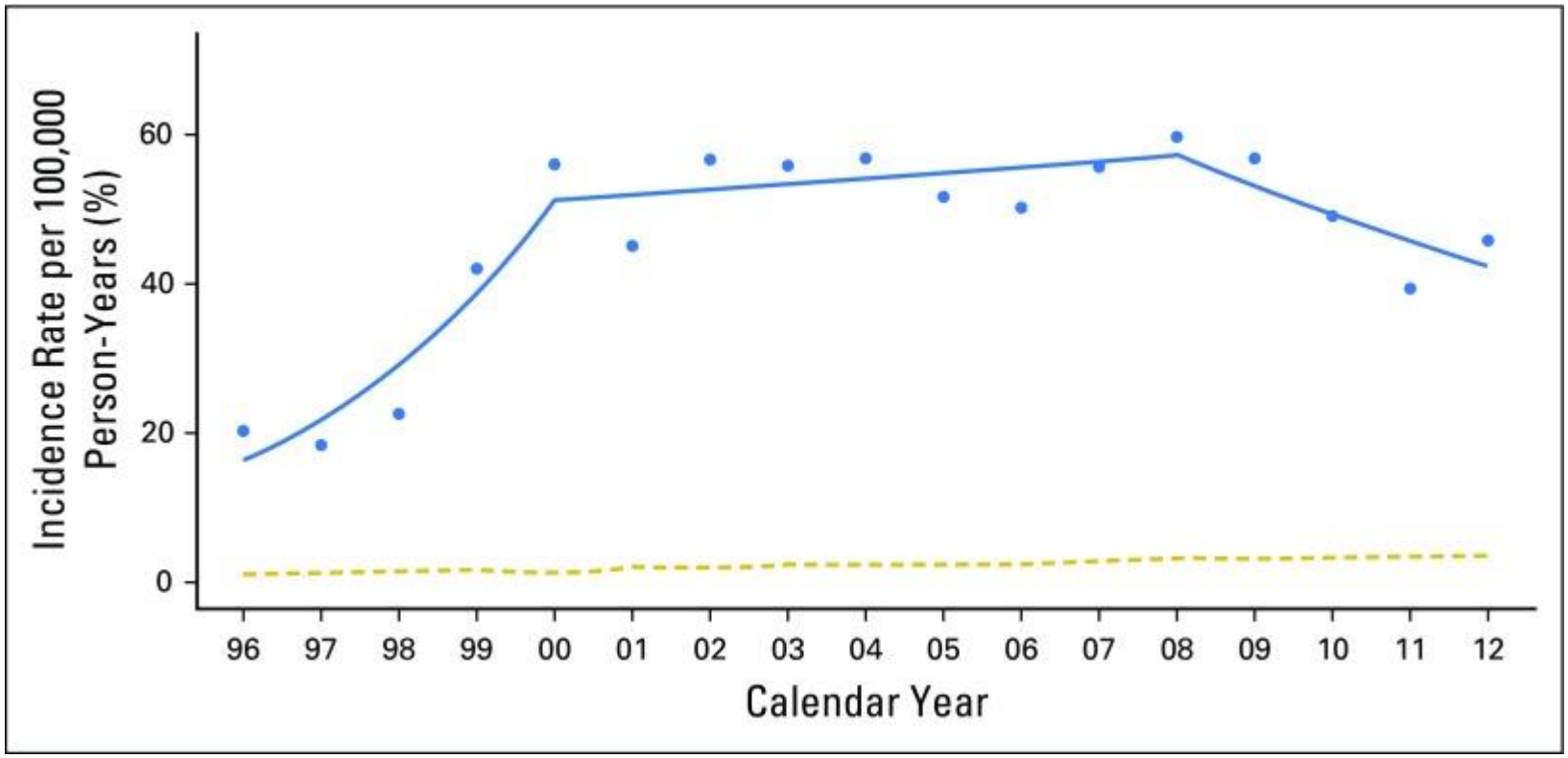
de Martel C et al AIDS 2015

Calendar Trends in Standardized Incidence Ratios (SIRs) for selected cancers in HIV-infected people in the USA during the modern cART era (1996-2012



Hernandez-Ramirez RU et al Lancet HIV 2018

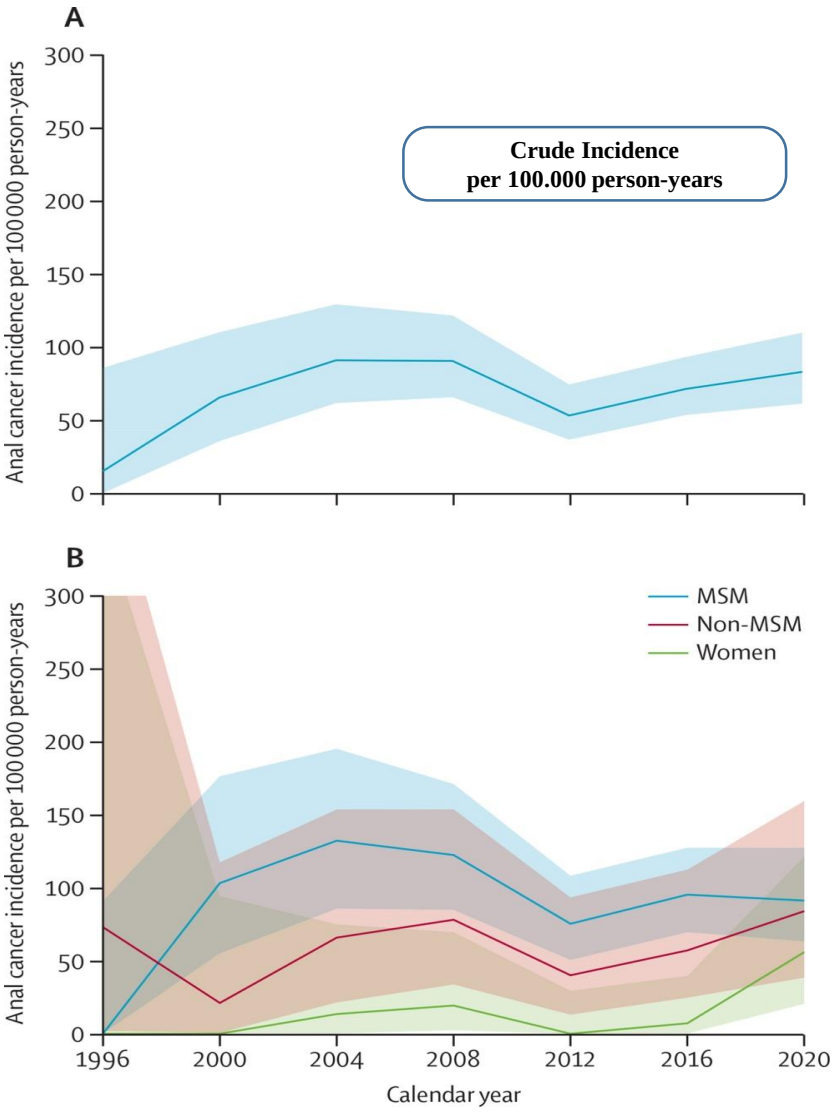
Anal Cancer Risk among 447.953 People with HIV Infection in the USA (1996-2012)



Anal cancer incidence increased steeply during 1996 to 2000 (annual percentage change +33%), reached a plateau during 2001-2008 and declined during 2008-2012 (annual percentage change -7%. Groups at high risk (i.e MSM) may benefit from screening.

Colon-Lopez V et al J Clin Oncol 2018

Anal Cancer Incidence among 28.175 Persons Living with HIV in the Netherlands (Athena Cohort-1996-2020)



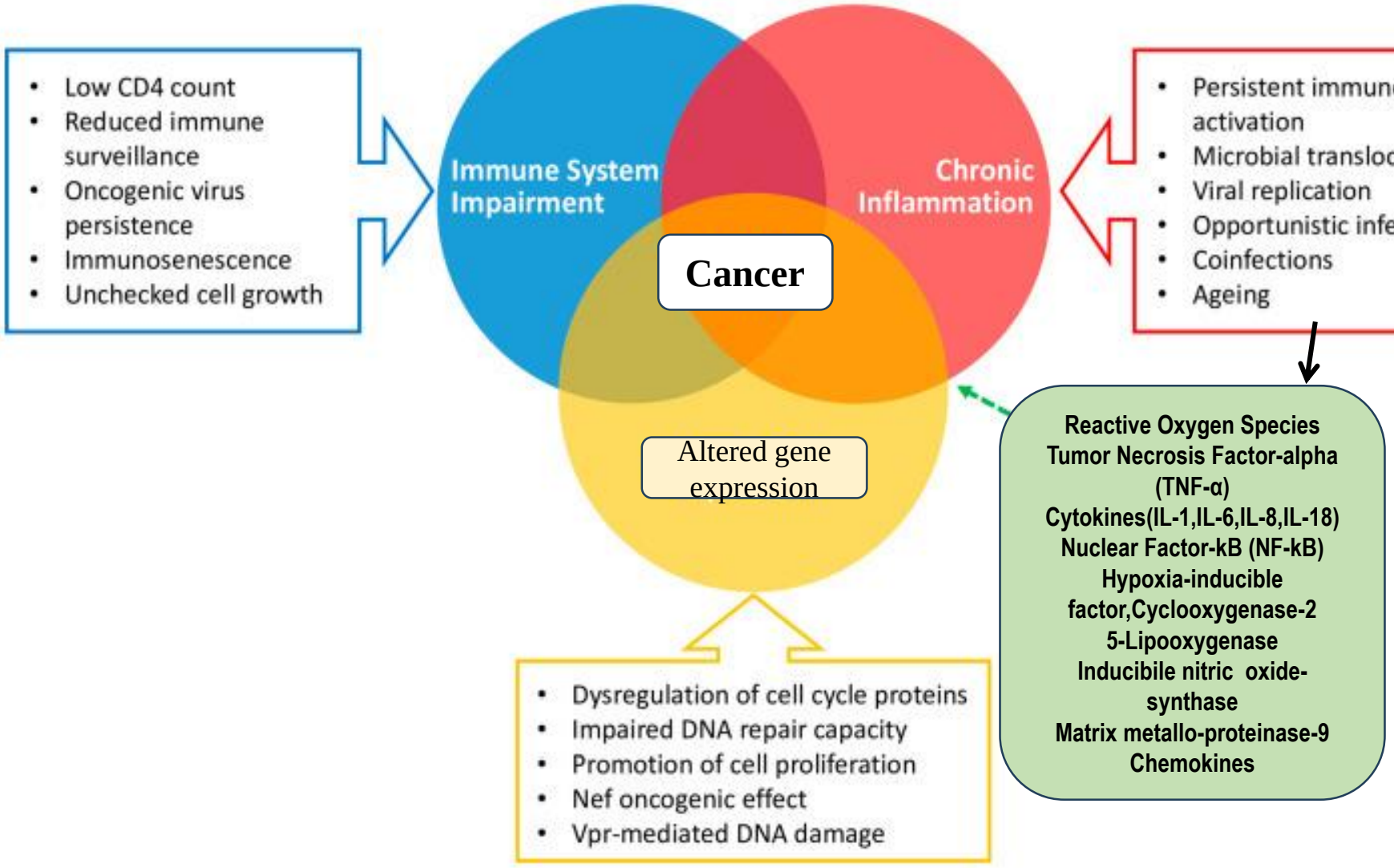
Age-adjusted Incidence Rate Ratios (RR) (95% CI) over time

	MSM	Men non-MSM	Women
1996-2005	1 (ref)	1 (ref)	1(ref)
2006-2012	**0.75** (0.49-1.14)	**0.98** (0.38-2.55)	**1.03** (0.09-11.53)
2013-2020	**0.62** (0.41-0.92)	**1.03** (0.42-2.55)	**1.94** (0.22-16.98)

As anal cancer incidence is slowly declining in MSM but not in non.MSM and women, health-care professionals should not focus only on MSM for anal cancer prevention

van der Zee RP Lancet HIV 2023

Major Features of Cancer Pathogenesis in PLWH



Dickey B et al JAIDS 2023; Omar A et al. Cancers 2024

Chronic Inflammation and Cancer

There is a strong link between chronic inflammation and cancer.

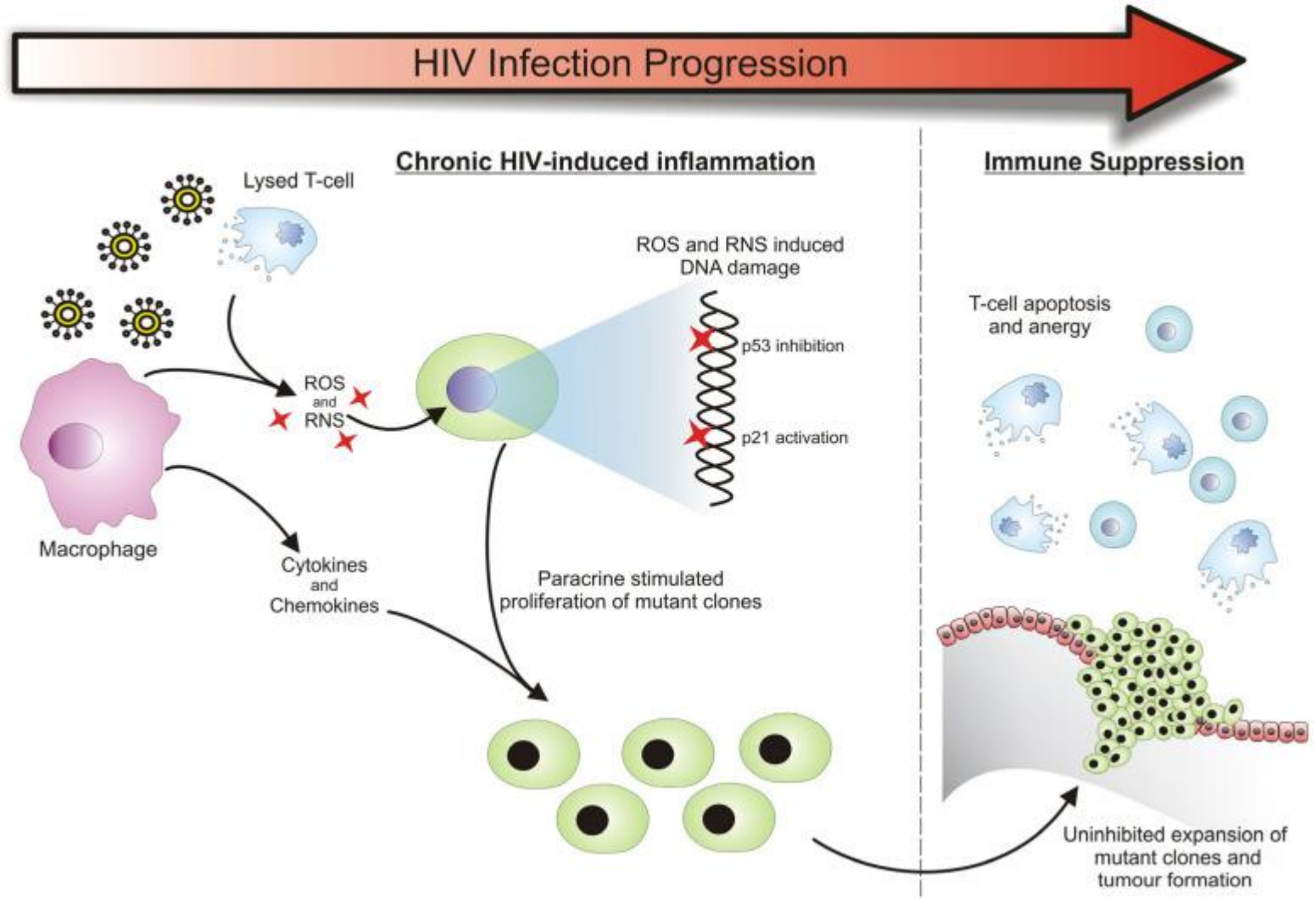
-An inflammatory microenvironment, either conferred by an underlying overt or smoldering inflammatory condition constitutes a prerequisite and fuel to essentially all cancer.

-Chronic inflammation predisposes to the development of cancer and promotes all stages of tumorigenesis.

- In the general population, around 15-20% of all cancer cases are preceded by infection, chronic inflammation, or autoimmunity at the same tissue or organ site.

- -Moreover, cancers previously defined as “non-inflammatory” recruit immune cells and increase expression of inflammatory mediators to support tumour growth and re-shape tumour microenvironment to their benefit

HIV-related Chronic Inflammation in the Development of Cancer



Chronic inflammaging leads to the depletion of the naïve T-ceell population and the accumulation of differentiated and anergic T-cells.
Large amounts of reactive oxygen and nitrogen species (ROS and RNS) can initiate the carcinogenic process by damage to cellular genomic DNA and genetic instability.In addition, cytokines, chemokines and growth factors can support the growth and proliferation of the transformed cells

HIV-related Kaposi Sarcoma

Major Features

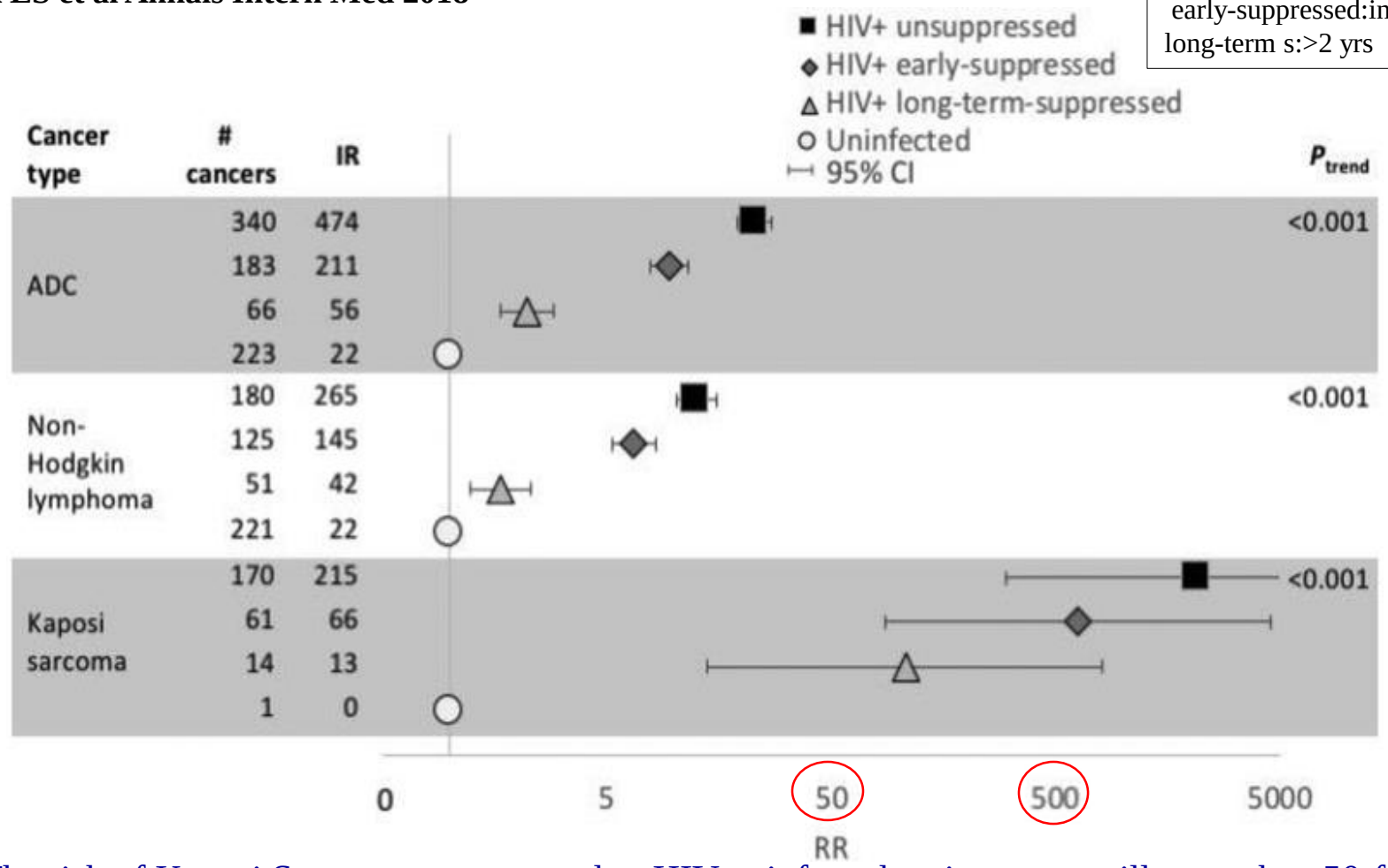
Clinically, Ks most commonly involves adults with a male predilection, and lesions evolve from early macules (patch stage) to plaques (plaque stage) and larger nodules (tumour stage). They typically involve mucocutaneous sites but may also involve visceral locations (gastrointestinal tract >50%, lung 20%).All organs may be affected by KS

Heterogeneous clinical course ranging from an indolent state to a severe, progressive disease leading to significant morbidity and mortality

Viral Suppression is Associated with Decreased Cancer Incidence in the Veteran Prospective Cohort (1999-2015)

Park LS et al Annals Intern Med 2018

early-suppressed:initial 2 yrs
long-term s:>2 yrs



The risk of Kaposi Sarcoma as compared to HIV-uninfected patients was still more than 50-fold in PLWH despite long-term viral suppression and more than 500-fold in those with early-suppression.

Deleterious effects of HIV infection persist i the presence of long-term cART, such as chronic immune activation/inflammation or immune-senescence.

Standardized Incidence Ratio (SIR) for AIDS-Defining Cancers in PLWH on cART with CD4≥500/µL and Persistent (≥2yrs) Controlled HIV Viremia

Results from the FHDH-ANRS CO4 Cohort (France 1992-2009)

Cancer Type	N° of PY o HIV Patients	IR in HIV-pos.Pts (95%CI) per 100.000 PY	IR in HIV-neg Pts (95%CI) per 100.000 PY	SIR (95% CI)
Kaposi Sarcoma	55.633	**21.6** (11.2-37.7)	**0.6** (5-6)	**35.4** (18.3-61.9)
NHL	56.493	15.9 (7.3-30.2)	13.8 (13.5-14.1)	1 (0.4-11.8)
Cervical cancer	14.825	20.2 (4.2-59.1)	12.9 (12.5-13.4)	……..

PY:person-year; IR: Incidence Rate;

In PLWH with restored immunity and persistent controlled HIV viremia, the risk remained significantly elevated for Kaposi Sarcoma and was similar to that of the general population for NHL

Hleyhel M et al CID 2013

CD4/CD8 Ratio and the Risk of Kaposi Sarcoma in 56.708 HIV-Suppressed PLWH. 20 European Cohort Studies (2000-2014)

Caby F et al CID 2021

	Whole population (221 incident KS)	PLWH with CD4>500 at baseline (65 incident KS)
Immune-Virological Factors	**Adjusted °Hazard Ratio (95% CI)**	**Adjusted° Hazard Ratio (95% CI)**
CD4/CD8 Ratio from baseline*:		
CD4/CD8:1	1	1
CD4/CD8: 0.8	1.18 (0.98-1.42)	**1.38** (1.00-1.91)
CD4/CD8: 0.5	**1.64** (1.10-2.45)	**2.35** (1.33-4.14)
CD4/CD8: 0.3	**2.02** (1.23-3.31)	**3.27** (1.60-6.56)
CD4 count/µL from baseline*		
350	**1.57** (1.09-2.25)	
500	1	1
800	0.68 (0.39-1.20)	0.49 (0.22-1.09)
1000	0.74 (0.38-1.45)	0.33 (0.11-0.97)
Virological Failure from baseline	**2.77** (1.90-4.06	**2.69** (1.31-5.29)

°adjusted for age,sex,risk group,calendar period of cART and virological failure; *within 6 monthsfollowing virological control

HIV-related immune activation, reflected by CD4/CD8 ratio,may contribute to Kaposi Sarcoma development in PLWH on efficient cART

Evolving Spectrum of Kaposi Sarcoma (KS) in the cART era

Major features:
-High prevalence of systemic symptoms
- High HHV8 viral load
- Rapidly progressive KS
-High mortality
-Treatment: chemotherapy and/or immunotherapy +cART

KS+KICS
KS+MCD
KS+PEL

Major features:
Skin and visceral involvement

-Aggressive course
-Good prognosis in the cART era

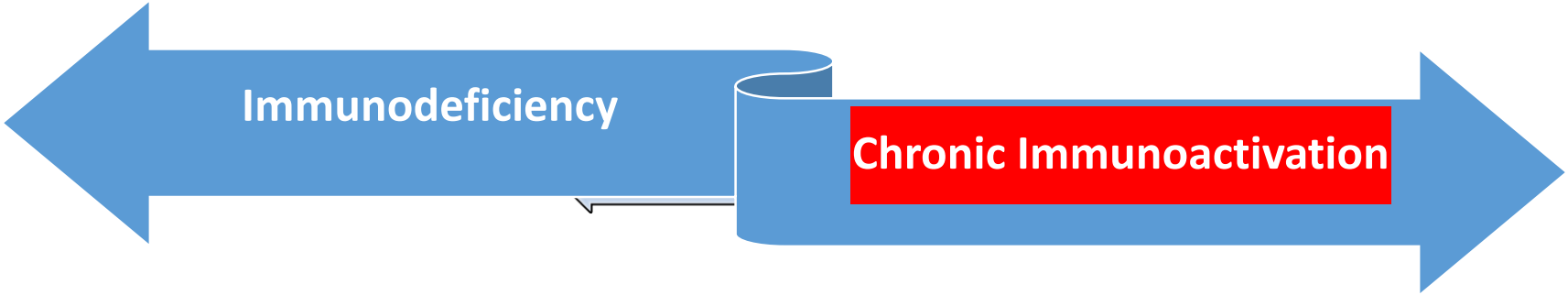
Low CD4 count and/or high HIV viremia

Major features:
***KS progression or unmasking KS**
*Prevalence:10-40%
*Agressive clinical course
*High mortality
*Treatment: immediate chemotherapy +cART

IRIS-KS

Major features:
*Prevalence 19-20%
*Chemotherapy refractory /relapsing disease

KS with high CD4 count and undetectable HIV-RNA



Kaposi Sarcoma in Virally Suppressed People Living with HIV and with High CD4 count

The proportion of KS cases occurring in virally suppressed PLWH and with high CD4 count is rising in the cART era

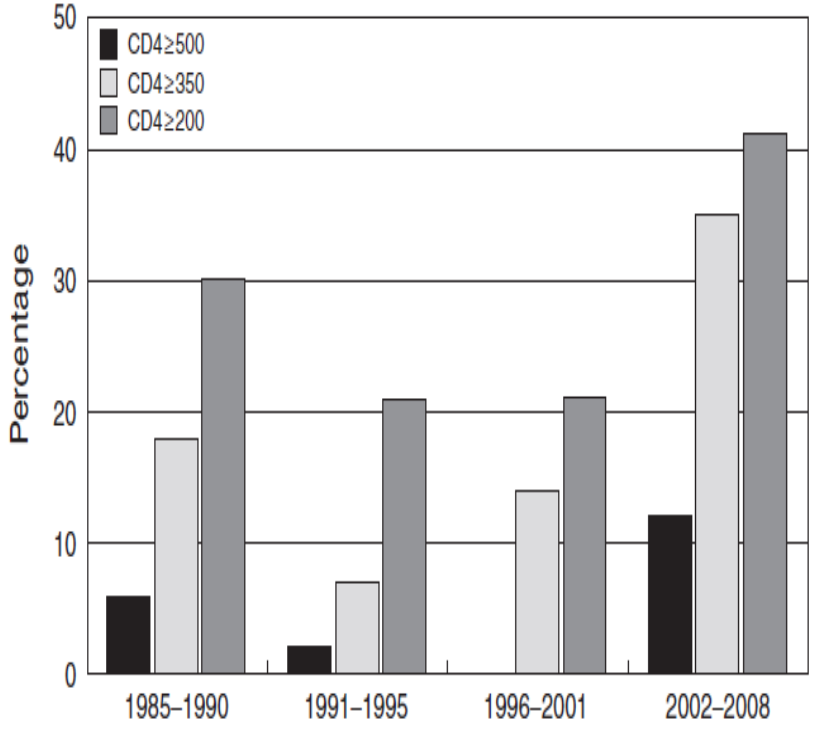


Fig. 1. CD4 cell count at diagnosis of Kaposi's sarcoma during the course of the HIV epidemic (1985–2008).

CD4 cells	Cluster KS % (N°19)	HIV+ Controls % (n°47)	P value°
CD57+	41.5	27.7	0.005
CD28-	60.5	51.3	0.04
CD27+CD28+ CD45RA*	11.3	20.7	0.02
CCR5	43.1	28.3	<0.001

Increased frequency of T cells with Immunosenecence phenotype and lower naive T cells* are associated with Kaposi's Sarcoma among effectively treated patients

Crum-Cianflone NF et al, AIDS, 2010;Unemor P AIDS 2013

Kaposi Sarcoma in Virally Suppressed PLWH with High CD4 Count
Major Case Series-I

	Mani D (2009)	Palich R (2020)	Severin D (2021)
Total n°	20	21	12
Sex: M/F n°	19/1	17/4	12/12
Age ,yrs, median	42 (25-69)	54 (35-61)	54 (38-60)
CD4 Count/µL (range)	483 (300-625)	449 (211-625)	723 (520-881)
CD4 /µL nadir, median	216 (4-431)	196 (81.329)	NA
cART Duration, median	5 yrs (1-12)	≥12 months	NA
Site of Disease n° (%) Skin Lymph nodes Visceral involvement	 12 (60) 0 8 (40)	 21 (100) 6 (27) 11 (52)	 12 (100) 1 (8) 1 (8)

Mani DJ et al Int Assoc Physicians AIDS Care 2009; Palich R et al CID 2020; Severin D et al AIDS 2021

Kaposi Sarcoma in Virally Suppressed PLWH with High CD4 Count Major Case Series-II

	Mani D (2009)	Palich R (2020)	Severin D (2021)
Total n°	20	21	12
Treatment: n° (%) Chemotherapy Local Therapy	 14 (70) 4 (20)	 21 (100) 1 (5)	 2 (17) 4 (33)
Response: n° (%) CR SD NR	 13 (65) 4 (20) 3 (15)	 6/16 (37) 6/16 (37) 4 (25)	 NA
Followup Duration Media,mos	39 (6-120)	17 (9-20)	NA
Recurrences n° (%)	NA	13 (65)	NA

KS in virally suppressed HIV patients represents a clinical and biological entity tha is still poor understood. These clinical forms are a therapeutic challenges without short-term improvement of anti-HHV8 immunity and no active replication of HIV to control.

Mani DJ et al Int Assoc Physicians AIDS Care 2009; Palich R et al CID 2020; Severin D et al AIDS 2021

A Comparative Study of Classical and HIV-Viremic and Aviremic KS (France 2000-2007)

N° of Patients: Classical KS:n° 62 ; Viremic KS:68; Aviremic KS: 12

Major Results

There were no significant differences between aviremic AIDS-KS and Classical KS (CKS) groups in terms of clinical presentation, except for the age at diagnosis (54 vs 71 yrs ,$P < 0.0001$) .

Both groups predominantly had a localized indolent disease, but 17% of aviremic AIDS-KS and 12% of CKS had disseminated disease (stage III and IV Kriegel). The distribution of skin lesions was similar in both groups, in lower limbs for 75% in aviremic AIDS-KS and 84% in CKS. Most persons presented less than five skin lesions (67% in aviremic AIDS-KS and 54% in CKS)

There was a tendency for viremic AIDS-KS PLHIV to have more aggressive presentation in comparison with aviremic AIDS-KS, as 14 PLHIV (22%) had a Kriegel score of 4 versus 1 PLHIV (8%) for aviremic AIDS-KS

Severin D et al AIDS 2021

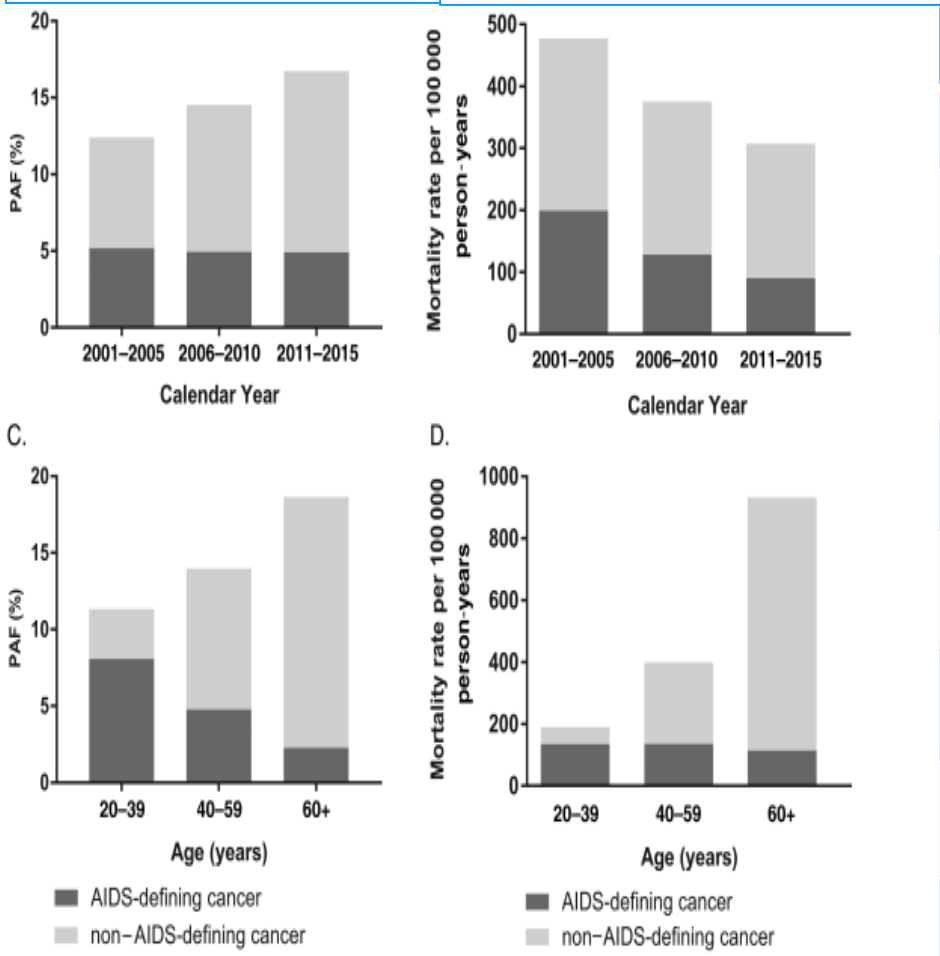
Survival of major HIV-Cancer

What is the natural history of cancers in HIV-suppressed PLWH on cART?

Deaths Attributable to Cancer in the US HIV Population (2001-2015)

31.614 cancers /521.623 Persons Living with HIV- Median followup: 6.8 yrs

PAF (%) | **Mortality Rate per 100.000 py**



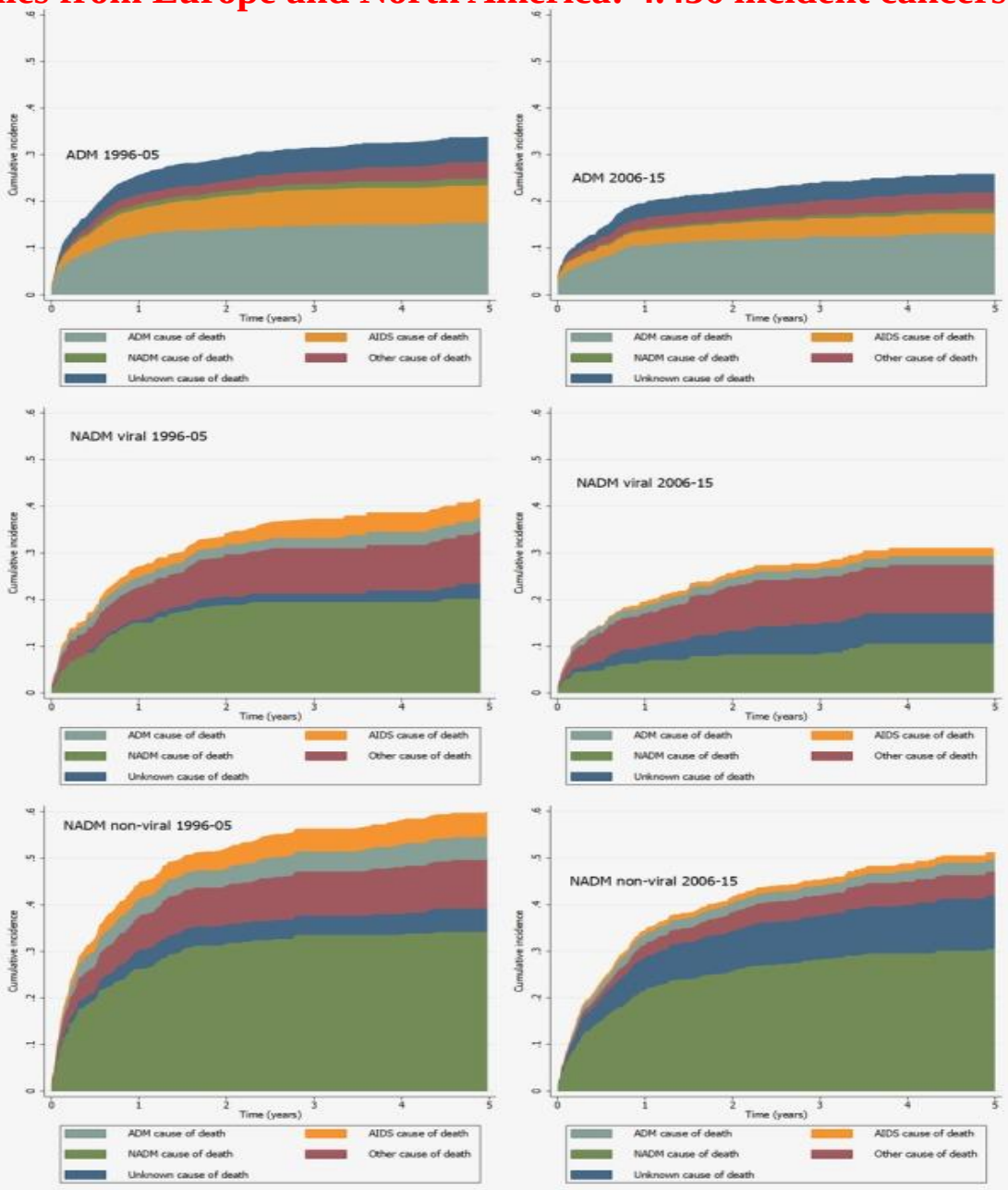
Cancers	PAF (%) (95% CI)
All cancers	**14.5** (13.6-15.4)
AIDS-Defining Cancers	**5** (4.4-5.6)
Non-AIDS Def Cancers	**9.2** (8.5-9.9)
Cancer Site	
NHL	**3.5** (3.0-3.9)
Lung	**2.4** (2.0-2.7)
Cervix	**2.0** (1.0-4.0)
Kaposi Sarcoma	**1.3** (8.5-9.9)
Liver	**1,1** (0.9-1.6)

Population-Attributable Fractions (PAF):proportional contributions of cancer to mortality

Although cancer mortality is declined over time, it remains high and represents a growing fraction of deaths in the US HIV population. NHL is a leading cause of cancer-attributable deaths

Horner MJ et al CID 2021

Cause-specific Mortality after Diagnosis of Cancer among 83,585 HIV-positive Patients: 10 Cohort Studies from Europe and North America: 4.436 incident cancers (Mortality Rate Ratio, MRR)

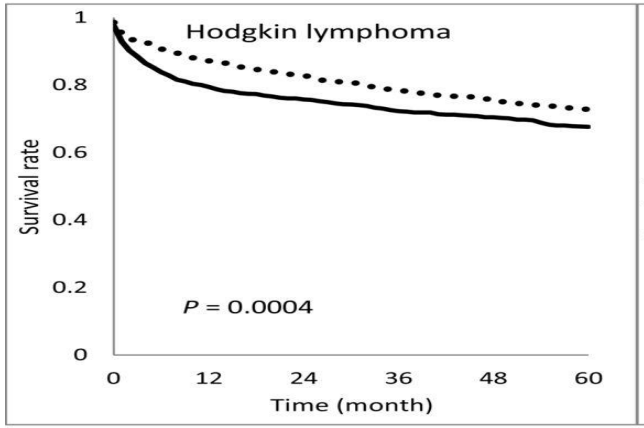


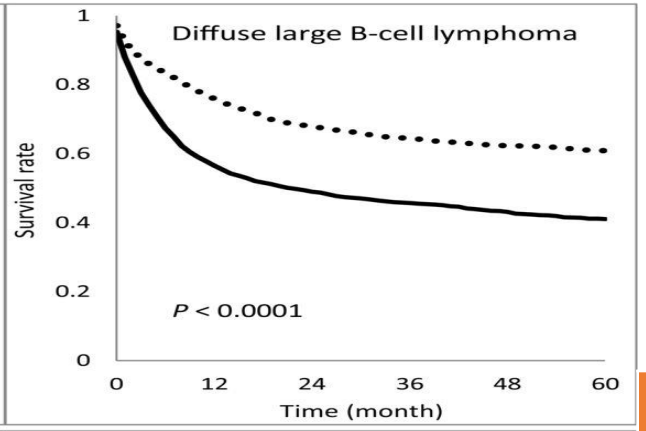
2006-2015 vs 1996-2005	
Cancer	**Adjusted MRR (95% CI)**
ADM	**0.77** (0.61-0.86)
Viral NADCS	**0.76** (0.54-1.07)
Nonviral-NADCs	**0.84** (070-1.00)

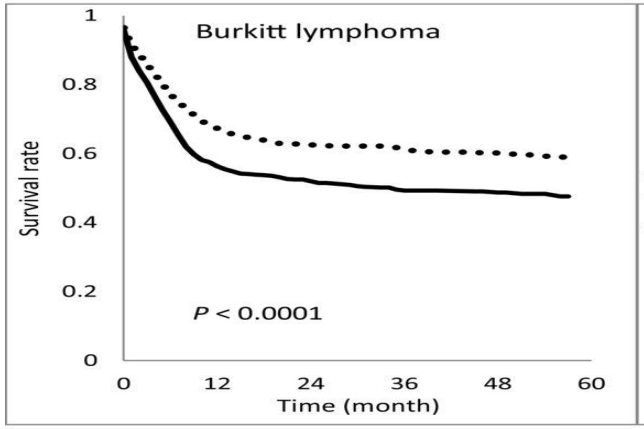
adjusted for sex, risk group,age,CD4 count,HIV viral load at cancer diagnosis

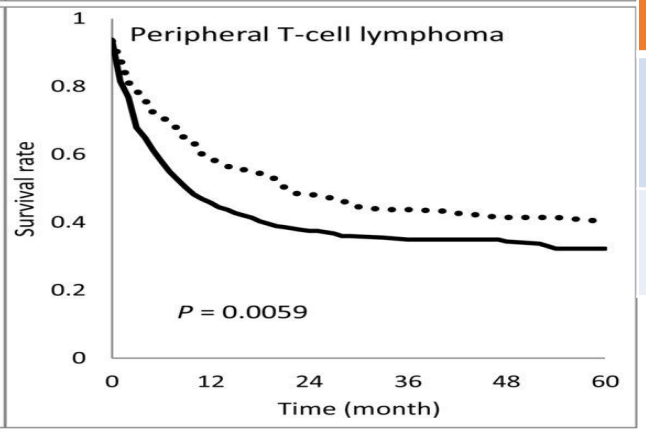
Trickey A Int J Cancer 2020

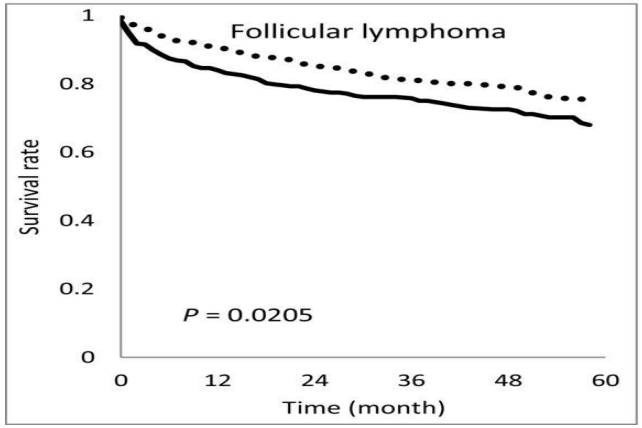
Overall Survival by HIV status among 179.520 Patients with Lymphoma - (USA-National Cancer Database 2004-2011)









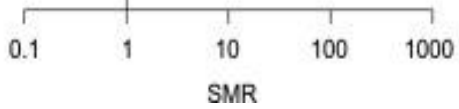


	HIV-pos Pts	HIV-neg Pts
No Therapy %	16*	8
CT use %	82*	87

*p<0.0001

Meta-analysis of Standardized Mortality Ratio (SMR) for non-AIDS-defining Cancers among People Living with HIV (1992-2022)

Type of Cancer	SMR (95%CI)	Number of studies	Number of effect sizes	Number of observed cancers	Heterogenity I^2(%)
A. Infection-related cancers					
Anus and anal canal	124.07 (27.31-563.72)	2	3	43	92
Hodgkin lymphoma	41.03 (2.91-577.88)	2	3	49	98
Liver	8.36 (3.86-18.11)	3	10	342	76
Stomach	1.74 (0.49-6.16)	2	3	18	80
B. Non-infection related cancers					
Trachea, bronchus, and lung	3.95 (1.52-10.26)	4	9	605	87
Leukemia	2.62 (0.70-9.83)	2	2	14	83
Brain and central nervous system	3.82 (1.01-14.49)	2	2	28	92
Pancreas	1.27 (0.59-2.75)	2	2	17	55
Melanoma of skin	3.95 (1.28-12.20)	2	2	16	75
Colon and rectum	2.53 (0.96-6.69)	4	6	146	89



Yuan T et al Thelancet.com 2022

Outcomes after Cancer Diagnosis for HIV-Infected Patients compared to the General Population (1996-2010)

Coghill A et al J clin Oncol 2015

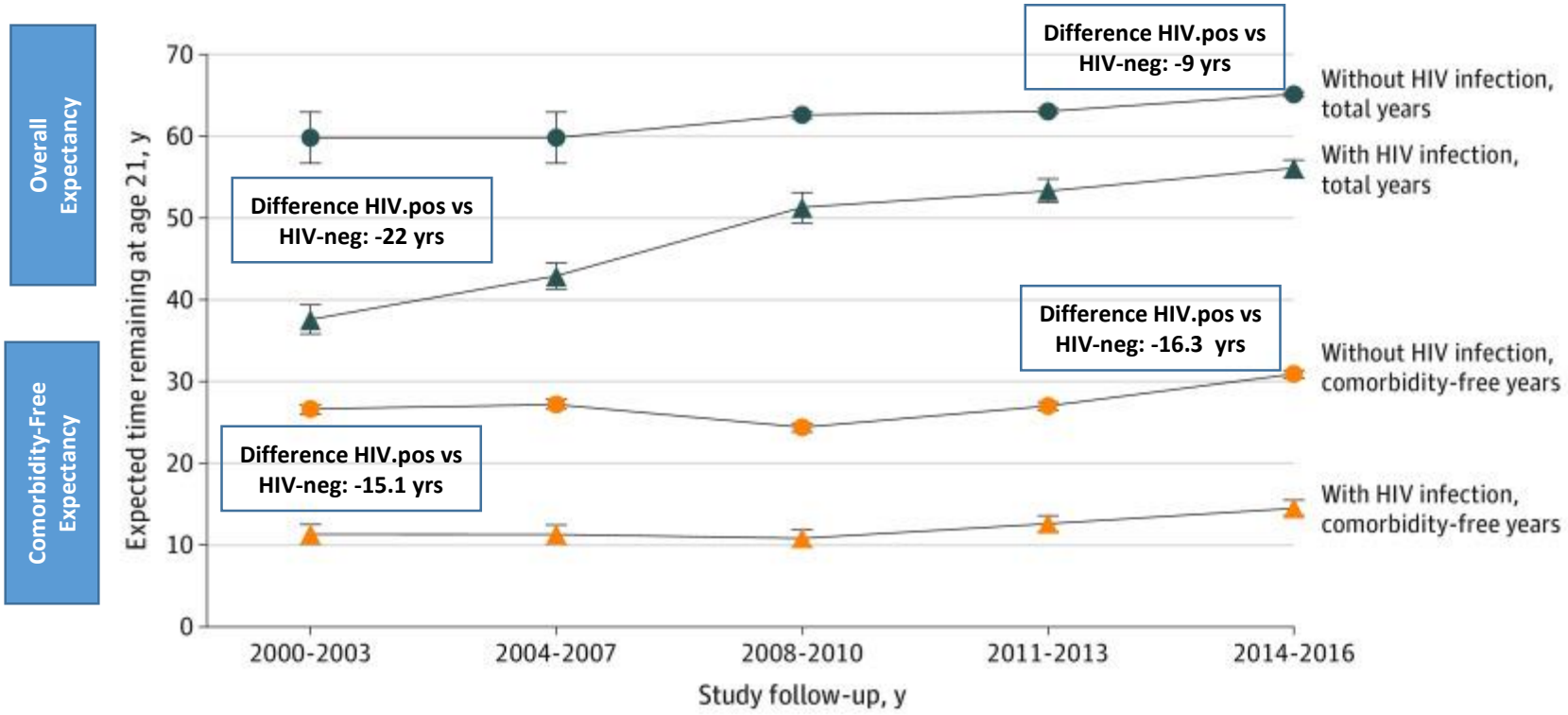
Cancer	Overal Death HR (95%CI	Cancer Specific Death HR (95%CI
Lung	**1.85** (1.73-1.97)	**1.28** (1.17-1.39)
Prostate	**2.59** (2.14-3.14)	**1.57** (1.02-2.41)
Breast	**4.62** (3.92-5.45)	**2.61** (2.06-3.31)
Colorectal	**2.26** (1.95-2.61)	**1.49** (1.21-1.84)
Liver	**1.50** (1.32-1.70)	1.17 (0.99-1.39)
Anal	**1.86** (1.60-2.16)	0.97 (0.75-1.25)
Head Neck	**2.46** (2.09-2.88)	1.31 (0.94-1.83)
Hodgkin L.	**4.19** (3.65 -491)	0.86 (0.61.21)1
DLBCL	**3.55** (3.31-3.81)	0.88 (0.76-1.01)

HIV was associated with increased cancer-specific mortality for lung, prostate,breast and colorectal cancer cancer.

Treatment Guidelines for HIV-related Cancers

Treatment Strategies	HIV-Specific Issues
The treatment strategy for cancers in patients receiving effective cART should not be influenced by HIV status	Potential pharmacokinetic interactions between cART and anticancer or supportive care drugs
All PLWH with cancer must receive cART during antineoplastic treatment	The need to maximize supportive care, particularly prophylaxis against opportunistic infections and support with hematopoietic growth factor, in high risk patients
PLWH with cancer should not be excluded from cancer clinical trials of the general population.	The management of comorbity in aging PLWH (Alert: higher comorbidity rate in PLWH compared to general population

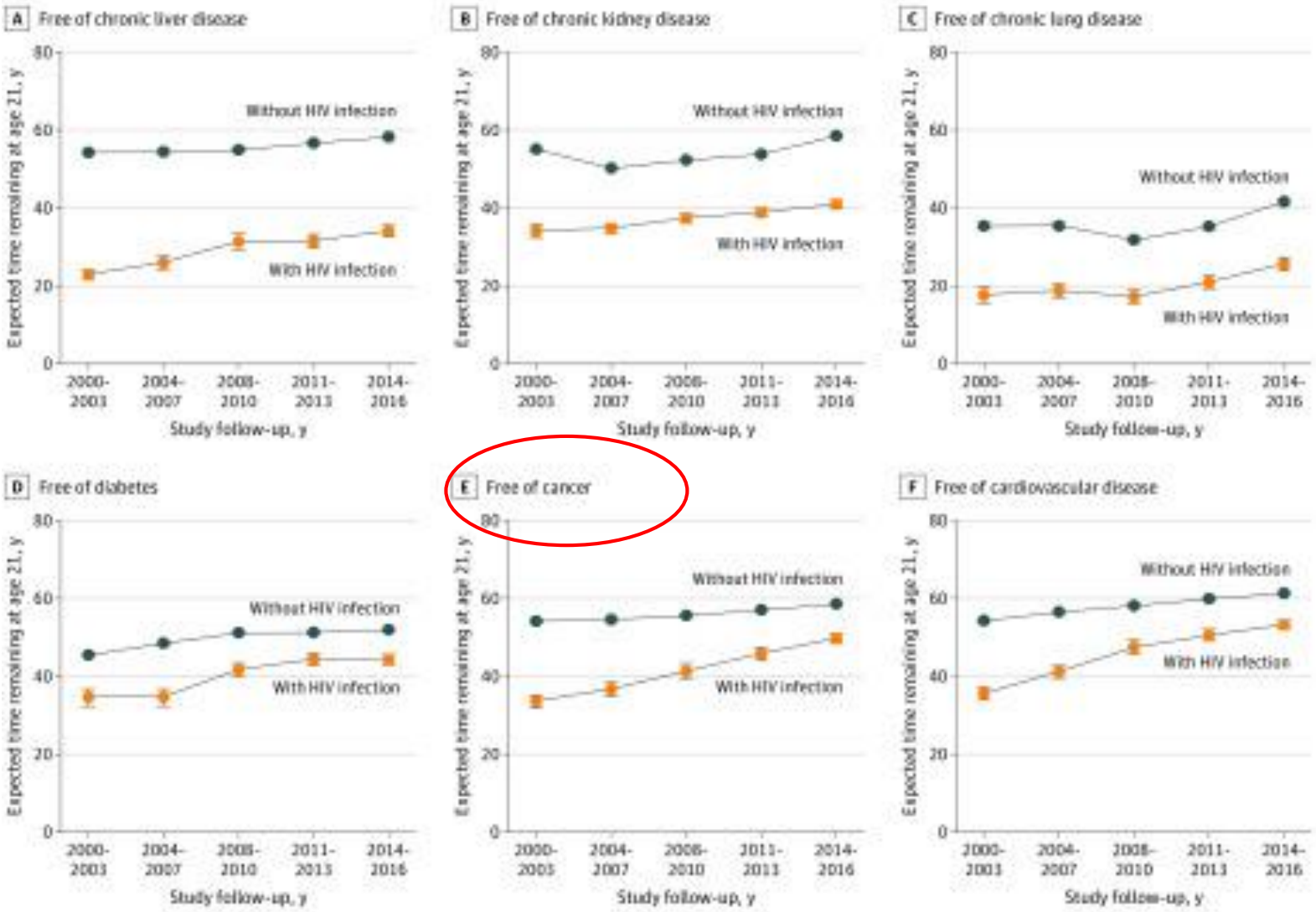
Overall and Comorbidity-Free Life Expectancy at Age 21 years for Persons with and without HIV Infection (Kaiser Permanente Chort:39.000 PLWH and 387.785 uninfected Persons) (2000-2016)



Life expectancy of adults with HIV infection may be near that of life expectancy of individuals without HIV infection, but greater attention is needed to prevention of comorbidities among Persons Living with HIV (PLWH)

Marcus JL et al JAMA 2020

Overall and Comorbidity-Free Life Expectancy at Age 21 years for Persons with and without HIV Infection (Kaiser Permanente Chort: 39.000 PLWH and 387.785 uninfected Persons) (2000-2016)



Differences in Comorbidty-Free Expectancy by HIV status persisted over time, although the gap narrowed over time for several comorbidities, most notably daibetes, cancers and cardiovascular disease The positive changes may be associated with frequent health care visits, which can facilitate access to preventive care, including cancer screening.

HIV-related Solid Tumours
focus on Screening Programs and Preventive Strategies

Major Features:

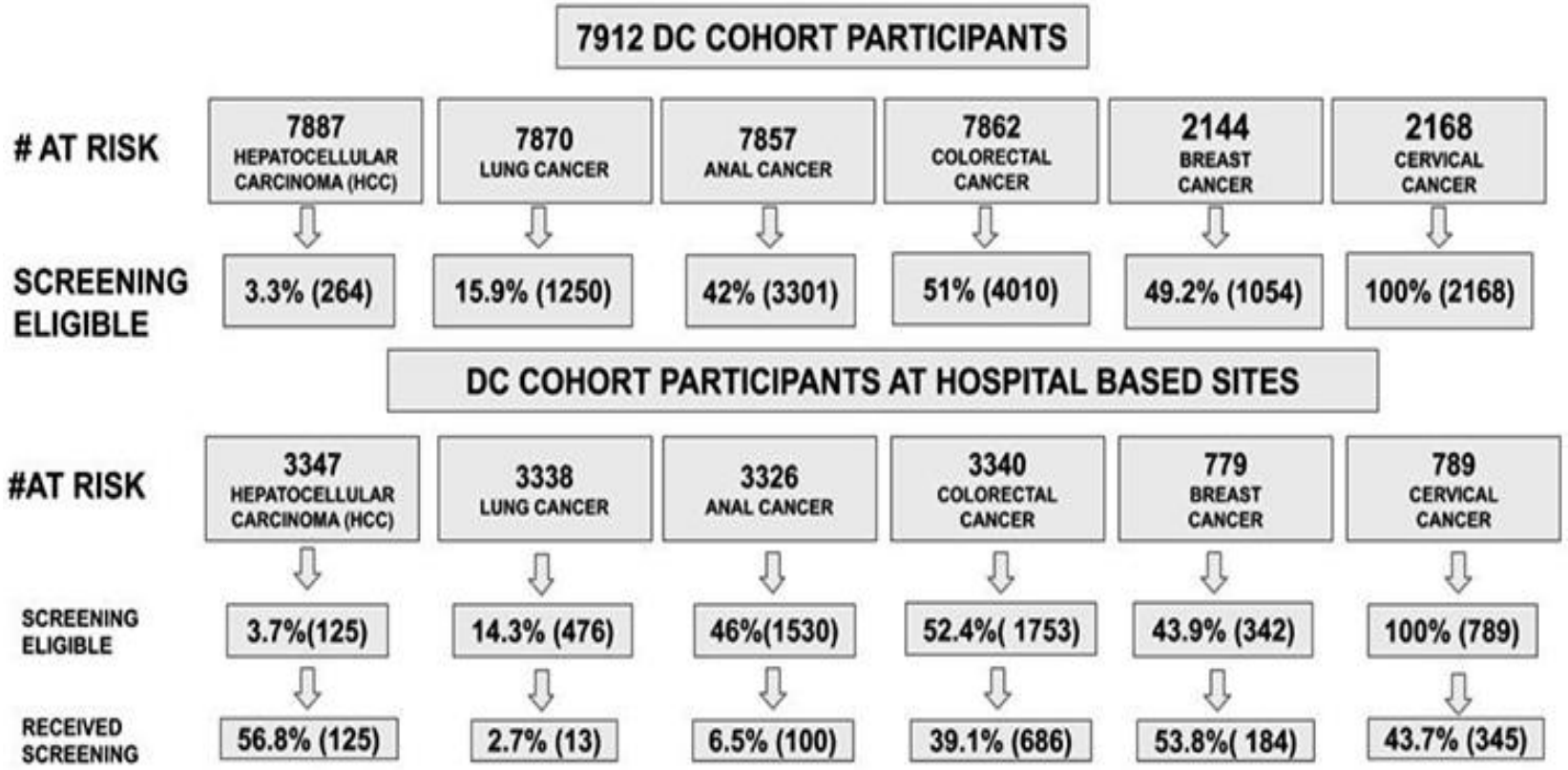
-Few trials for cancer prevention have be done to provide guidance on HIV-specific surveillance programs for patients with solid tumours.

-European and US guidelines recomended cancer screening that is appropriates for age and risk factors

-New target population: Long-term survivor patients with prior malignancies

CRO 2024

Cancer Screening Practice among a Cohort of Persons Receiving HIV Care in Washington,DC (2011-2017)



*Participants were considered at risk for HCC screening if they did not have a prior history of HCC; lung cancer if they did not have a prior history of lung cancer, anal cancer if they did not have a prior history of anal cancer, colorectal cancer if they did not have a prior history of colorectal cancer, breast cancer if they were female and did not have a history of breast cancer, and cervical cancer if they were female

**Screening eligibility was determined based on published guidelines as outlined in the methods and TABLE 1.

Despite a large elegible population there were low rates of screening. Implementation of cancer screening is an important component of care among Persons Living with HIV.

Anal Screening Programs Controversial Issues

	*Sensitivity %	*Specificity %	Level of Evidence
Anal Pap test	**84**	**32-60**	BII
hrHPV test	**94**	**35**	BII
Cotesting°	**92**	**32**	BII

*for HGAIN in MSM; °Pap test+HPV test

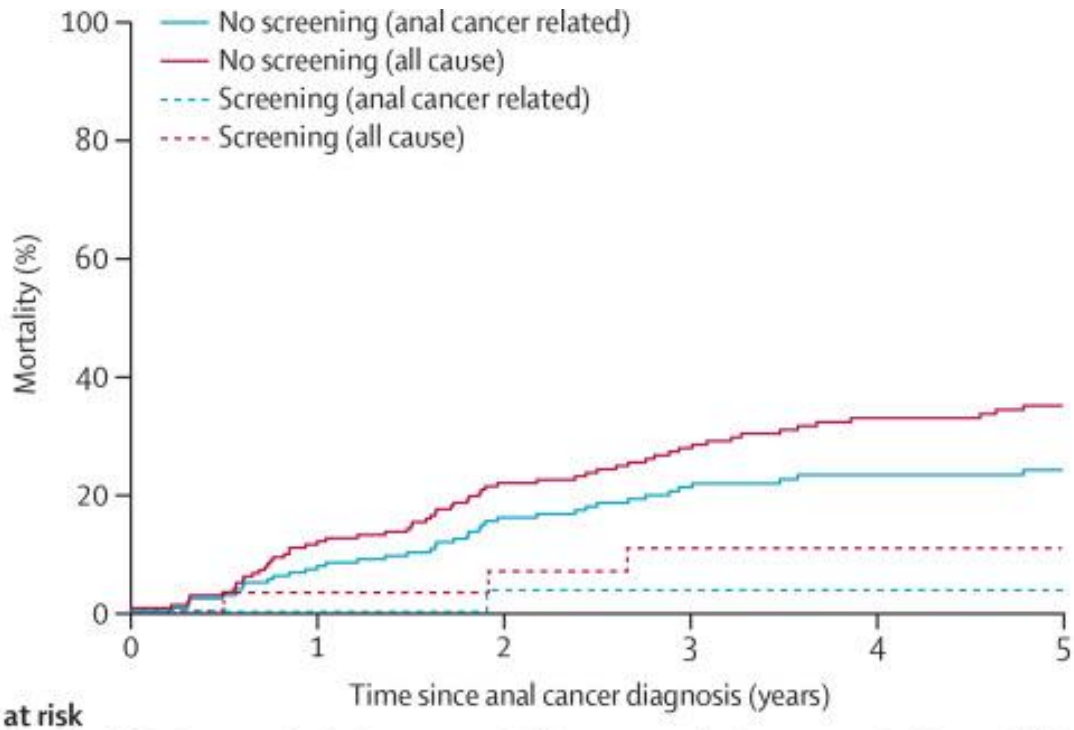
Primary screening test with hrHPV test:
-The efficency is limited in population with high HPV prevalence (e.g MSM HIV+). This strategy could be considered in setting with no cyttology infrastrutture, or to reduce HRA (for patients testing hrHPV negative).
-HPV16 genotype shows high specificity (92%), but low sensibility (44%)

- **High Resolution Anoscopy is the gold standard test for anal cancer screening**
- **Limited n°of clinicians with necessary expertise /limited equipment availability**
- **Paucity of cost-effectiveness data on anal screening approaches**

There are no formalized anal screening programs

Clark MA Int J Cancer 2022,Stier AE Int J cancer 2024)

Effect of the Introduction of Anal Screening in Persons Living with HIV: a Nationwide Cohort Study

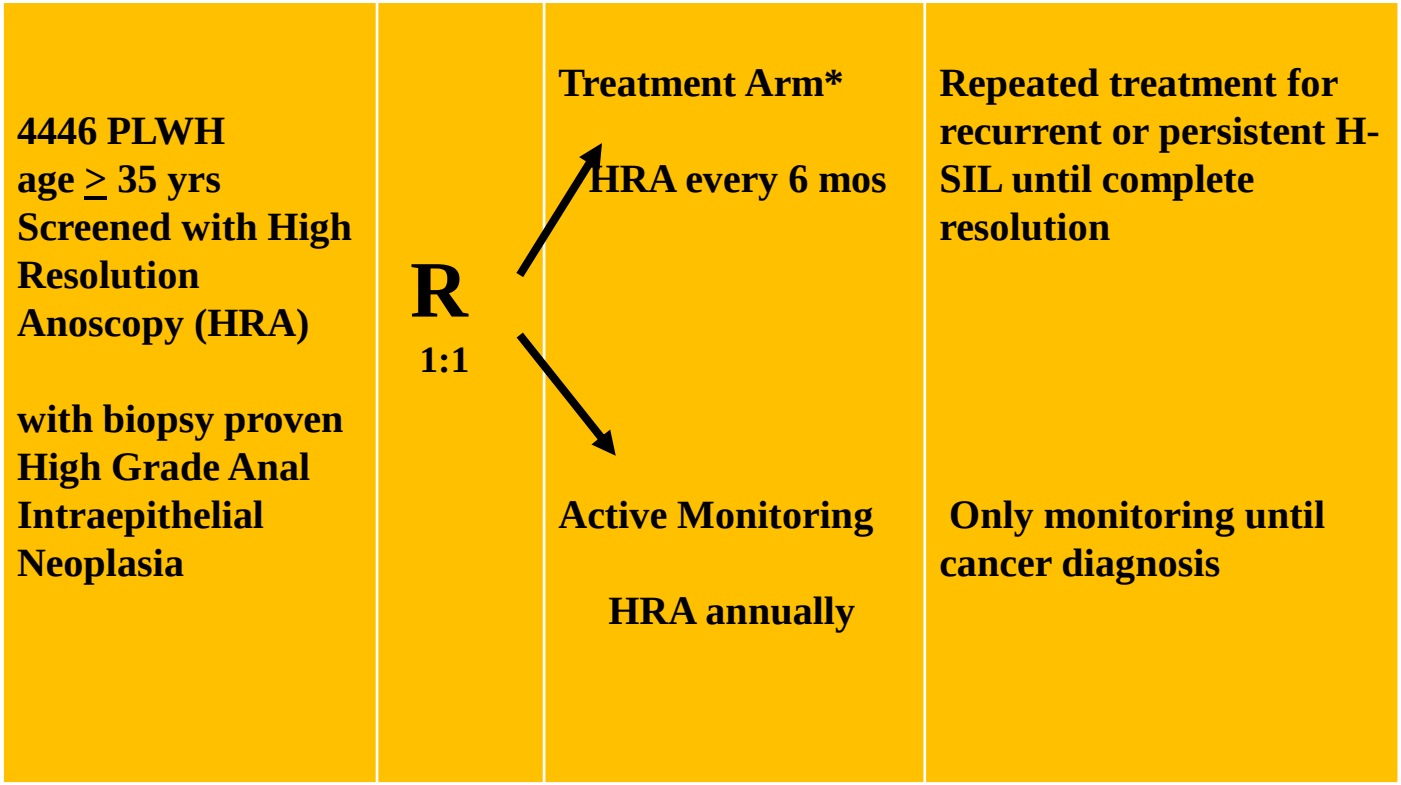


Number at risk						
No screening (anal cancer related)	187 (0)	163 (11)	141 (18)	120 (31)	100 (48)	88 (147)
No screening (all cause)	187 (0)	163 (3)	141 (6)	120 (17)	100 (29)	88 (126)
Screening (anal cancer related)	30 (0)	29 (1)	26 (3)	22 (7)	17 (12)	12 (29)
Screening (all cause)	30 (0)	29 (0)	26 (2)	22 (5)	17 (10)	12 (27)

Van der Zee RP et al Lancet 2023

CRO 2024

Anal Cancer/H-SIL Outcomes Research (ANCHOR) Study in Persons Living With HIV (PLWH) (USA 2014-2021)



* electrocautery in most cases

Palefsky J NEJM 2022

Anal Cancer/H-SIL Outcomes Research (ANCHOR) Study in Persons Living With HIV (PLWH) (USA 2014-2021)

Median Followup: 26 months

	Treatment Arm n°2227	Active Monitoring Arm n°2219
Anal cancer		
n° cases	**9**	**21**
Incidence/100.000 PY	**173**	**402**
REDUCTION 57% (95% CI 6-80%) p 0.03		
Adverse Events n° (%)	**683**	**635**

Palefsky J NEJM 2022

International Anal Neoplasia Society's Consensus Guidelines for Anal Cancer Screening

Populations for Screening

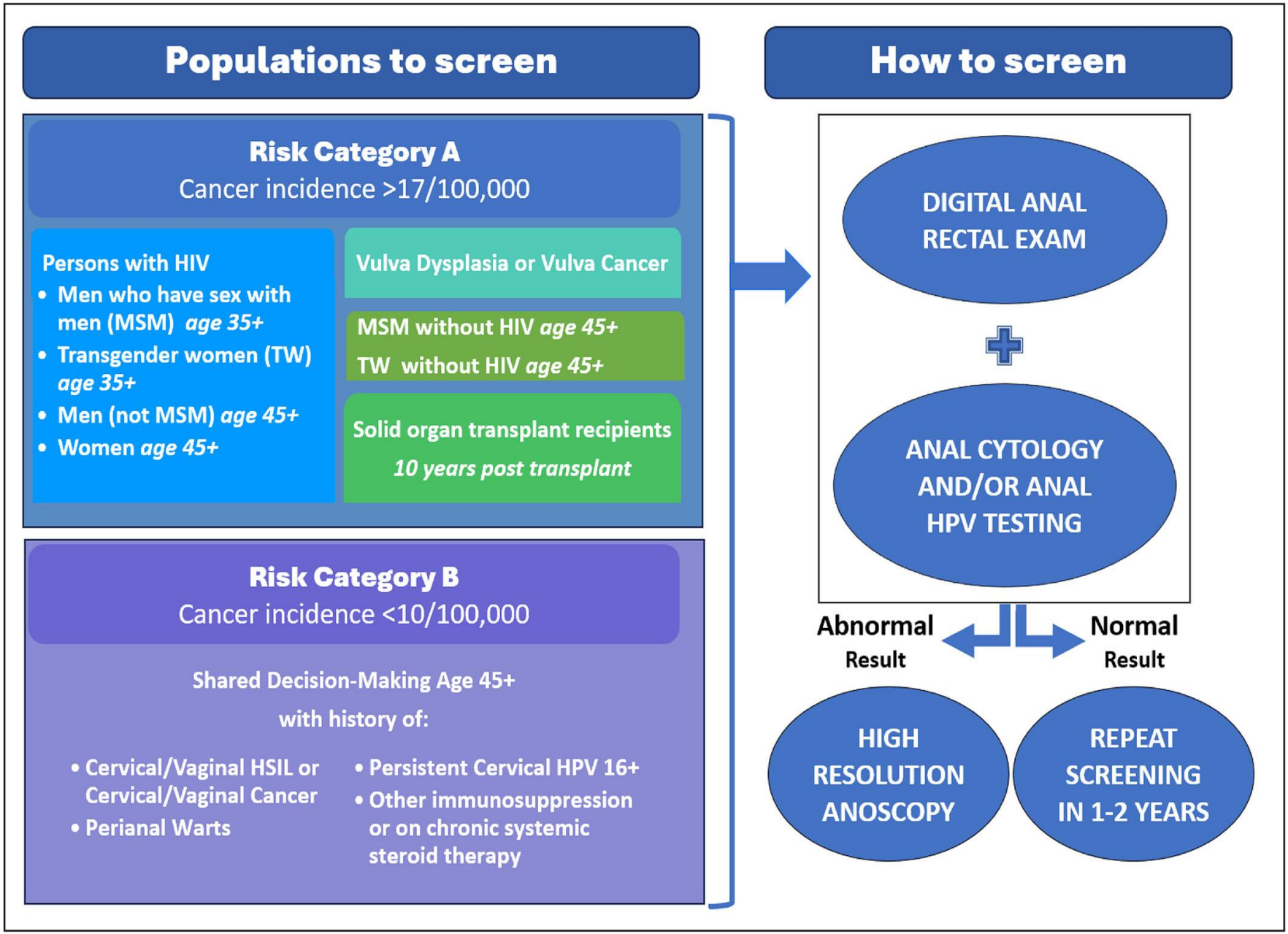
Risk Category A (incidence ≥10 fold compared to the general population

Populations	When	Anal Cancer Incidence per 100.000 person-year
MSM and Transgender Women IW) with HIV	Age 35	>70/100.000 age 30-44 >100/100-000 age 45+
Women with HIV	Age 45	>25/100.000 age 45+
MSW with HIV	Age 45	> 40/100.000 age 45+
MSW and TW not with HIV	Age 45	> 18/100.000 age 45-59 > 34/100.000 age 60+
History of vulvar HSIl or cancer	Within 1 yr of diagnosis	> 40/100.000
Solid Organ Transplant Recipients	10 yrs post-transplant	> 25/100.000

MSM: Men with sex with men: MSW: Men with sex with women

Stier EA et al Int J Cancer 2024

International Anal Neoplasia Society's Consensus Guidelines for Anal Cancer Screening



Stier EA et al Int J Cancer 2024

International Anal Neoplasia Society's Consensus Guidelines for Anal Cancer Screening:Management

Primary Screening Test	Triage Test	Results	Management	Modification for low HRA capacity
Cytology	None	Negative ASC-US or worse	Repeat 12 mos HRA	Repeat 12-24 mos -ASC-US/LSIL repeat 12 mos -HSIL ,ASC-H: HRA
Cytology	hrHPV testing of ASC-US or worse	ASC-US/LSIL and hrHPV neg ASC-US/LSIL and hrHPV positive ASC-H/HSIL (rergardless of HPV)	Repeat 12 mos HRA HRA	Repeat 12 mos If HPV non 16:repeat 12 mos If HPV16pos: HRA HRA
hrHPV testing (HPV16 genotype)	None	Negative Positive	Repeat 12-24 mos HRA	Repeat 24 mos If HPV non 16:repeat 12 mos; If HPV16pos: HRA
hrHPV testing (HPV16 genotype)	Cytology of hrHPV positive	Neg/ HPV non 16 pos ASC-US or worse /hrHPV positive If HPV16 pos	HRA or Repeat 12 mos HRA HRA	Repeat 12 mos ASC-US/LSIL and HPV non 16 pos:repeat 12 mos HRA i other cases
Co-testing	None	-Both negative -ASC-US/hrHPV neg -Neg/hrHPV pos (non16) -LSIL/HPVneg -ASC-US/LSIL/hrHPVpos HSIL,ASC-H or HPV16 pos	Repeat 12 -24 mos Repeat 12 mos HRA or repeat 12 mos HRA or repeat 12 mos HRA HRA	Repeat 24 mos Repeat 24 mos Repeat 12 mos Repeat 12-24 mos ASC-US/LSIL ,HPV non 16 pos:repeat 12 mos -HRA

Evolving Features of HIV-Malignancies
Conclusions

- 1. Treatment of HIV-malignancies has evolved over time, in line with better control of HIV replication and recovery of immune function by cART. The overall survival for these patients has dramatically improved in the modern cART era.

2. However, data from large population-based studies have shown that HIV infection remains associated with higher risk of death in patients with all malignancies compared to general population
Disparities in practice pattern based on HIV status may influence outcomes in this population that is still excluded from prospective clinical trials of the general population.

3. Dissemination of effective management strategies is mandatory to improve patient outcome.

4. HIV infection alone should no longer be an exclusion criterion in any clinical trial.