

# Changing Trends in HIV AIDS Kaposi's Sarcoma

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# Introduction

- Commonest cancer in men and second commonest in women
- The incidence of KS in Africa has increased with the exponential spread of HIV and poor HAART coverage
- In KZN, incidence increased 30 fold
  - 19.7/100 00 in men
  - 11.5/100 00 in women

*Wabinga et al Br J Cancer 2000*

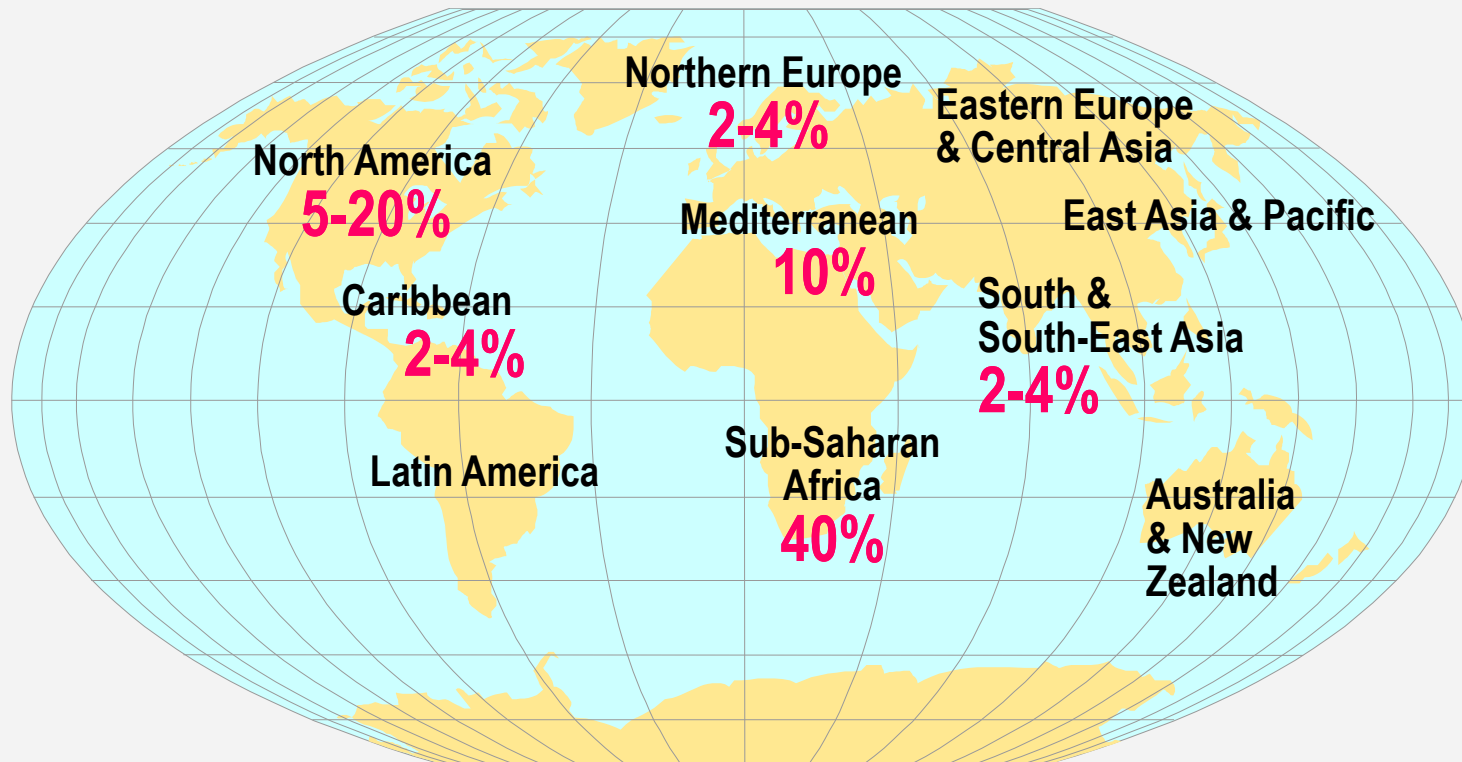
*Mosam et al IJSA 2009*

Site	ALL			Age 18-49		
	n	% Total	Rank	n	% Total	Rank
Breast	1590	17.8	1	540	17.7	2
Cervix	1565	17.5	2	673	22.1	1
Head and Neck	1029	11.5	3	257	11.8	4
Lung	720	8	4	137	4.5	6
Kaposi Sarcoma	468	5.2	5	417	13.7	3
Colorectal	393	4.4	6	119	3.9	8
Oesophagus	358	4	7	54	1.8	10
Lymphoid Malignancy*	354	4	8	138	4.5	5
Unknown Primary	311	3.5	9	93	3.1	9
Uterine	269	3	10	39	1.3	12
Sarcoma	256	2.9	11	127	4.1	7
Prostate	255	2.8	12	4	0.1	16
Ovary	172	1.9	13	54	1.8	11
Skin **	160	1.8	14	38	1.2	13
Stomach	128	1.4	15	35	1.1	14
Melanoma**	127	1.4	16	33	1.5	15
Other	800	8.9	NA	287	9.4	NA
TOTAL	8955	100		3045	100	

Distribution of Cancers  
KZN  
Jan 2001 to June 2004  
All vs 18- 49 yrs

*Unpublished data*

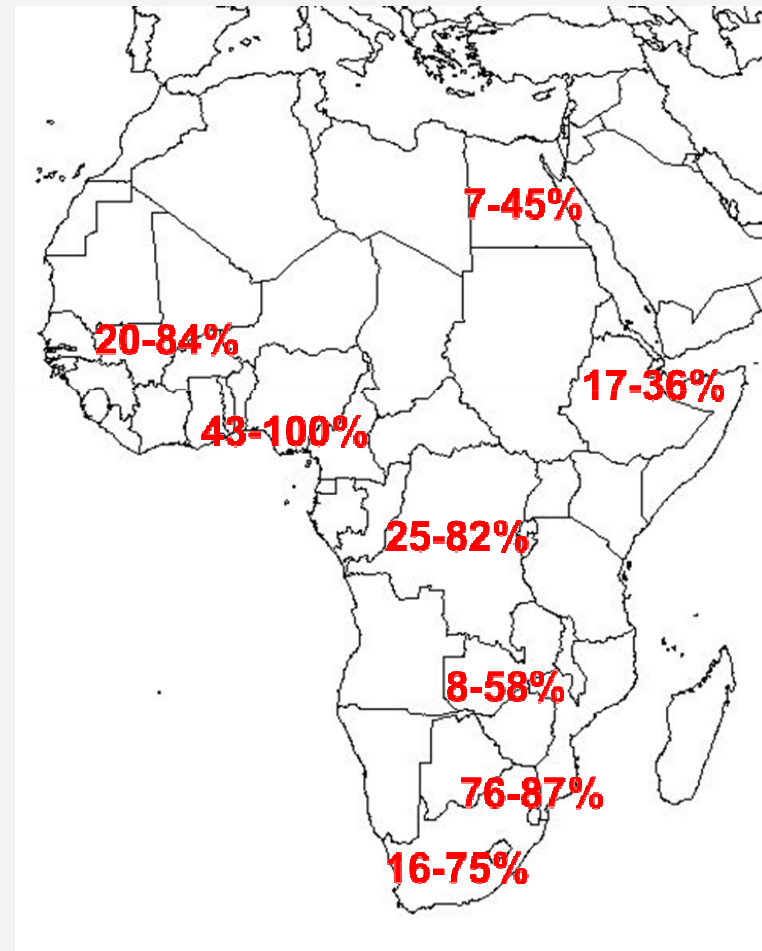
# Global HHV 8 Seroprevalence



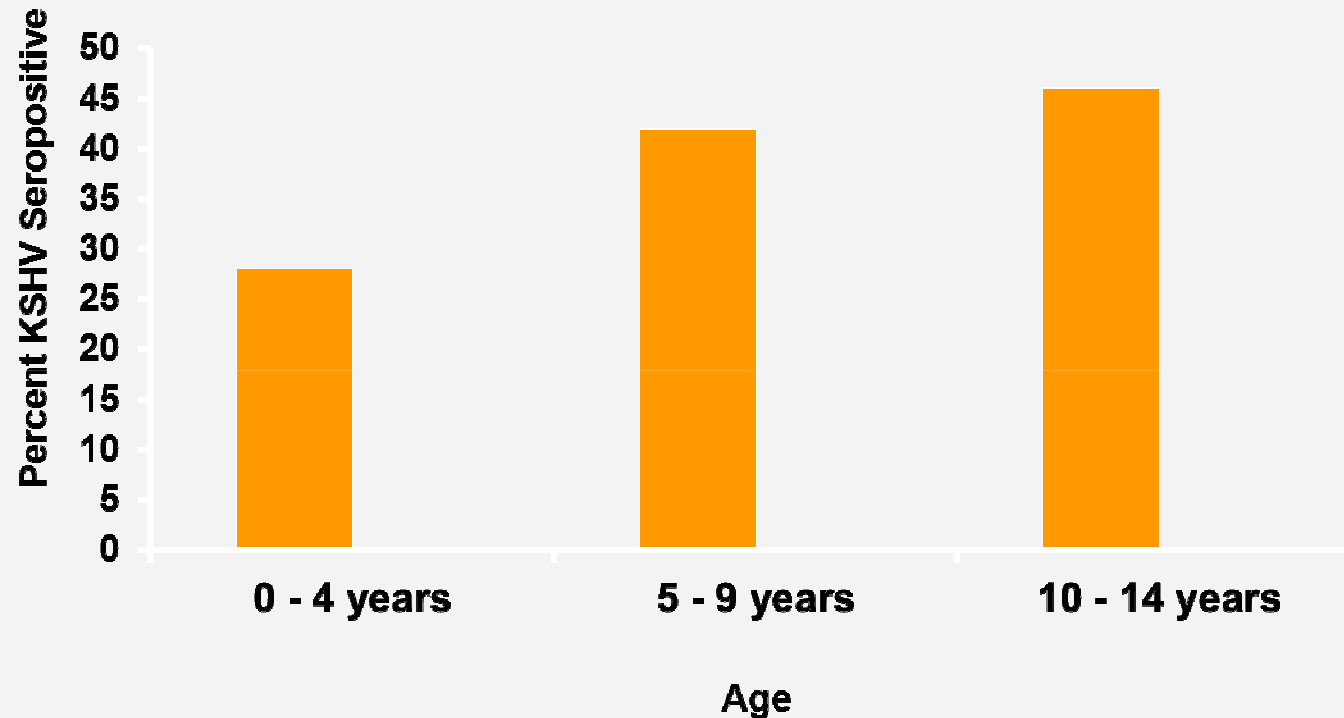
*Chatlynne LG, Semin Cancer Biol 1999 (3) : 175 - 178*

# HHV8 in Africa

- Different assays used by different studies
- No clear evidence of geographic difference
- Common in Uganda & Cameroon pre HIV era
- Botswana and Gambia KS was rare before onset of HIV



# HHV8 Seroprevalence in Uganda

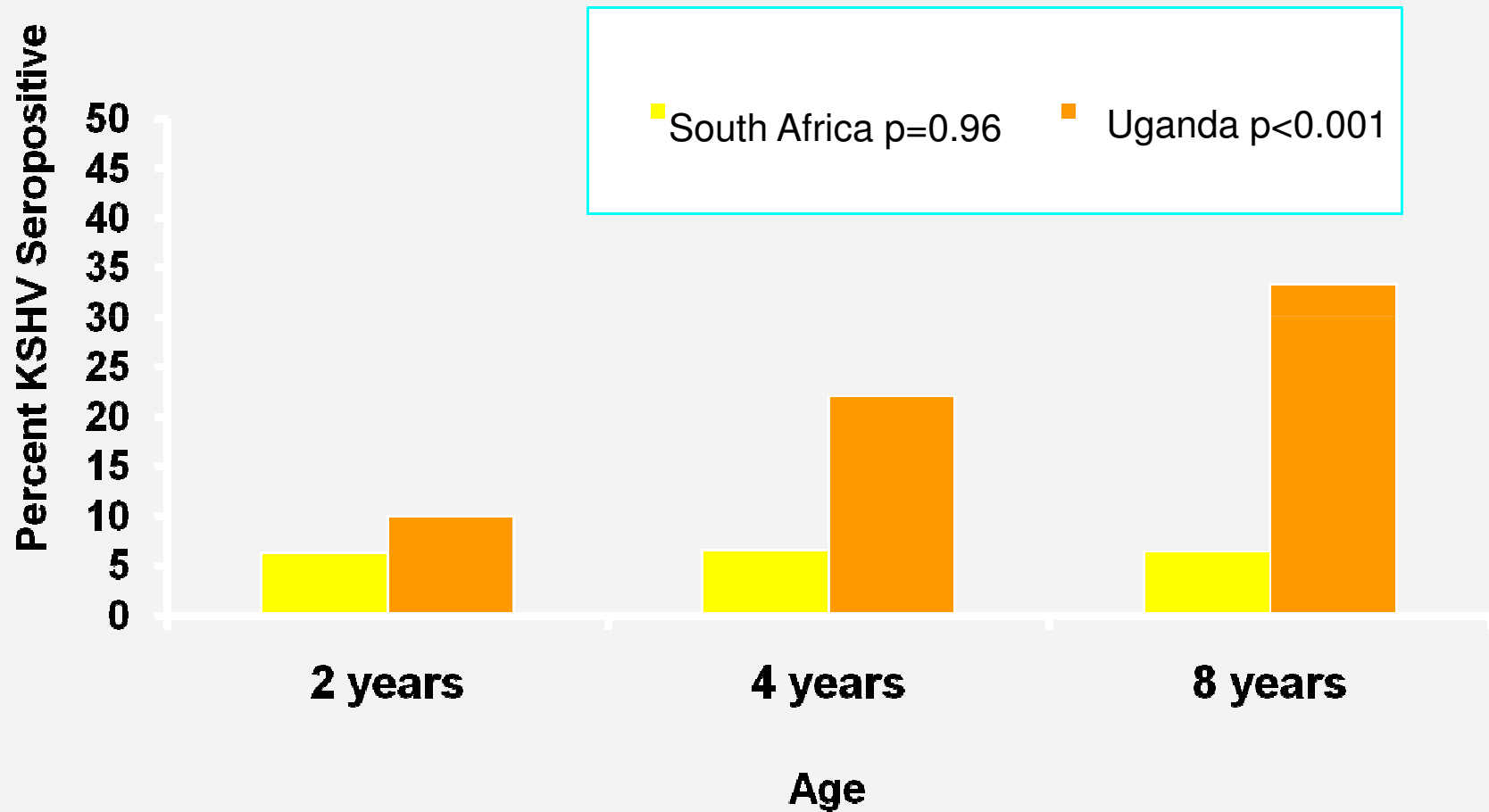


**Age-dependent increase in hhv8 prevalence in children under age 10**

Increases from early childhood reaching near adult prevalence before puberty

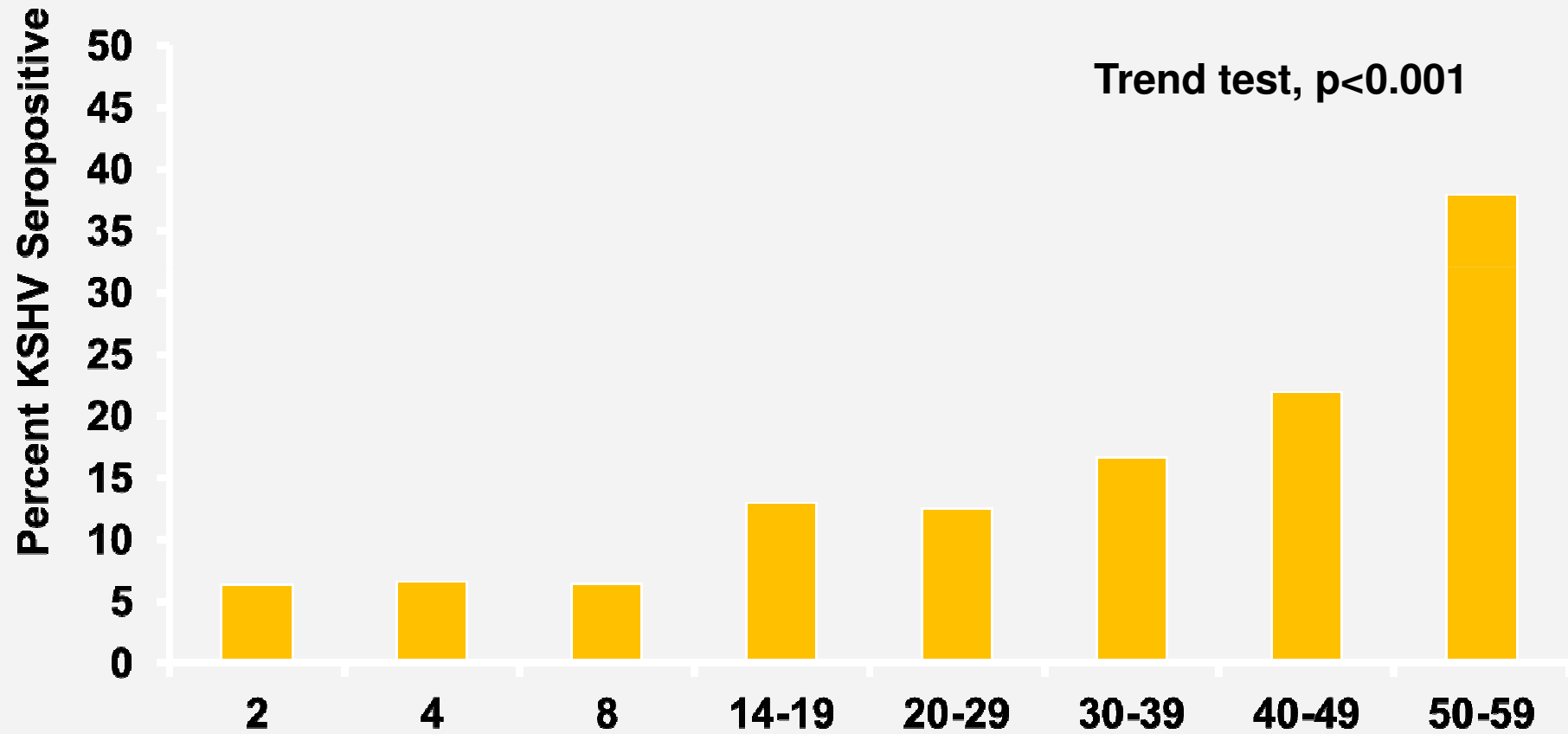
The inferred mode of transmission is ongoing horizontal transmission in childhood

# HHV8 Seroprevalence in Children SA and Uganda



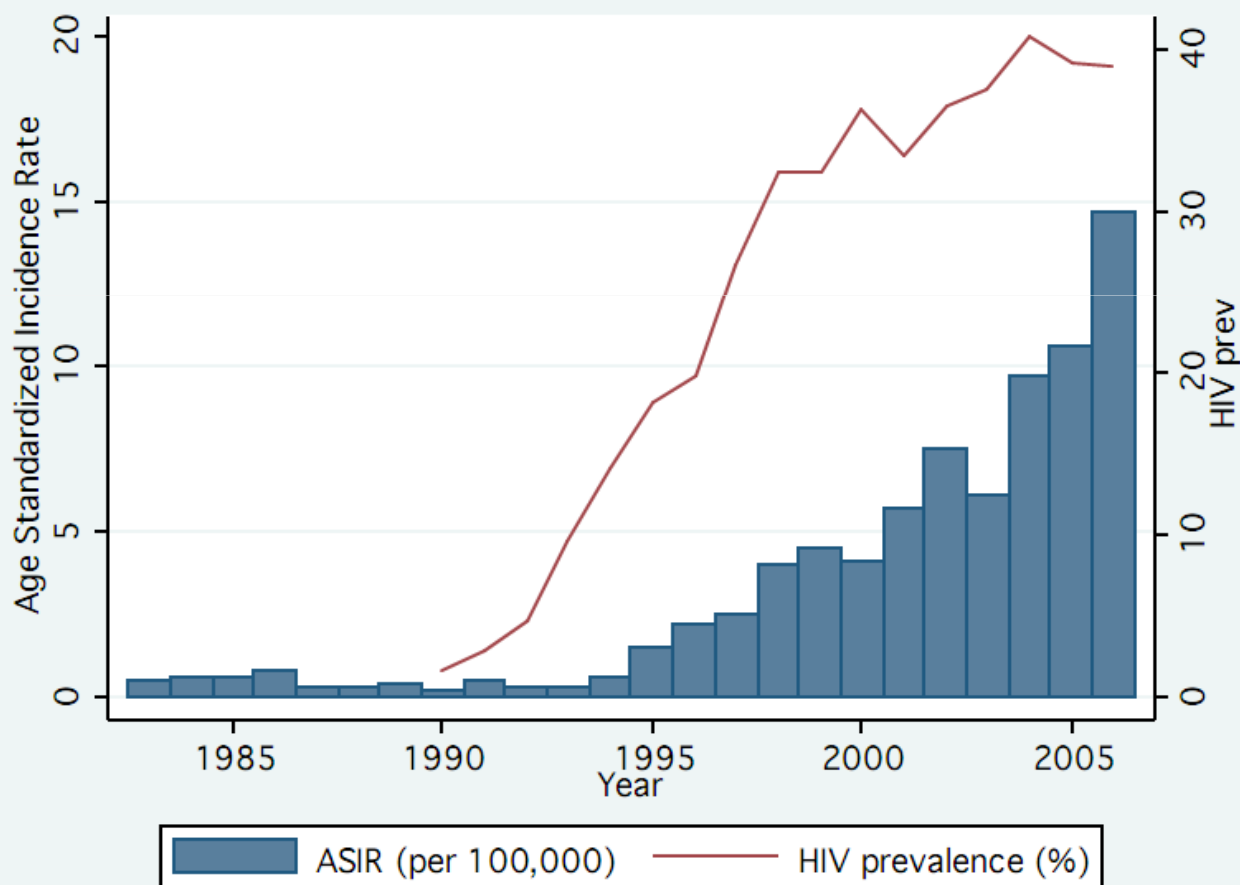


# HHV8 Seroprevalence Children vs Adult caregivers



*Dollard Int J Cancer 2010 Nov 15;127(10):2395-401*

# Age Standardised Incidence of KS



ASIR / 100 000

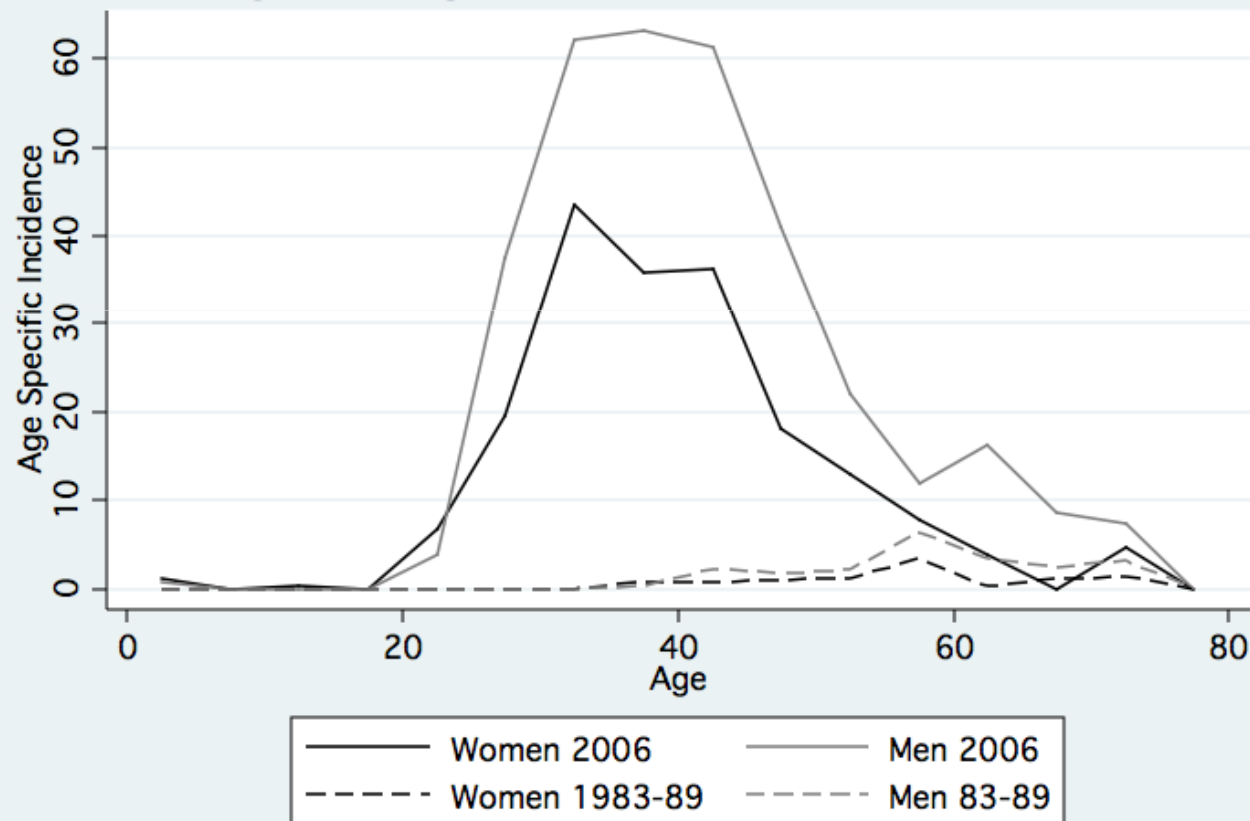
1983 - 0.52  
2003 - 14.76

HIV  
seroprevalence

1989 - 1.6%  
2006 - 39%

# KS Age Specific Incidence Pre-AIDS vs AIDS Epidemic

Figure 2. Age Specific Incidence per 100 000



## Peak Incidence

**Pre-HIV era**  
(1983-1989)  
55-60 yrs

**HIV eras**  
fourth and fifth  
decades of life

# Cutaneous Features

- Asymptomatic pink to purple or brown
- Patches, papules, plaques, nodules or tumours
- Round, oval, elongated, fusiform
- Undiagnosed or overlooked

# Early lesions



# Sites



# Advanced Lesions



# Mucosal Involvement

- Oral cavity in 20% at diagnosis
- Tongue, hard & soft palate
- Associated with GIT KS





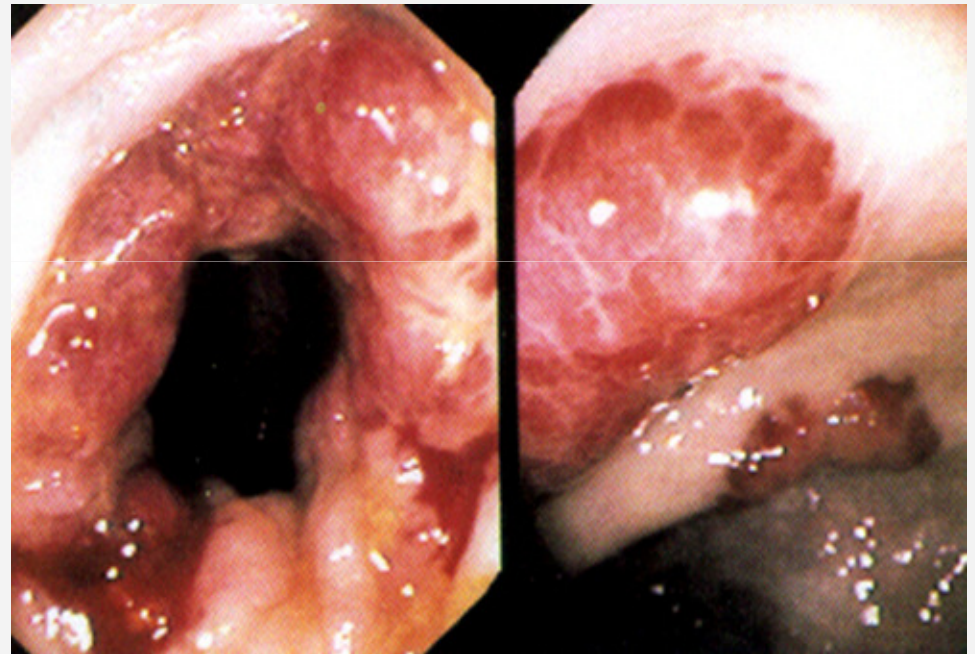
# Lymphatic Involvement

- Lymphadenopathy
- Lymphoedema
- Woody hard induration
- Non-pitting oedema



# Visceral Involvement: GIT

- >50% clinically
- 80% at autopsy
- May be asymptomatic
- Symptoms: Abd pain, bloody stools, LOW



# Pulmonary

- 30% clinically
- 50% at autopsy
- Symptoms:  
dyspnoea, cough,  
effusions
- Survival poor



# KS mimickers

## Patch stage

- Bruises
- Purpura
- Haemangioma
- Naevi



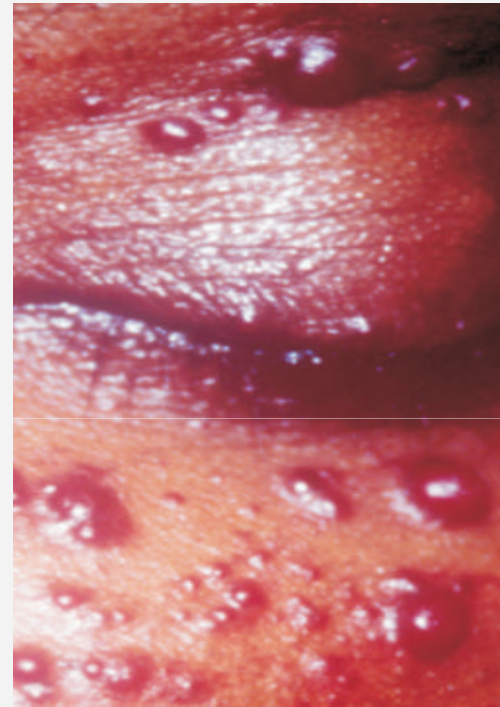
# Papules/ Plaques

- Discoid Lupus
- Lichen planus
- Keloids
- Chromomycosis



# Nodules

- Pyogenic granuloma
- Bacillary angiomatosis
- Deep fungal
- Erythema nodosum

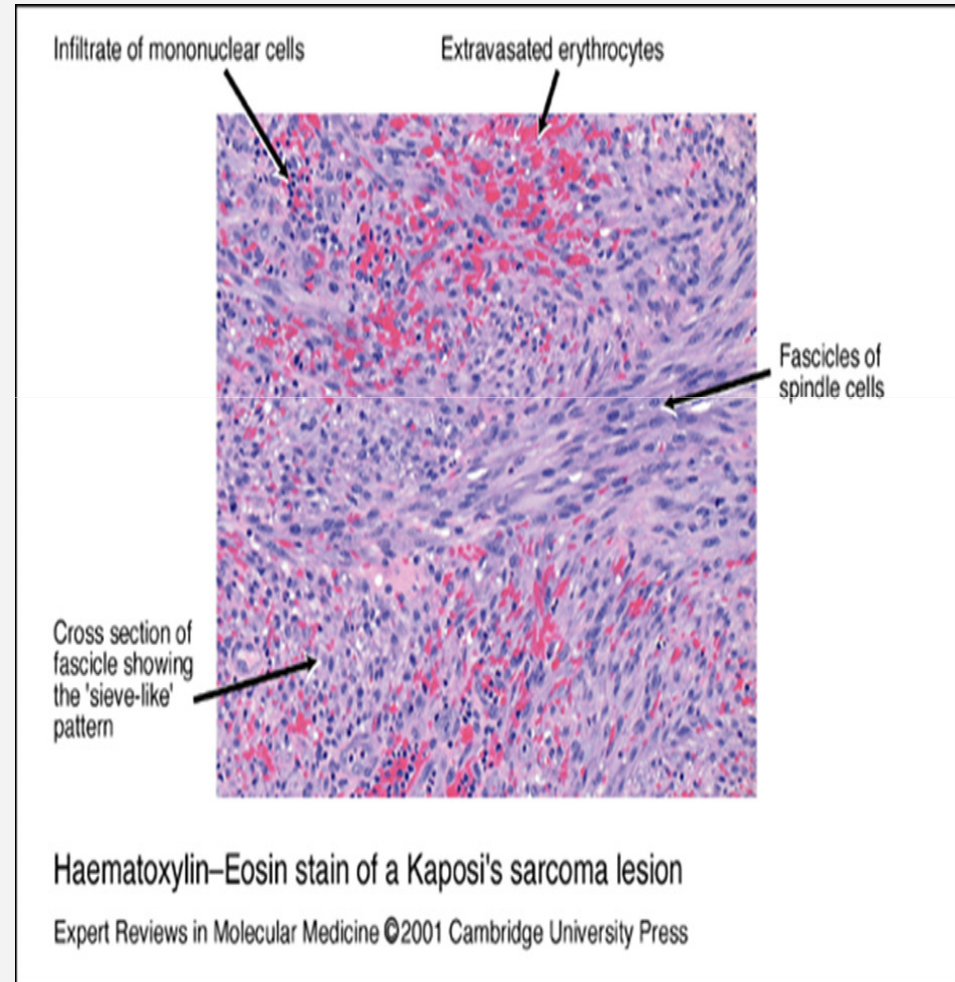




# Diagnosis

Biopsy: Skin, endoscopic or transbronchial

- Proliferation of abnormal vascular spaces, lymphoplasmacytic infiltrates
- Endothelial cells contain HHV 8
- Spindle cells predominate





# Investigations

- CD4 and HIV-1 viral load
- CXR
- Stool occult blood
- Sputa MCS and AFB
- If GIT symptoms, endoscopy
- If abnormal CXR or symptoms, bronchoscopy

# Staging Classification- “TIS”

	Good Risk (All)	Poor Risk (Any)
T (Tumor)	T0: 27 mo survival Skin, minimal oral mucosa, lymph node only	T1: 15 month survival Edema or ulceration Extensive oral mucosa Visceral KS
I (Immune System)	I0: 40 month survival CD4>150	I1: 13 month survival CD4<150
S (Systemic Illness)	S0:22 month survival No OI's or thrush No B symptoms Karnofosky >70%	S1: 16 month survival Hx of OI's or thrush B symptoms present Karnofosky<70% Other HIV related disease

# Efficacy of HAART

- All patients with HIV-KS should receive HAART
- HAART has been associated with:
  - Decrease in new KS lesions
  - Regression in size of existing KS lesions
  - Improved survival
- Mechanism:
  - Likely immune reconstitution
  - Antiangiogenic properties of PIs
- May be associated with immune reconstitution inflammatory syndrome

# HAART in AIDS-KS

- Response rates:
  - Up to 79% reported response rate for HAART alone
  - Can take up to a year
  - SA cohort, 39% response T1 disease
- Response most likely if:
  - T0 tumor
  - ART naïve
  - CD4 increase  $>150$  cells/mm<sup>3</sup>

# Treatment

- Major goals
  - Symptom palliation
  - Prevention of disease progression
  - Tumor shrinkage

# Indications for Systemic therapy

- Widespread skin involvement (>25 lesions)
- Extensive cutaneous KS unresponsive to local treatment
- Extensive oedema
- Symptomatic visceral involvement
- IRIS

# KS IRIS

- Worsening of existing KS or development of new lesions on HAART in 12 weeks
- Associated with rapid decline in HIV VL and increase in CD4
- Pulmonary involvement fatal
- CXT
- British cohort of 150 KS 6.6% developed IRIS KS
- Higher CD4, KS oedema, PI + NNRTI regimen
- SA cohort 112 21%

*Bower J Clin Oncol 2005 Aug 1;23(22):5224-8*

*Mosam JAIDS 2012 Jun 1;60(2):150-7.*

# Multinational Cohort HIV KS

- 3 SSA sites 1 UK
- Prevalence KS IRIS 13 %
- 2.5 X  $\times$ er risk in African cohorts
- Baseline KS IRIS predictors:
- Advanced T1 disease
- ART alone as KS therapy
- HIV-1 RNA VL  $> 5 \log_{10}$  copies/ml



# Corticosteroids and KS

- Corticosteroids have been associated with the induction or exacerbation of KS in HIV patients
- Generally, should be avoided
- Use only in:
  - acute respiratory distress syndrome accompanying HIV-related opportunistic pulmonary infection
  - tuberculosis meningitis or pericarditis
  - immune thrombocytopenic purpura, if necessary

# KS in Africa

- suboptimal HAART availability
- co-infections
- late presentation
- poor follow-up
- increased disease burden
- shortcomings of appropriate oncological services

# Cancer In Africa

- HAART provision cost effective intervention in decreasing the burden of HIV cancers
- especially KS
- potential for dramatic improvements in overall survival and quality of life for patients with HIV KS
- cancer control programmes in Africa are sparse
- provision of RXT, CXT & palliative care is inadequate

*Sitas et al Lancet Oncol 2008*

# Hypothesis

Rollout of HAART led to changes in  
the management of  
HIV KS in KZN

# Objectives

To assess temporal trends over 12 years  
1995-2006 at Addington Hospital

- Demography
- HIV serostatus
- Provision of HAART
- Provision of KS specific Rx: CXT/ RXT
- Outcomes of patients with HIV KS in KZN

# Method

- Anonymised record review
- 95 - 97 no HAART
- 98 - 00 no HAART
- 01 - 03 limited HAART
- 04 - 06 early HAART availability
- Demographics
- HIV status
- CD4 count
- HAART regimen
- Site of KS
- Extent of disease
- Therapy prescribed
- Outcome of KS

Growing AIDS epidemic

Mature AIDS epidemic

# Results

n=701

3 children (3, 14 & 17 yrs)

3 non Black Africans

F: M ratio = 1:1.1

# Characteristics

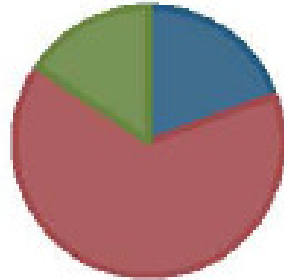
	<b>95- 97</b>	<b>98- 00</b>	<b>01- 03</b>	<b>04- 06</b>
<b>Number of Patients</b>	Total <b>76</b> Men 35 Women 40	Total <b>81</b> Men 54 Women 27	Total <b>165</b> Men 99 Women 66	Total <b>379</b> Men 148 Women 231
<b>Mean Age (Range)</b>	<b>36</b> (19-78)	<b>38</b> (21-79)	36 (17-76)	<b>35</b> (3-76)
<b>Disseminated Disease</b>	<b>47%</b>	<b>28%</b>	<b>37%</b>	<b>50%</b>
<b>Documented HIV +</b>	<b>65%</b>	<b>62%</b>	<b>86%</b>	<b>92%</b>
<b>CD4 Counts Available</b>	<b>0%</b>	<b>0%</b>	<b>28%</b>	<b>80%</b>
<b>Proportion CD4&lt;200</b>	<b>NA</b>	<b>NA</b>	<b>57%</b>	<b>54%</b>
<b>HAART</b>	<b>0%</b>	<b>0%</b>	<b>9.3%</b>	<b>44%</b>



# Documented HIV Status of Patients with KS

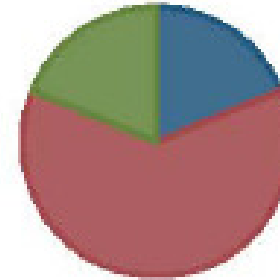
1995-1997

**HIV + 65%**  
**UK 20%**



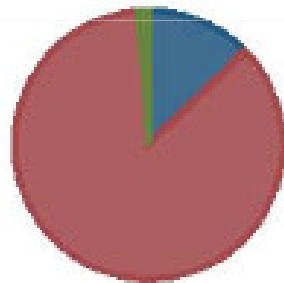
1998-2000

**HIV + 62%**  
**UK 19%**



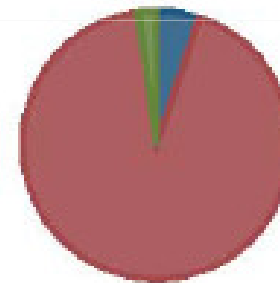
2001-2003

**HIV + 86%**  
**UK 13%**

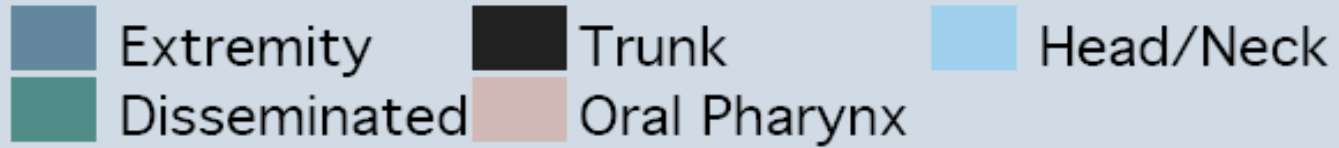


2004-2006

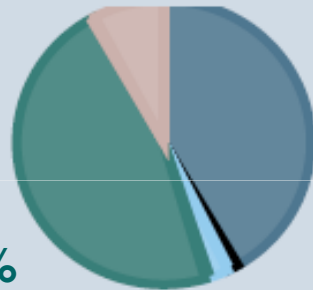
**HIV + 92%**  
**UK 5.3%**



# Clinical KS Distribution at Presentation

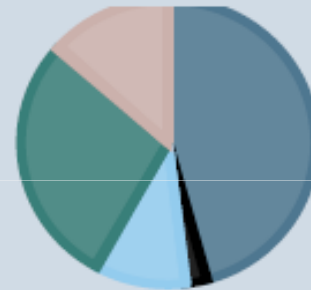


1995-1997



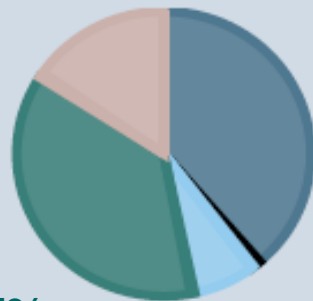
**Diss 47%**

1998-2000



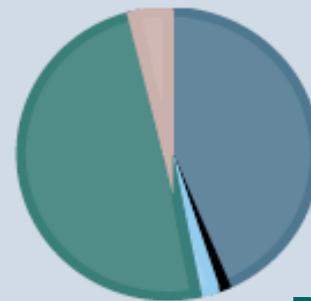
**Diss 28 %**

2001-2003



**Diss 37%**

2004-2006



**Diss 50 %**

# KS Specific Therapy Provided

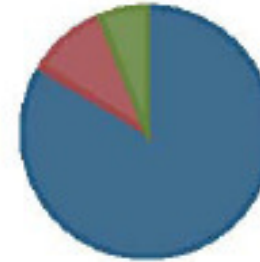
1995-1997



**CXT 23%**

**None 68%**

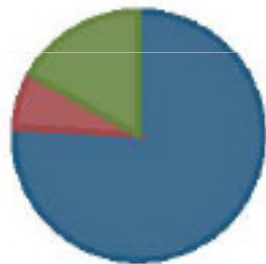
1998-2000



**CXT 5%**

**None 68%**

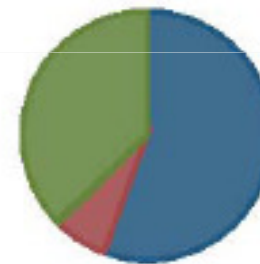
2001-2003



**CXT 17%**

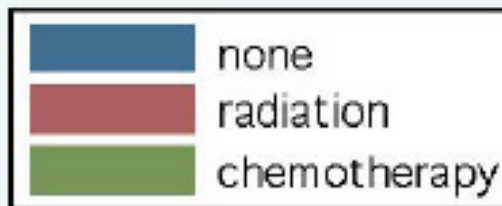
**None 76%**

2004-2006



**CXT 38%**

**None 56%**



# Planned vs Actual Therapy

Category	n	Palliative Care – Observation (%)		Radiation Therapy (%)		Chemotherapy (%)	
		Planned	Actual	Planned	Actual	Planned	Actual
Men (95-06)	336	35.7	61.9	28.7	9.5	36	28.6
Women (95-06)	363	31.4	67.7	32.2	5.6	36.4	26.6
1995-1997	77	11.7	67.5	16.8	9.1	71.4	23.4
1998-2000	81	59.3	68	33.3	8	7.4	5
2001-2003	166	42.2	75.9	39.8	7.2	18	16.9
2004-2006	379	28.7	55.7	28.1	6.9	43.2	37.5
No ARVs (95-06)	515	36.9	75.4	35.5	7.2	27.6	17.4
ARVs (95-06)	182	25.6	35.5	15.9	8.7	60.4	55.7

# Outcomes by HAART use

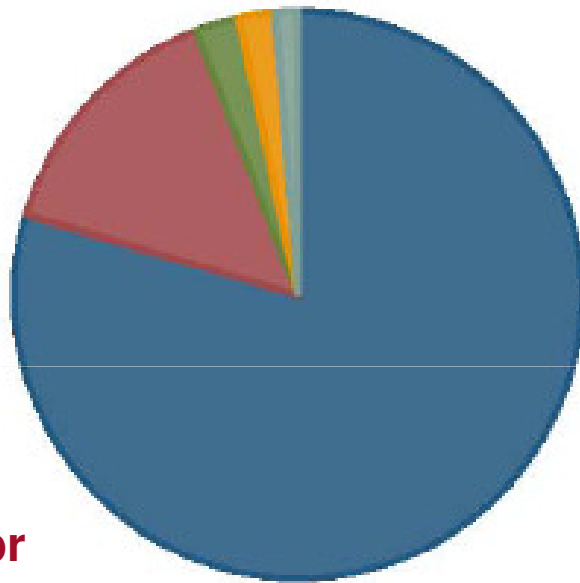
- HAART was associated with significantly higher CXT administration
- 56% vs 17%  $p < 0.001$
- HAART associated with fewer patients receiving palliative care
- 36% vs 75%  $p < 0.001$

# Outcomes by HAART use

- 38% of patients not on HAART missed planned therapies
- vs 13% of those receiving HAART
- HAART was associated with significantly fewer lost to follow up ( $p < 0.001$ )

## Outcomes by HAART Use

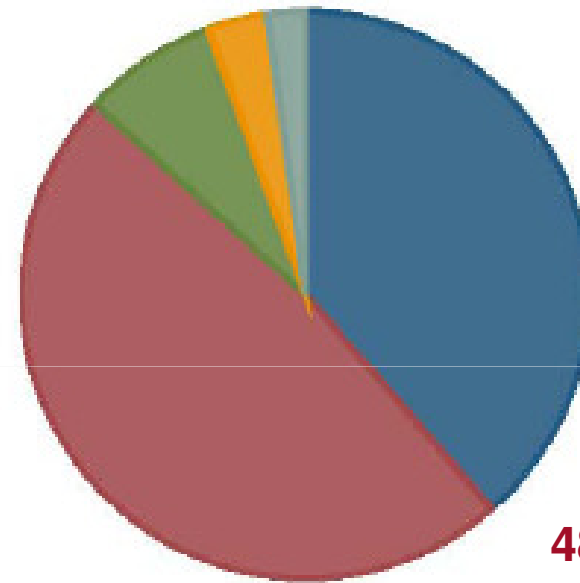
No HAART



**14% impr**

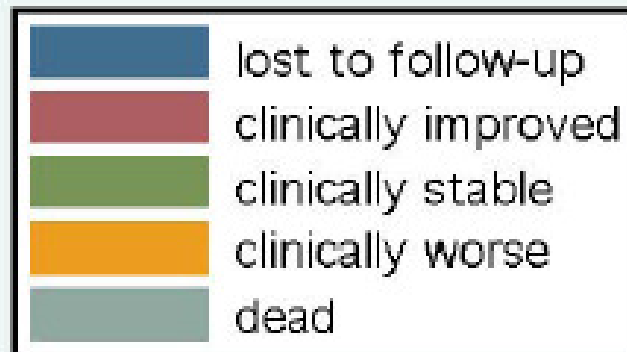
**79% lost**

HAART



**48% impr**

**38% lost**



# HAART in Hand in 2011

- Changes in KS presentation in KZN
- Addington Hospital in 2011
- 198 charts reviewed
- 194 HIV KS                      4 HIV –ve
- 100 % documented HIV (92% in 2006)
- 88.6% on HAART at first presentation to oncology ( 44% in 2006)



# HAART in Hand

- 58% presented within 3 months of histological diagnosis
- Mean CD4 266 cells/mm<sup>3</sup> ( 218 in 2006)
- 94% Poor Risk Disease
- Rural patients 3X more likely than urban patients to be on HAART
- Age > 30 yrs 3 X more likely than those < 30 of being on HAART

# Conclusion

- HIV KS important HIV surveillance tool in KZN
- HAART is associated with improved diagnostic evaluation, better follow-up, and increased chemotherapy use
- continued access to HAART and
- better access to CXT
- critical for the optimal management of HIV KS