HIV / AIDS Care in Africa: Achievements and Challenges

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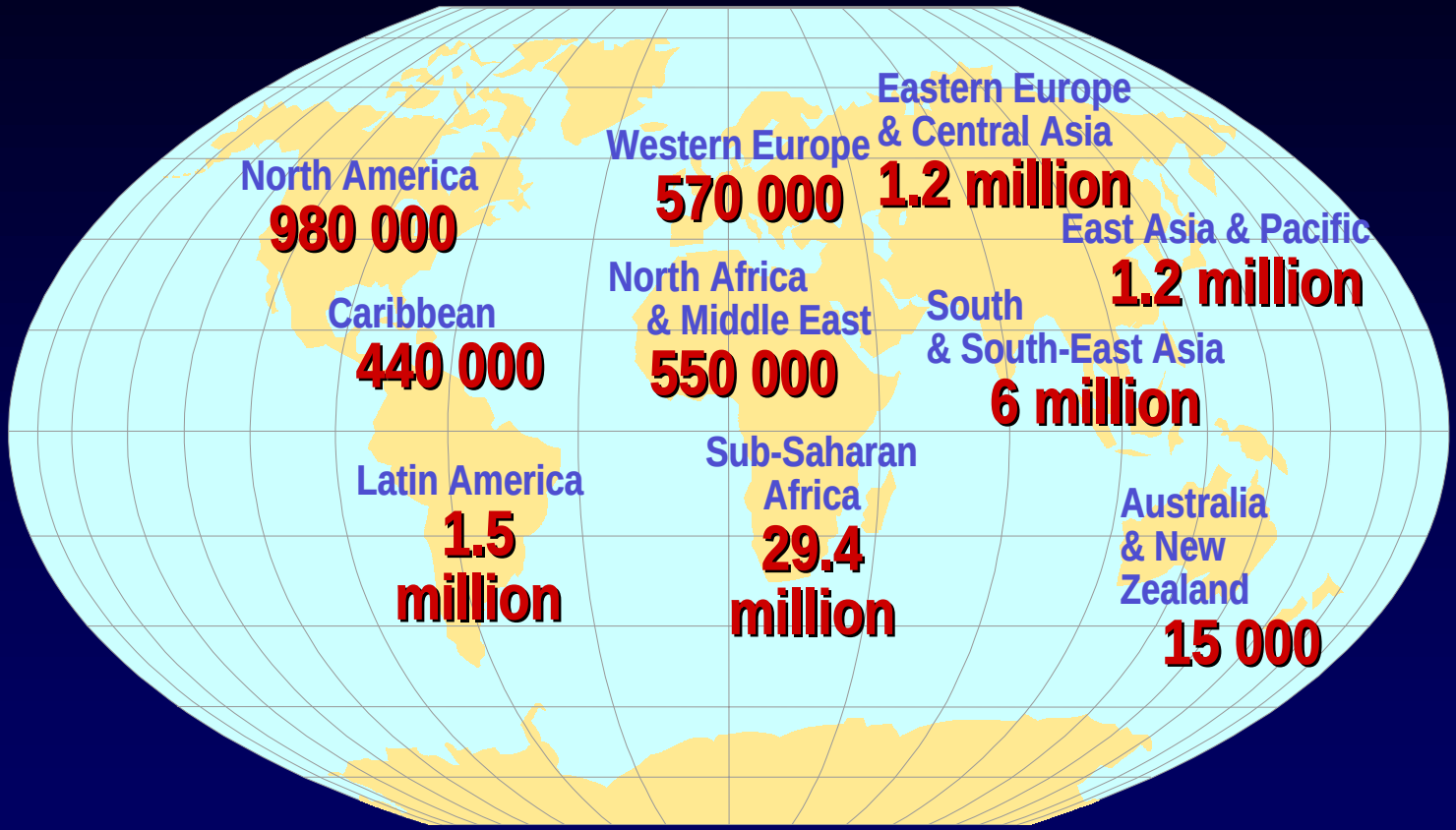
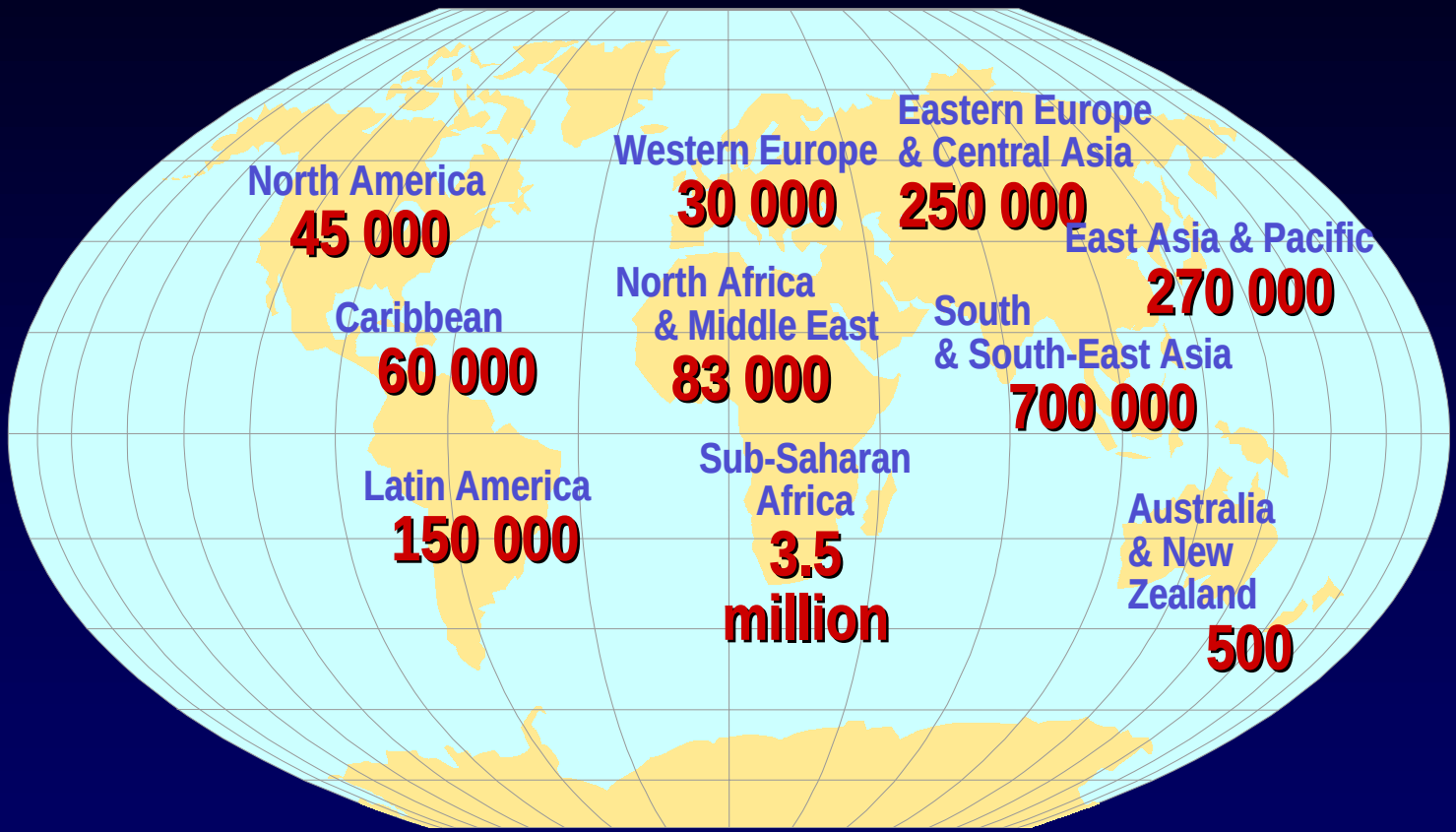
Adults and children estimated to be living with HIV/AIDS as of end 2002



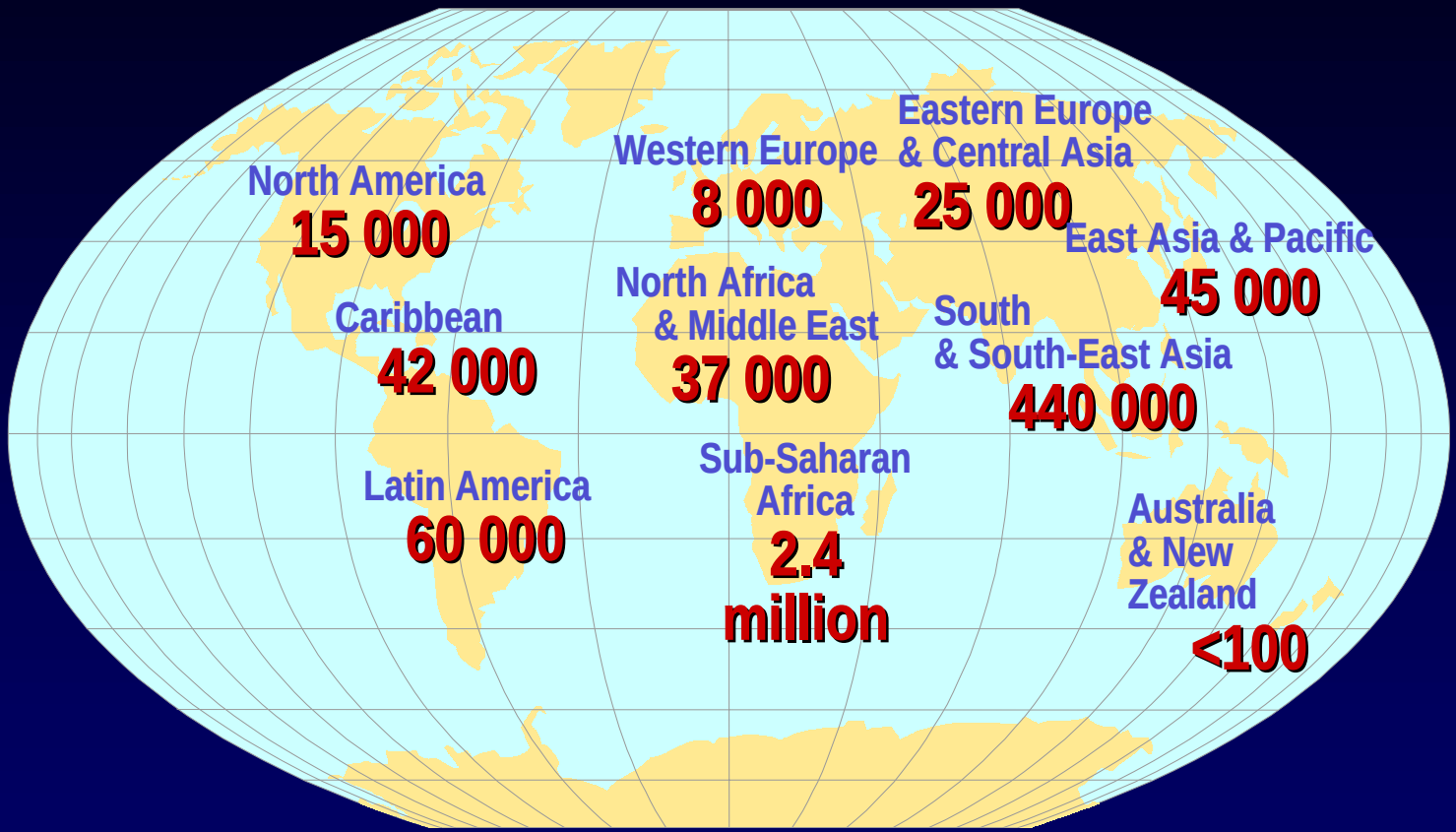
42 million

Estimated number of adults and children newly infected with HIV during 2002



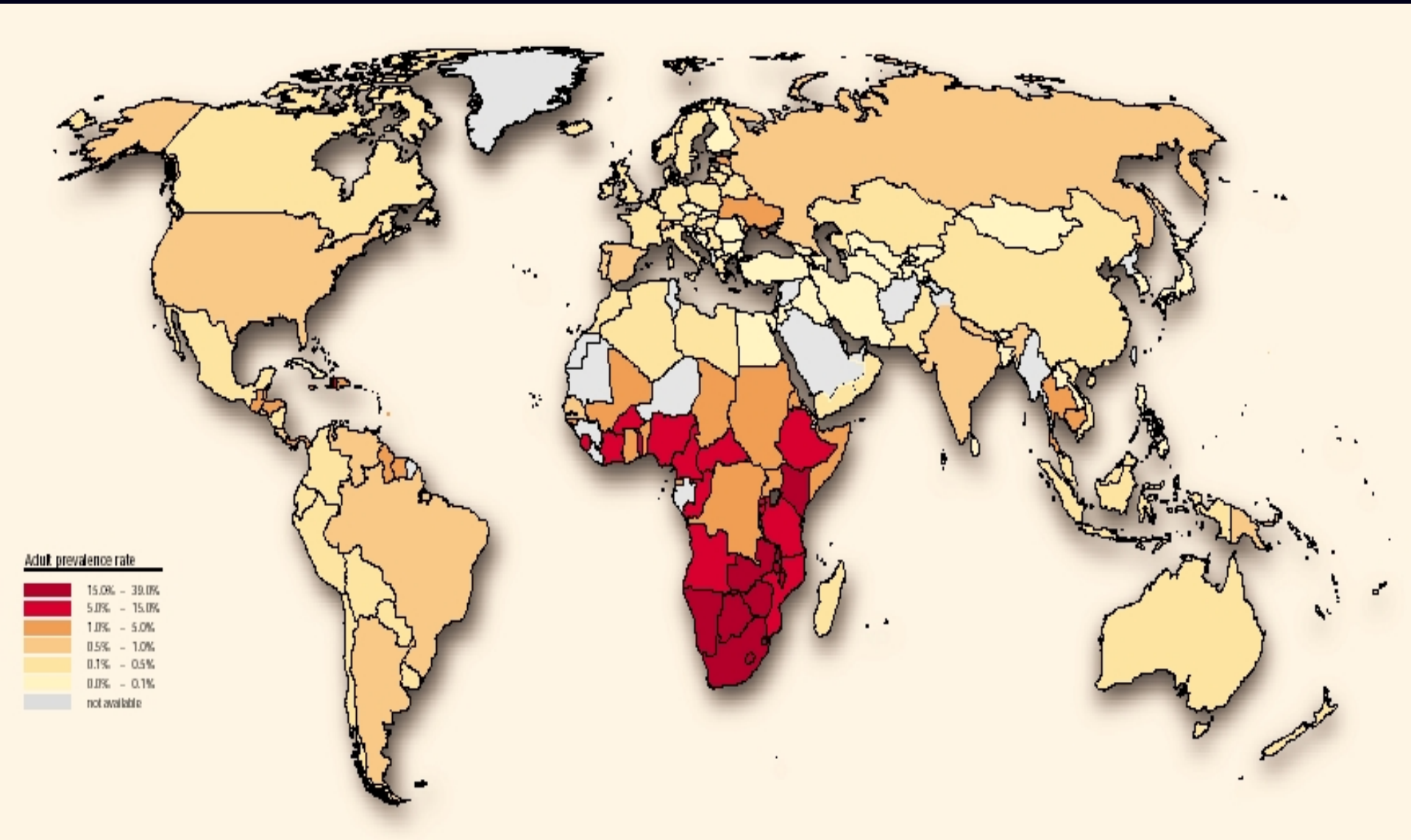
5 million

Estimated adults and child deaths due to HIV/AIDS during 2002

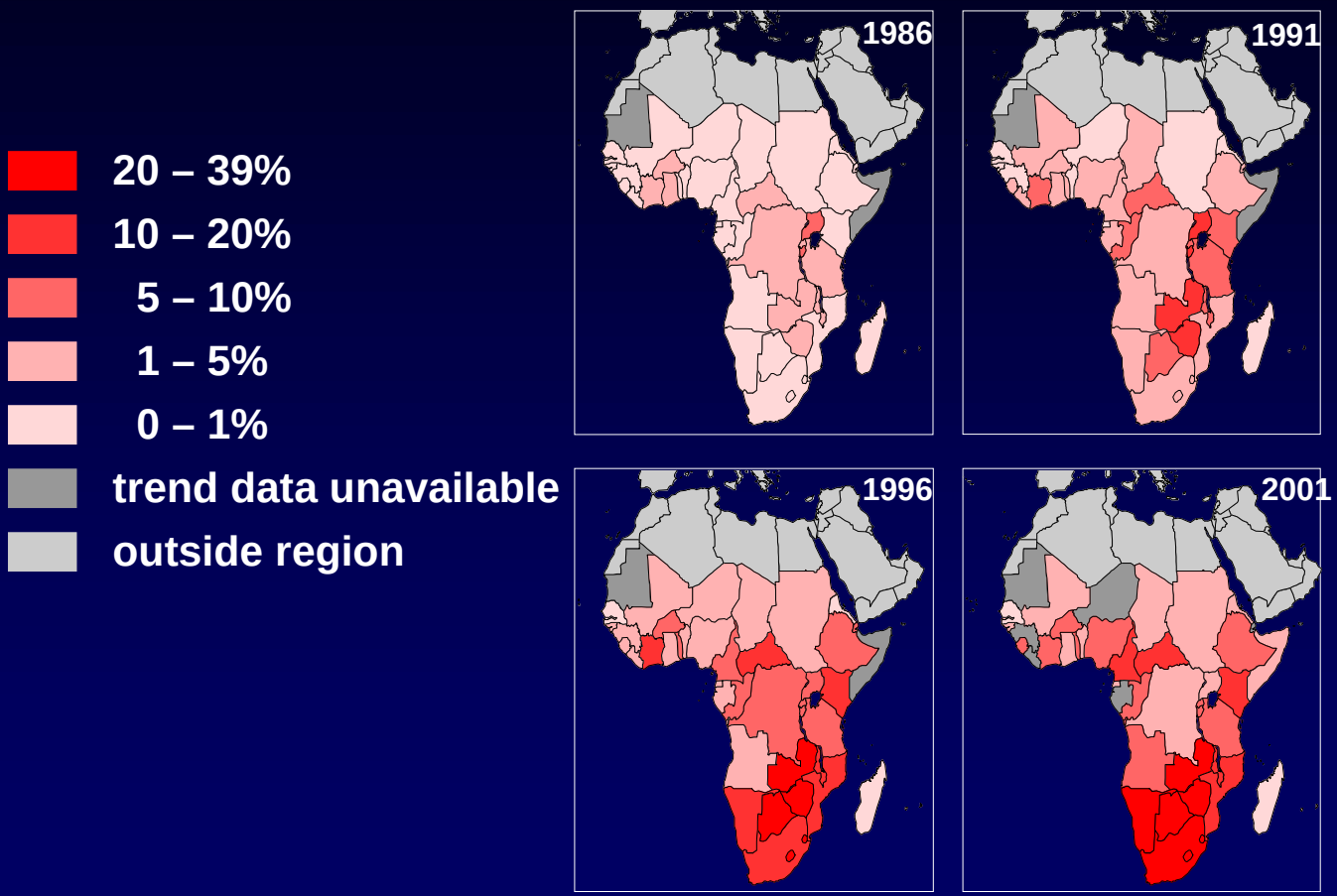


3.1 million

HIV Prevalence by Country, 2001



HIV prevalence in adults in sub-Saharan Africa, 1986-2001



Sub-Saharan Africa

- 28.5 million infected (2/3 world total)
- 17 million HIV deaths (83% world); 2.3 million died in 2001
- 90% of infected children around the globe
- 80% of all infected women
- At least 10% of the population is infected in 16 African countries; 36.2% in one area
- 8,000 new infections each day
- 75% of urban hospital beds occupied by AIDS patients
- Up to 800,000 children infected perinatally

HIV/AIDS:GLOBAL CRISIS

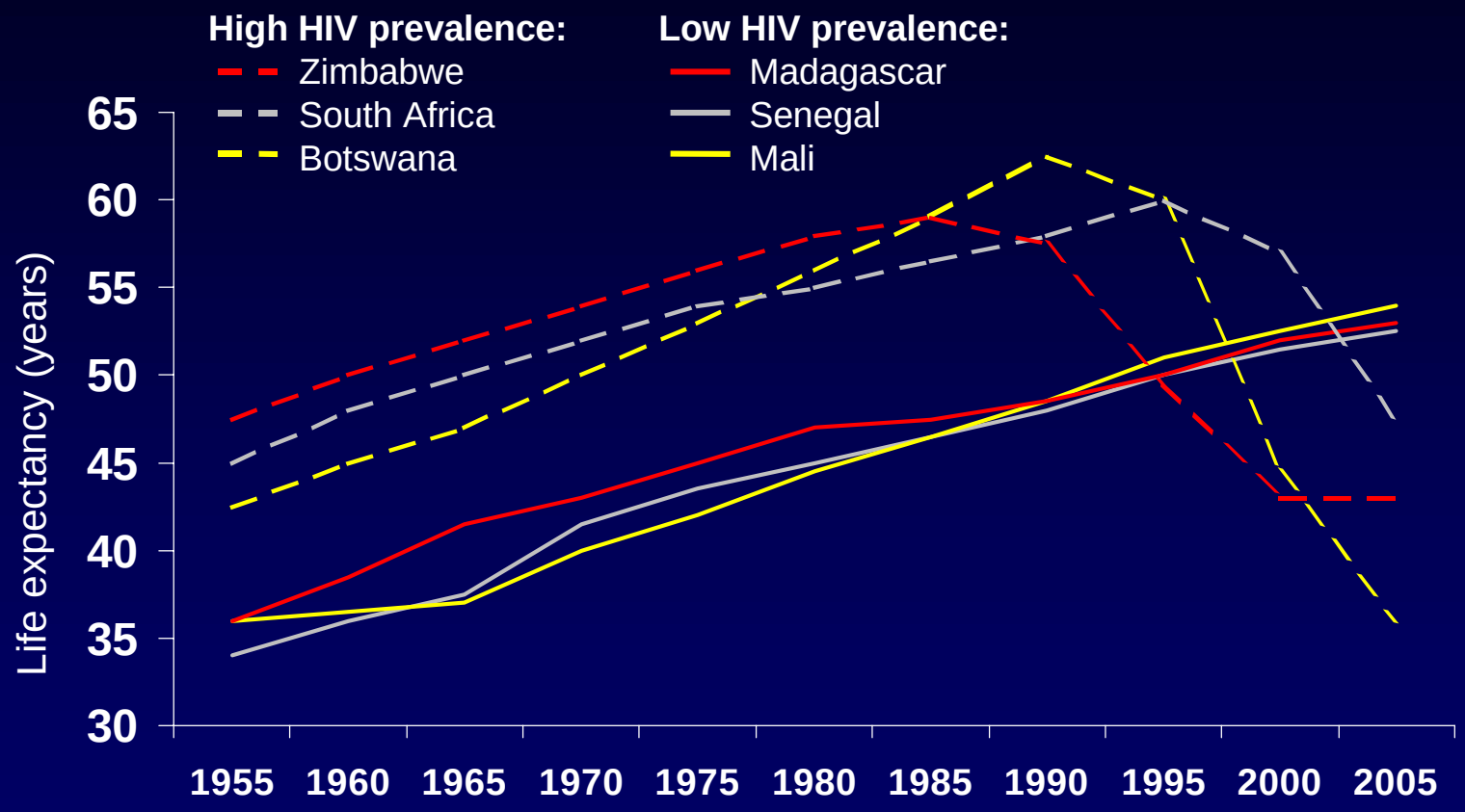
- DEVELOPMENT GAINS OF THREE DECADES REVERSED
- ECONOMIC DECLINE OF 10-40%
- HEALTH SYSTEM CHAOS
- POLITICAL INSTABILITY
- RAPIDLY INCREASING NUMBER ORPHANS
- IMMENSE HUMANITARIAN CONCERNS

Leading causes of death in Africa, 2001

Rank		% of total
1	HIV/AIDS	20.6
2	Acute lower respiratory infections	10.3
3	Malaria	9.1
4	Diarrhoeal diseases	7.3
5	Perinatal conditions	5.9
6	Measles	4.9
7	Tuberculosis	3.4
8	Cerebrovascular disease	3.2
9	Ischaemic heart disease	3.0
10	Maternal conditions	2.4

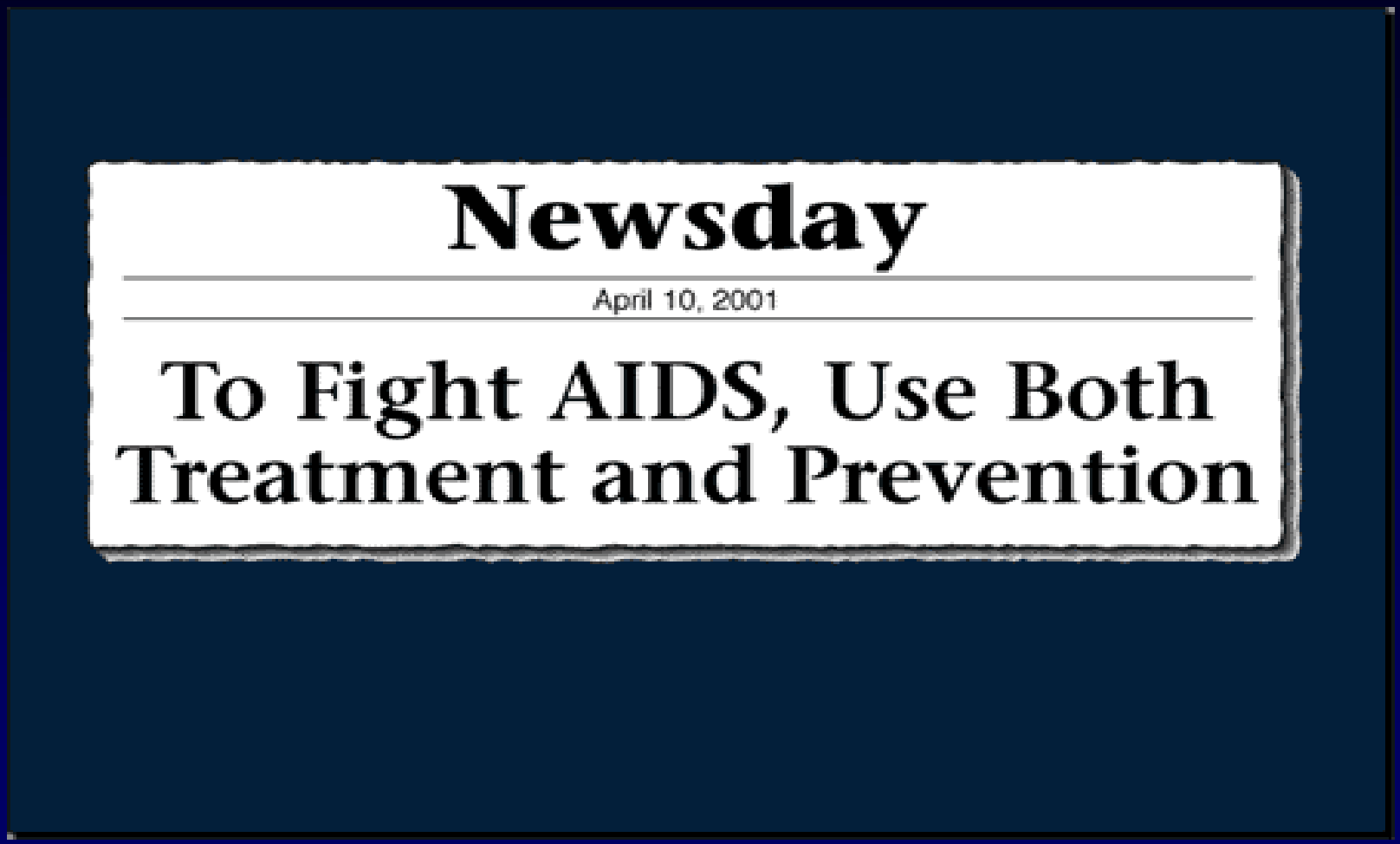
Source: *The World Health Report 2000, WHO*

Impact of HIV on life expectancy in Africa



Source: UN Department of Economic and Social Affairs (2001) *World Population Prospects, The 2000 Revision*

Prevention vs. Rx

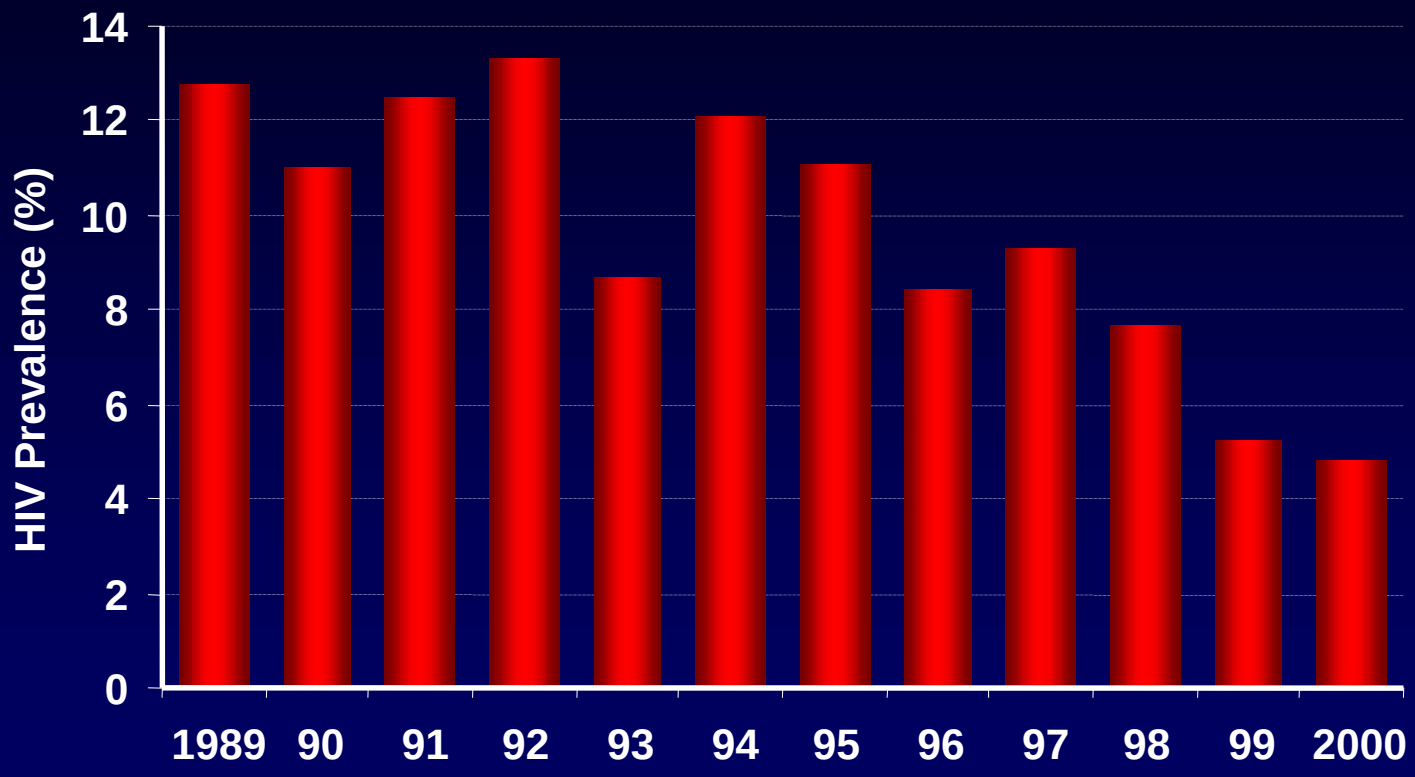


Newsday

April 10, 2001

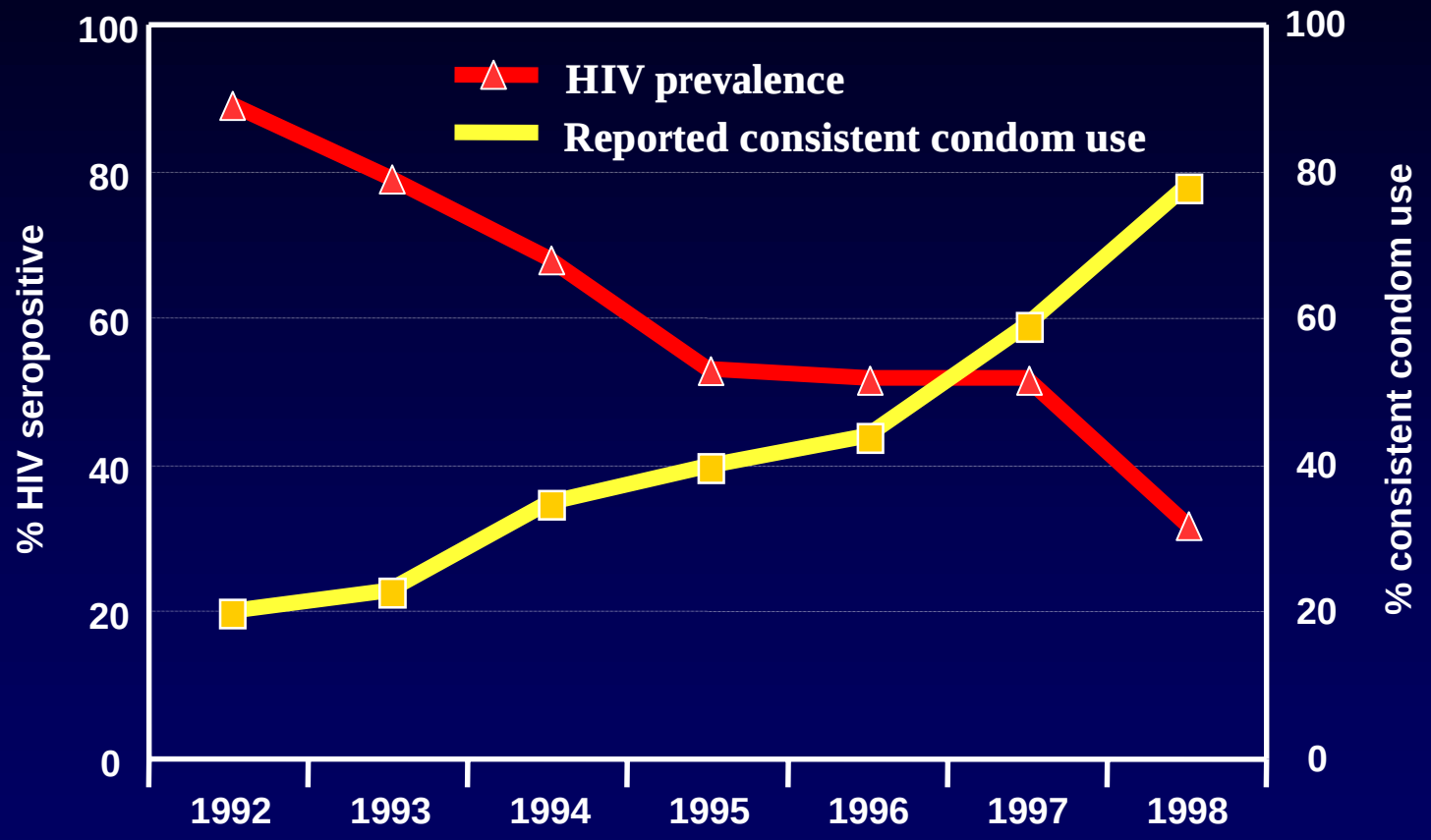
To Fight AIDS, Use Both Treatment and Prevention

Prevalence among pregnant women, outside major urban areas, Uganda



Source: Uganda National AIDS Programme

HIV prevalence and reported consistent condom use among female sex workers, Abidjan, Côte d'Ivoire, 1992-1998



Source: Ghys PD et al. (2002) *AIDS*

'Aids drugs made me well again'

LYNNE ALTENROXEL and JO-ANNE SMETHERHAM

DOCTORS gave Matthew Damane just a few years to live after he was diagnosed with HIV, the virus that causes Aids, in 1997.

At that time, life-saving Aids medicines, widely available in the West, were too expensive for poor people in countries like South Africa.

The brand-name medicines, which cost R1 400 a month, even with discounts offered by drug companies, are still too expensive.

But Damane, 35, from Khayelitsha, has had access to less expensive generic versions, imported from Brazil, and he credits the drugs with restoring his health.

"I am now well," he told a packed news conference in Johannesburg yesterday as he held up a plastic pill box. It has one pill compartment for each day of the week, helping him take his Aids medicines on schedule.

Damane, a nervous smile showing under his blue base-

activist groups announced it had imported the medicines from Brazil in violation of drug-company patent rights but with the full blessing of the Medicines Control Council (MCC).

Citing preliminary results from a pilot project in Khayelitsha, the activists said the Aids drugs had reduced the presence of the virus in people's bloodstreams to undetectable levels after less than one year of treatment. They said patients were getting off their deathbeds and returning to productive work and family lives.

"We literally resuscitated people," said Eric Goemaere, who heads the Aids clinic run by Médecins Sans Frontières (MSF) in Khayelitsha.

The preliminary results of the Khayelitsha pilot study – which has reported findings for 85 patients taking the Aids medicines – are the first evidence from a township clinic in South Africa that the Aids drugs can be taken on a long-term basis and can have the same dramatic effect in improving health as they have had in industrialised countries.

ment Action Campaign (TAC), Oxfam and Cosatu – pointed to the findings yesterday to urge the government to set up pilot projects to provide the drugs to symptomatic Aids patients in each province. They also referred to the results to support their argument that the government should follow Brazil's lead and make its own low-cost generic versions of the drugs.

"It is difficult but it is feasible in developing-country conditions," said Mark Heywood, TAC secretary.

The government did not comment on the activists' calls. It said the MCC would check whether the Brazil import was legal.

The drug companies that own the patent rights to the drugs do not have plans to sue the activists. Peter Moore, medical director at GlaxoSmithKline, said the company would wait for the MCC to act.

Boehringer-Ingelheim spokesman Kevin McKenna said he was not surprised at the developments.

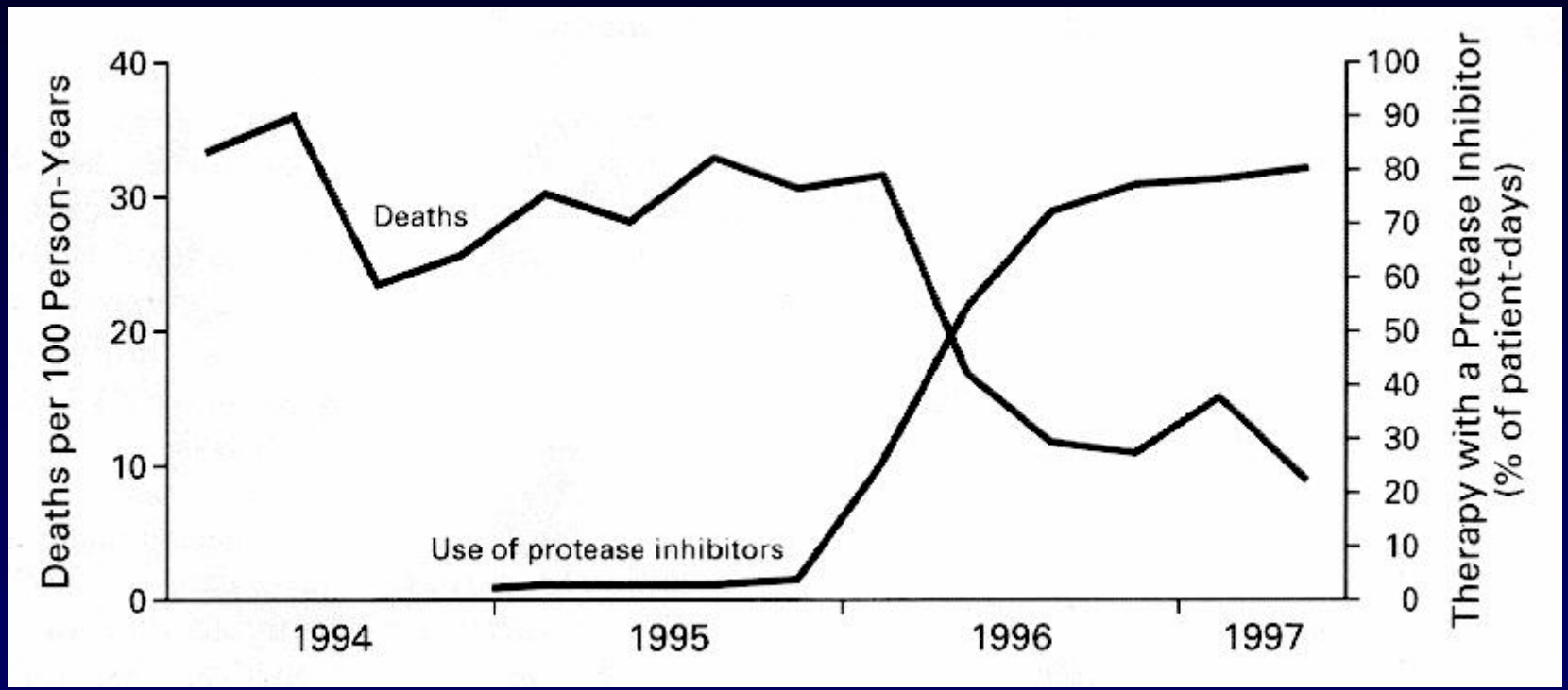
"I don't think we're falling off our chairs at the moment,"

Documented Benefits of HAART: Individual

- Increase Survival
- Decrease OIs
- Decrease Hospitalization
- Decrease in AIDS Incidence
- Decrease in Perinatal Transmission
- Restore Hope

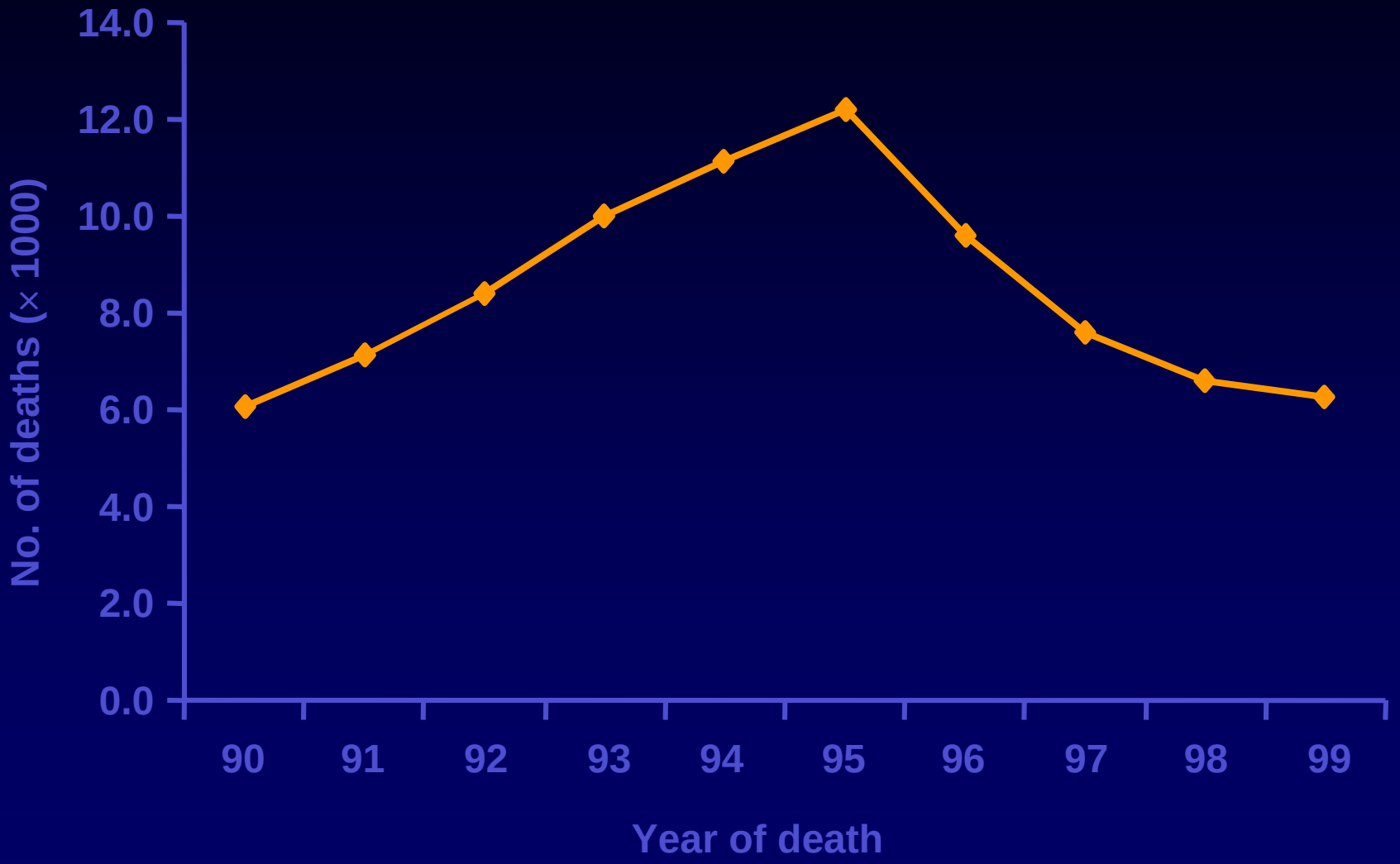
CFAR/UN Global Fund Special Consultation, Baltimore, October 2001

Mortality and PI-Containing Regimen Use in HIV-Infected Patients with <100 CD4 Cells, Jan. 1994-June 1997.

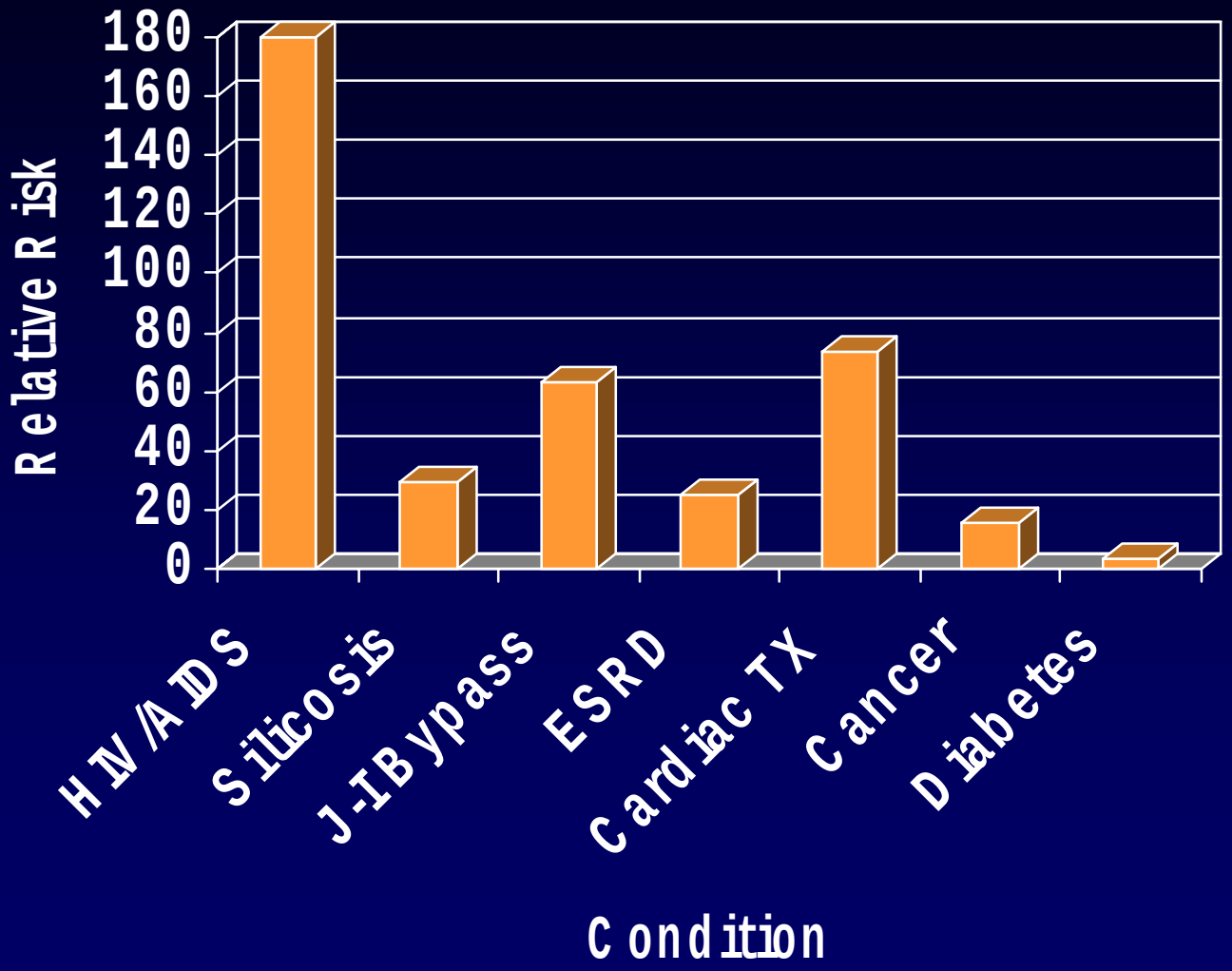


Palella, NEJM 1998

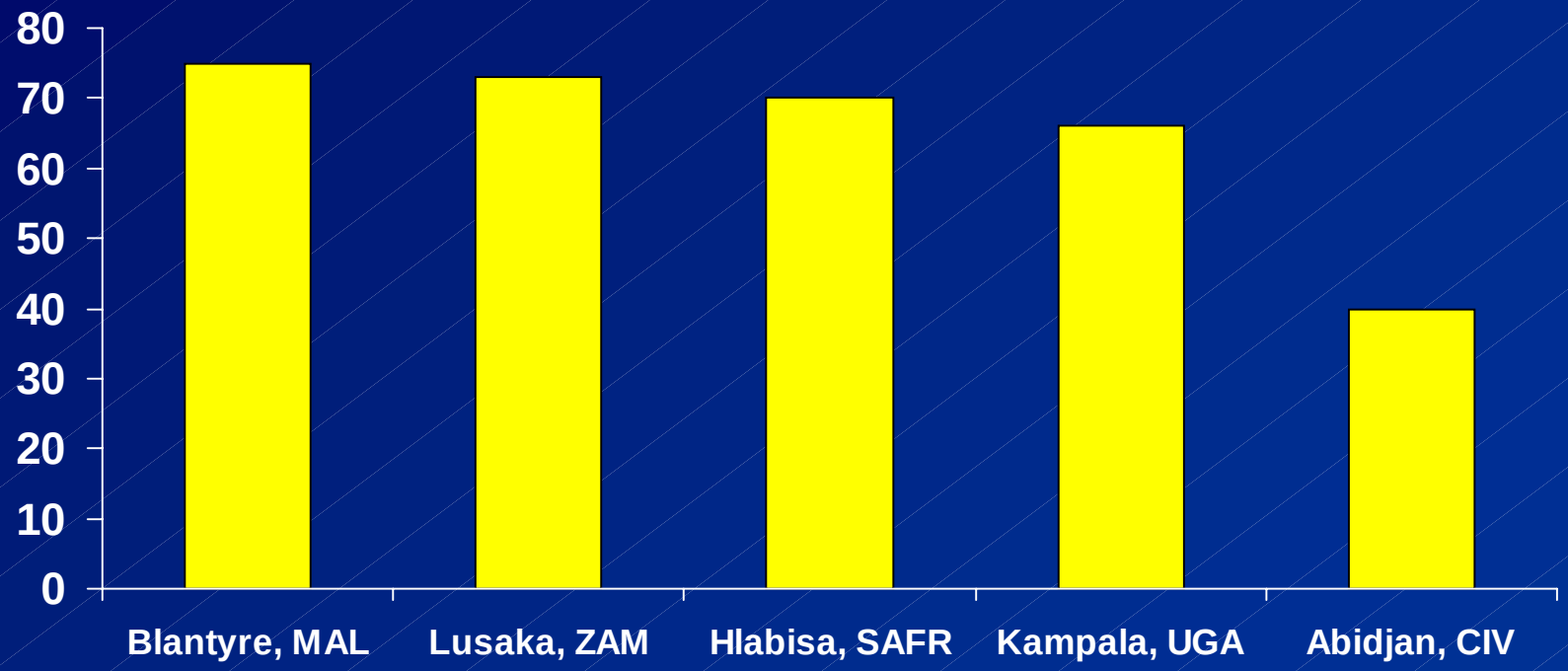
AIDS-related deaths
Brasil, 1990 - 1999



Relative Risks of Active TB



HIV Seroprevalence in TB Cases Africa, 1988-1997



TB is the major cause of death

- **Autopsy studies:**
  - **32% Cote d'Ivoire**
  - **38% Botswana**
- **Limited diagnostic facilities**
  - **Culture**
  - **Histopathology**
  - **Imaging**

AIDS 1993;7:1569
Int J Tuberc Lung Dis 2002;6:55

Tuberculosis Active Case Finding in MTCT HIV Prevention Program in Soweto, South Africa

Design:

- Cross-sectional Study
- May to Nov 2001

Setting:

- Chris Hani Baragwanath Hospital, Perinatal HIV Research Unit (PHRU)

Research Questions:

- Prevalence of active TB in a sub-sample of HIV-infected patients attending PHRU?

Nachega J., Coetzee J., Adendorff T., *et al*. *AIDS*, In press

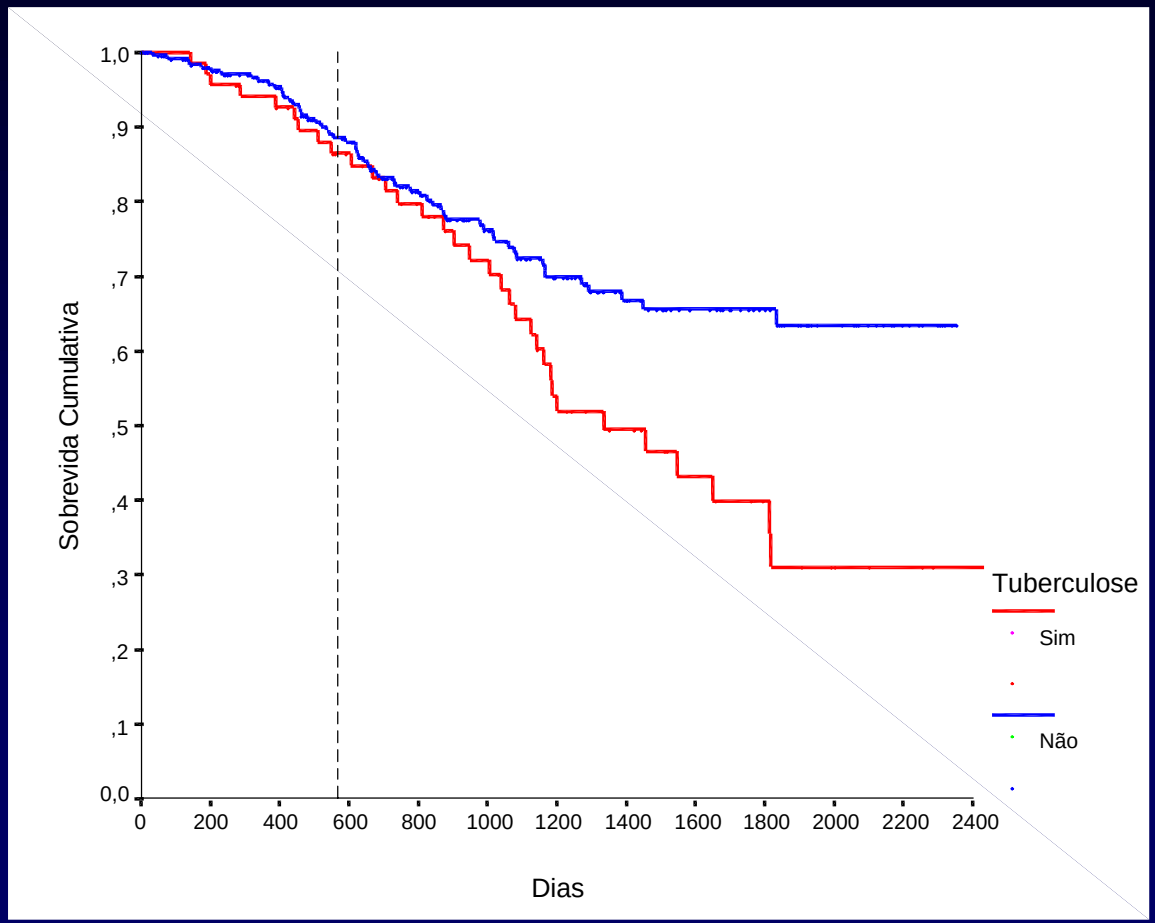
Tuberculosis Active Case Finding in MTCT HIV Prevention Program in Soweto, South Africa

Results:

- N = 438 HIV-infected adults
- mean age: 30 (±6.0); >95% were women
- Prevalence of latent TB (PPD+): 50%
- Prevalence of active TB in PPD+:13/120 (11%)

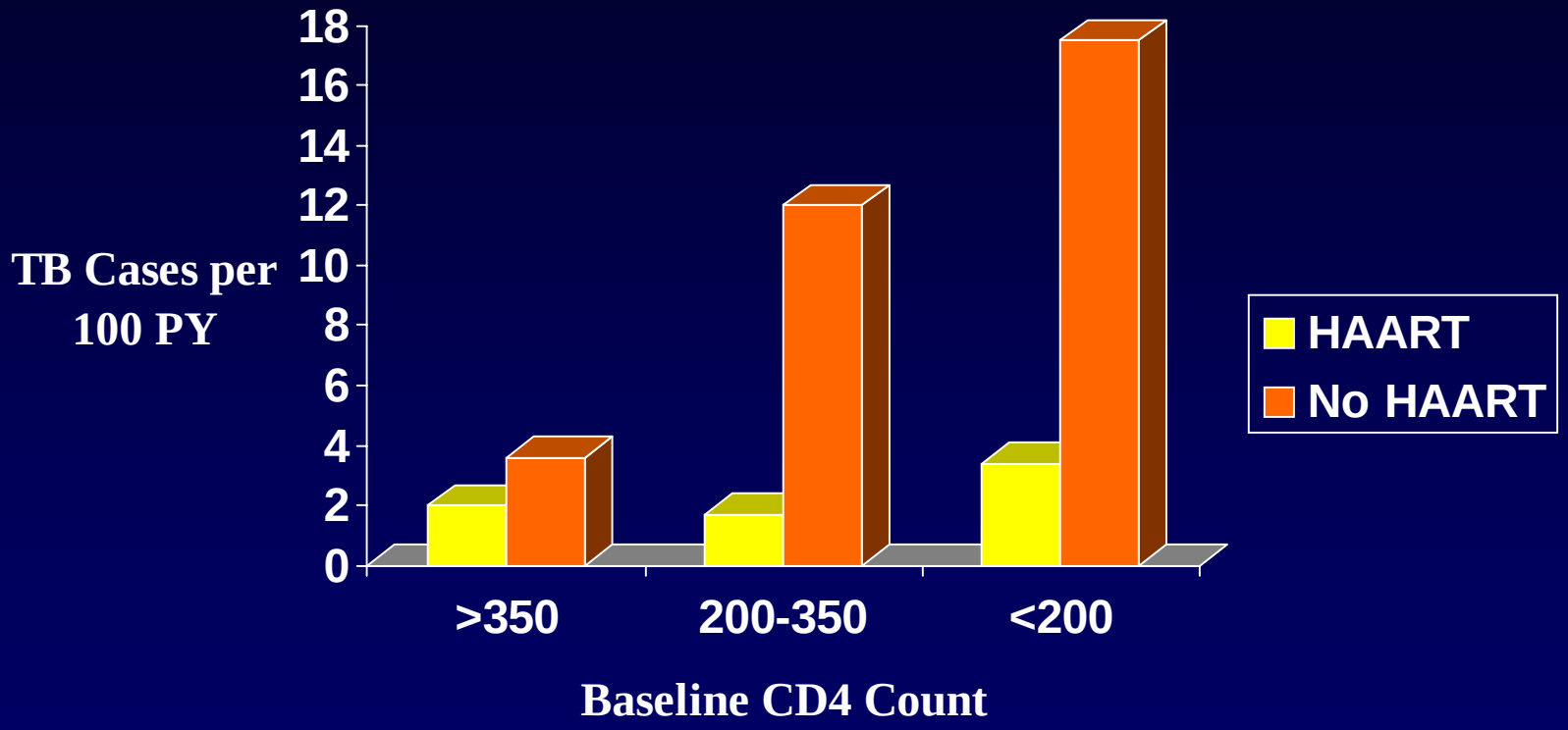
Nachega J., Coetzee J., Adendorff T., *et al*. *AIDS*, In press

Tuberculosis and Survival of 312 Individuals with Advanced HIV Disease (CD4+ < 15%)



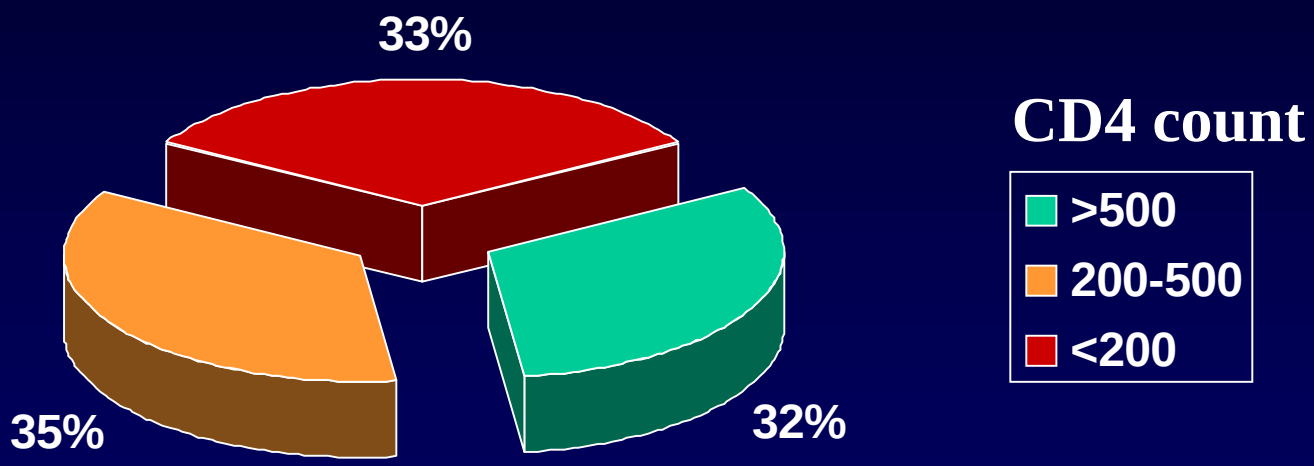
Santoro-Lopes, Clin Infect Dis 2002

Effect of highly active antiretroviral therapy on incidence of tuberculosis in South Africa: a cohort study



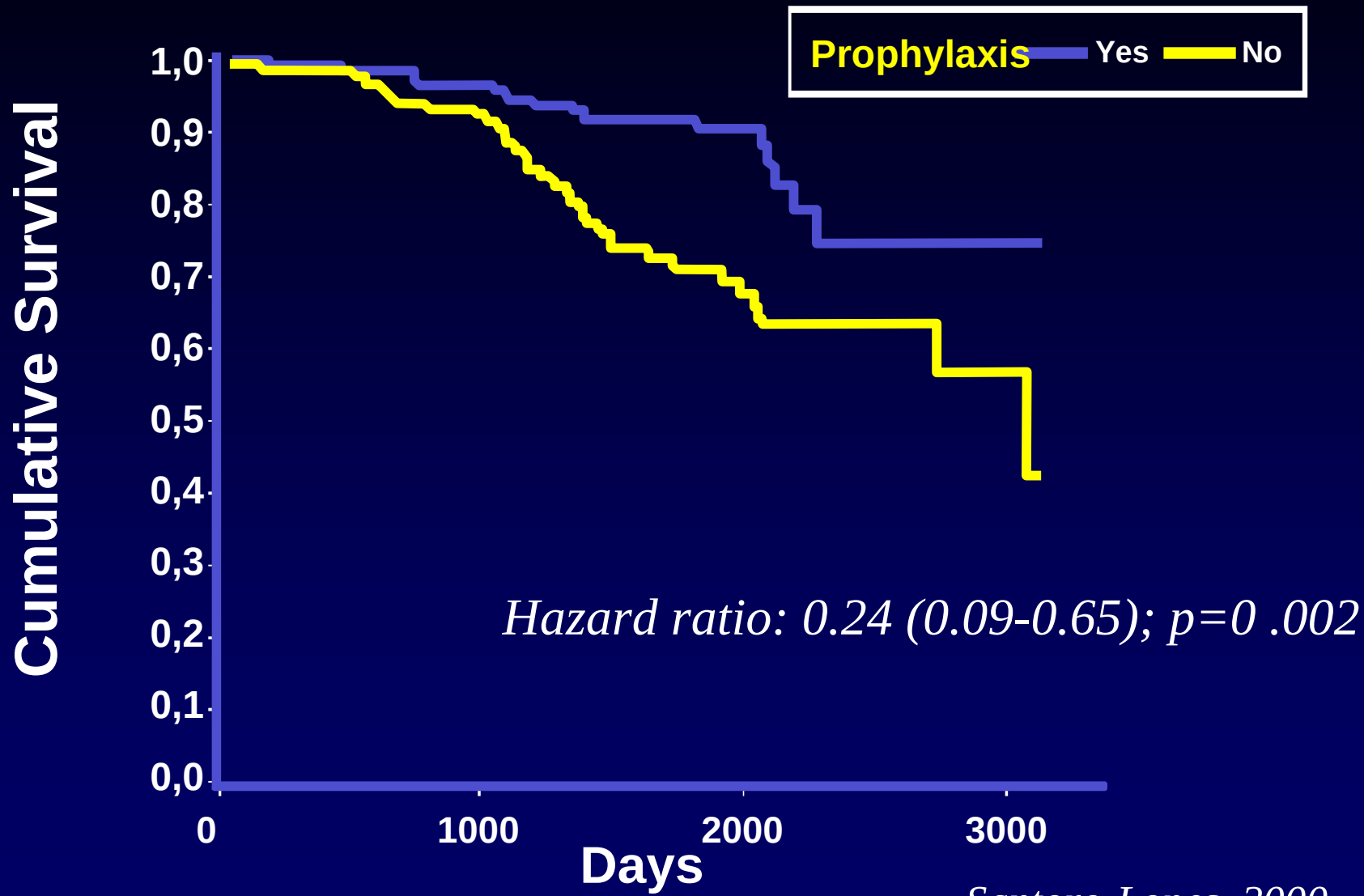
Badri et al. Lancet. 2002;359:2059-64

CD4 count of incident TB cases



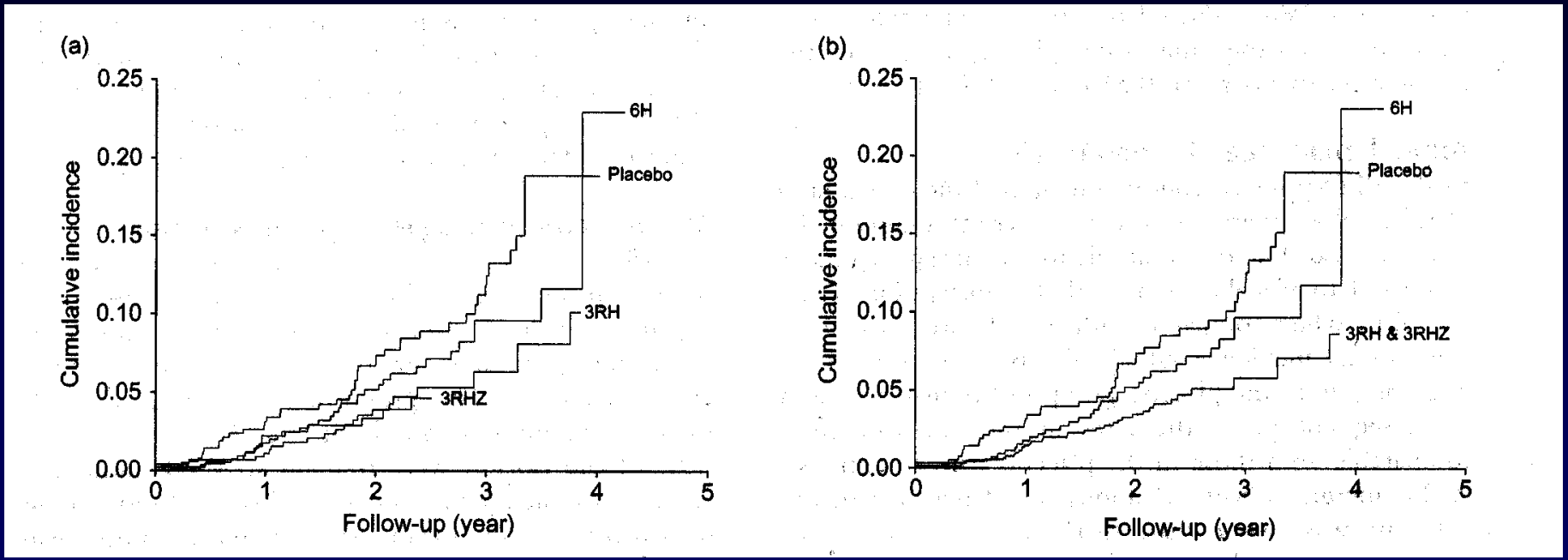
Badri et al. Int J Tuberc Lung Dis 2002;6:231-7

Tuberculosis: Prophylaxis and Survival



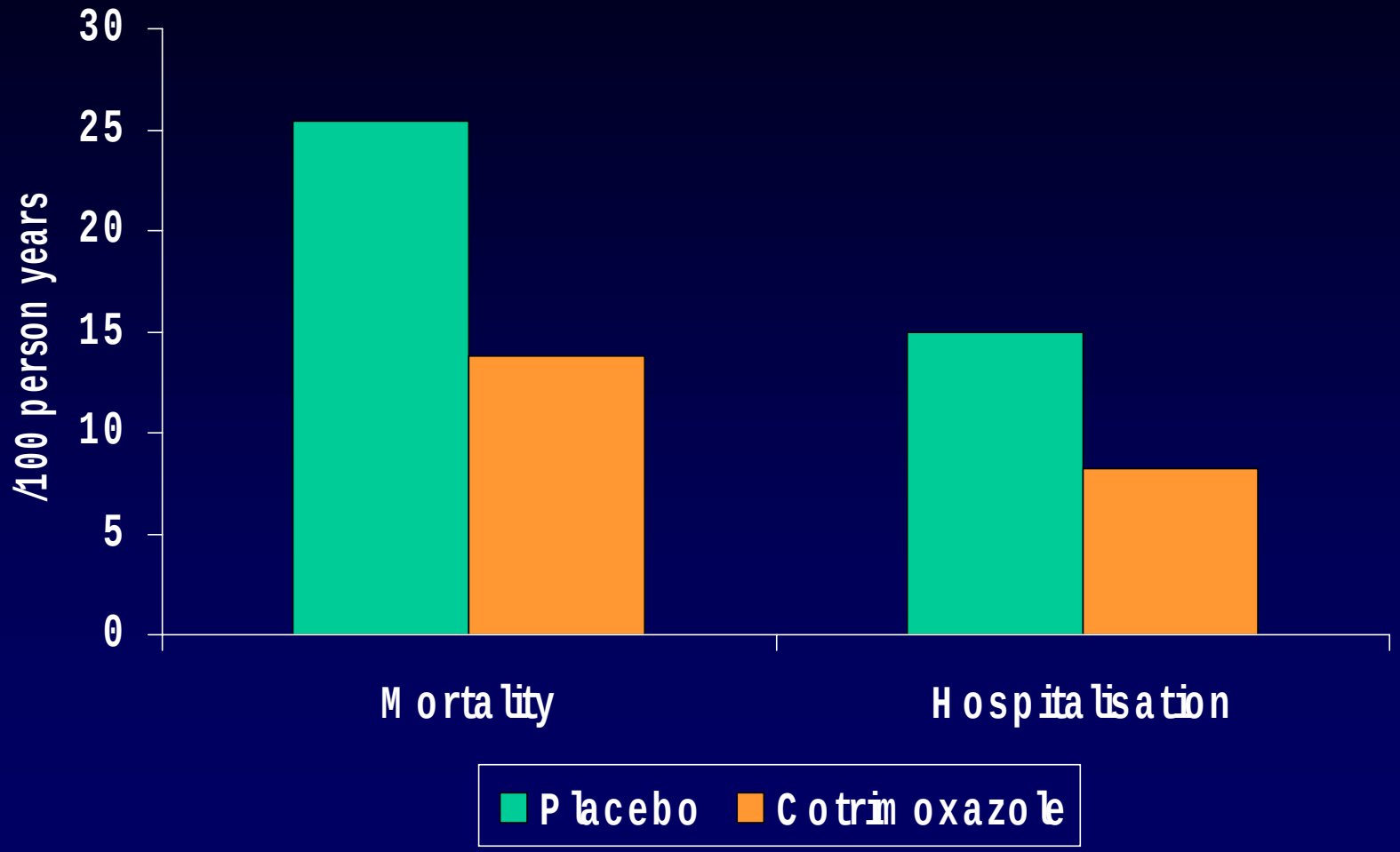
Santoro-Lopes, 2000

Duration of efficacy of treatment of latent tuberculosis infection in HIV-infected adults. Johnson et al. AIDS 2001;15:2137-2147



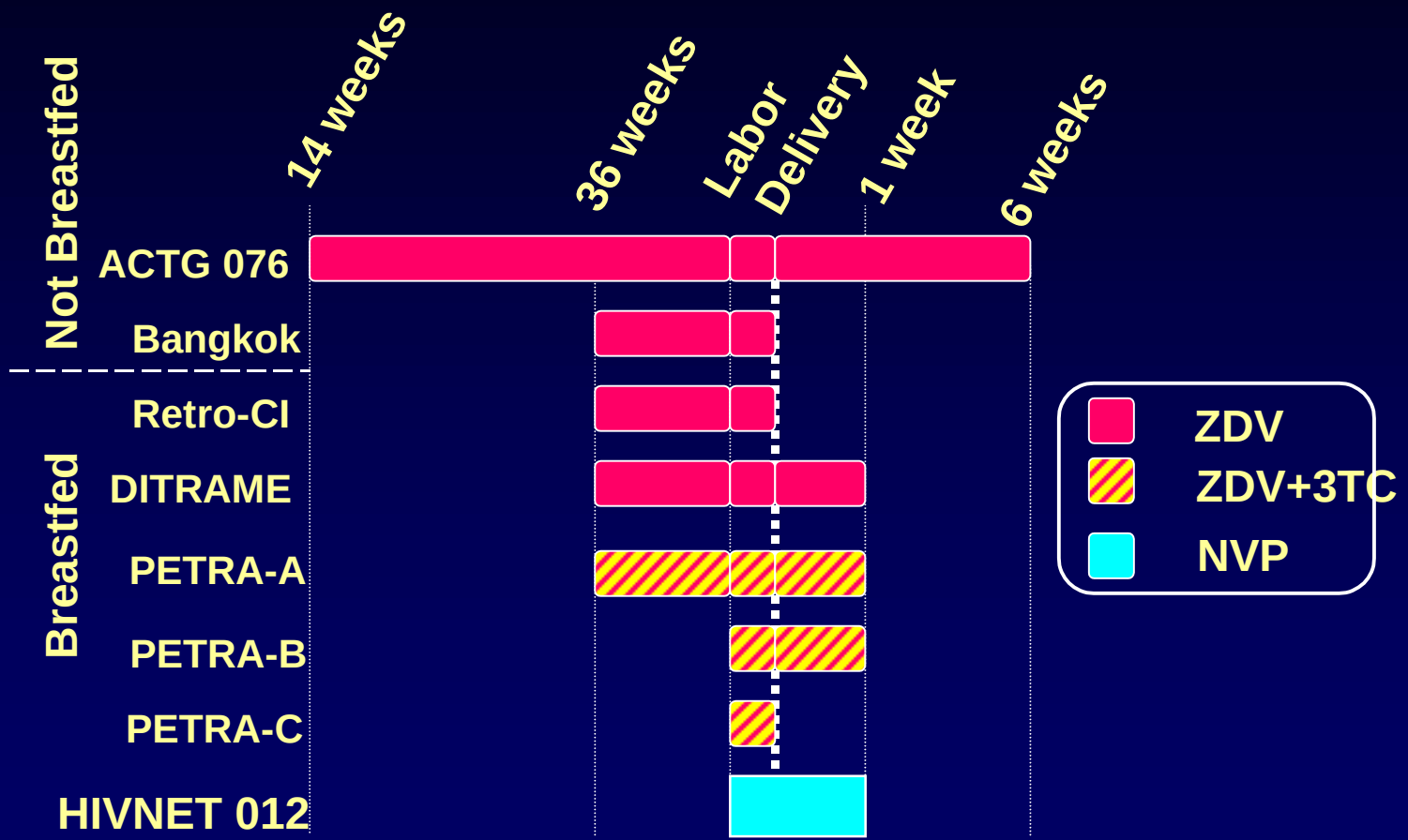
- Benefit of INH lost after 3 years
- Rifampin-based regimens have long-term benefit

Cotrimoxazole in TB/HIV



Lancet 1999;353:1469

Comparison of Timing of ACTG 076 and Short-course Antiretroviral Regimens



Documented Benefits of HAART: Socio- Economic

- Reduce number of orphans
- Increase work force
- Human capital
- Decrease need for retraining

JHU CFAR/UN Global Fund Special Consultation, Baltimore, October 2001

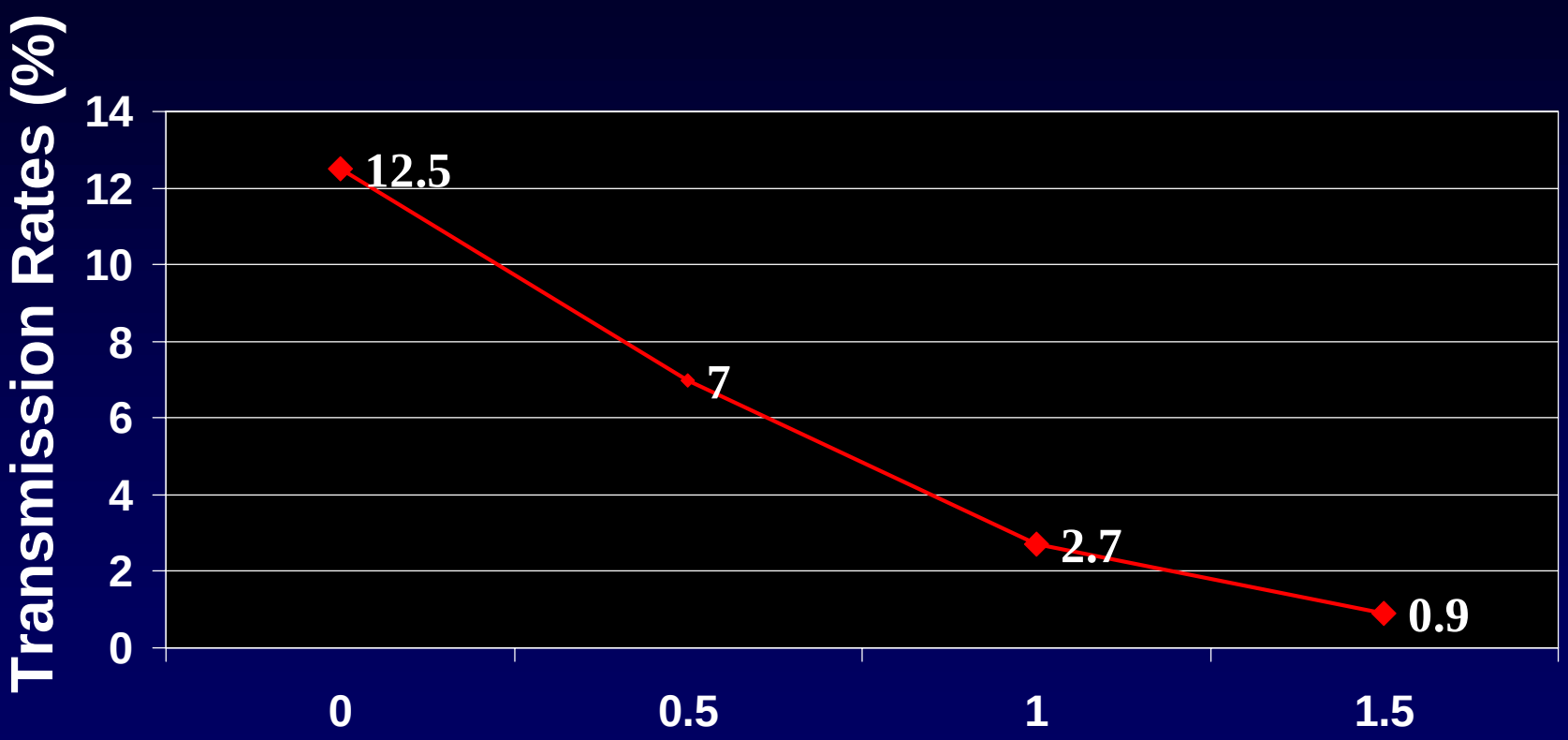
Documented Benefits of HAART: Public Health

- Decrease transmission of TB, HSV, HBV
- Build hope
- Greater participation in care among health care provider
- 1.5 Log reduction of VL reduce heterosexual transmission significantly

Importance for both HIV/AIDS Treatment and Prevention

- Incentive for VCT
- Decrease stigmatization of HIV infection
- Engagement/motivation of HC providers
- 1.5 Log reduction of VL reduce heterosexual transmission significantly
- Reduces STDs

Effect of Reduction in HIV-1 RNA Levels in Serodiscordant Ugandan Couples on HIV Transmission



Quinn TC et al. NEJM 2000, 342:921

Evaluation of UNAIDS HIV Drug Access Initiative Uganda and Côte d'Ivoire

Evaluation of pilot programs implemented by UNAIDS and national Ministries of Health

- **Capital cities of Uganda and Côte d'Ivoire**
- **August 1998-July 2000**
- **Patients paid for antiretroviral therapy and medical visits**
- **Côte d'Ivoire – subsidized treatment**
- **Laboratory monitoring supported by outside agencies**

AIDS Care and Support: Implementation and Accomplishments

UNAIDS Drug Access Initiative

Role of UNAIDS:

- **Negotiated drug prices**
- **Agreements with Ministries of Health**
- **Management of drug procurement and distribution through local NGO**
- **Identified standards for implementation, accredited hospitals**

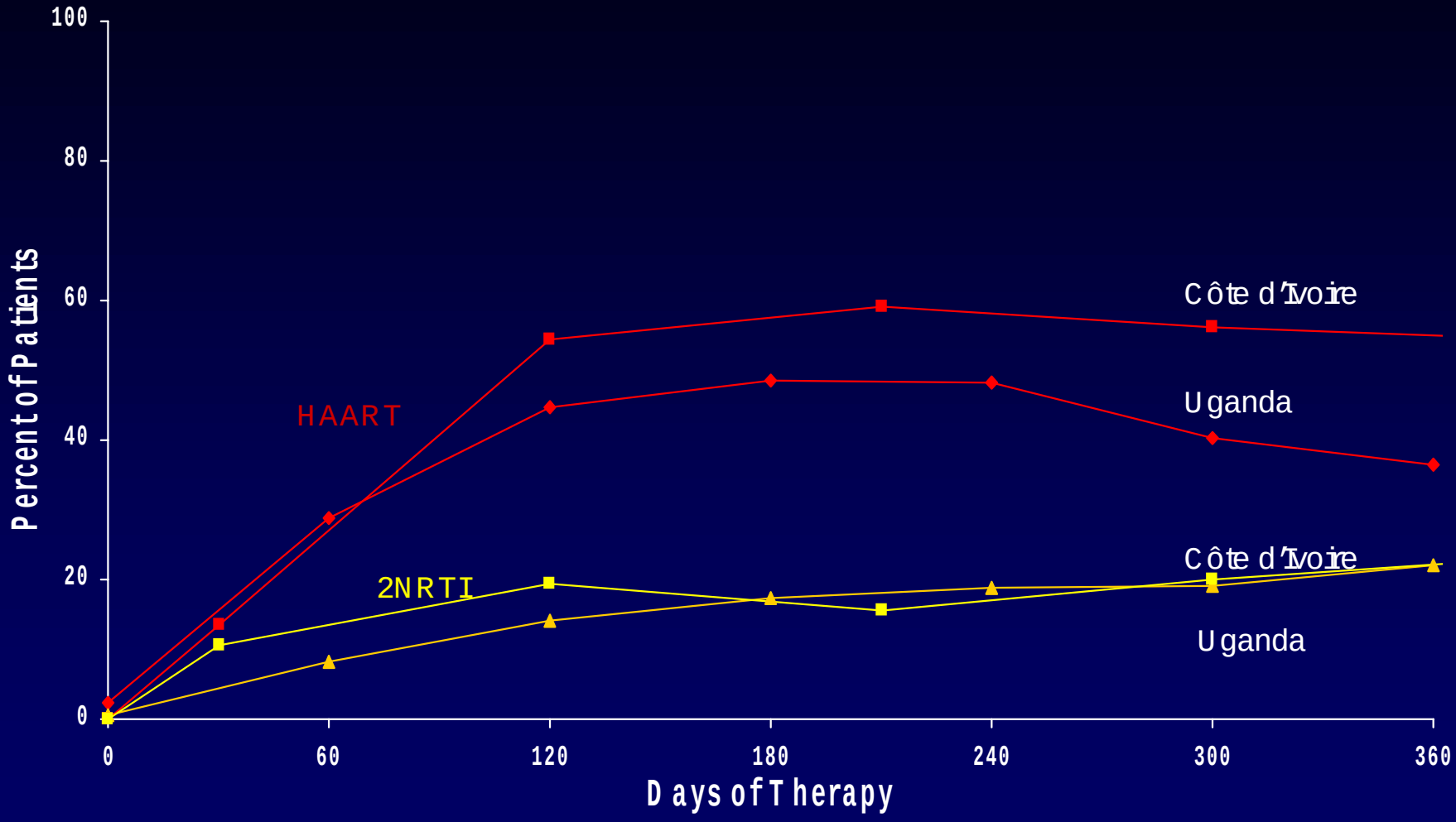
Background: Program Evaluation UNAIDS HIV Drug Access Initiative Uganda and Côte d'Ivoire

- **Patient response:**
  - **Clinical**
  - **Viral load**
  - **CD4+**
  - **Survival**
- **Genotypic and phenotypic resistance**

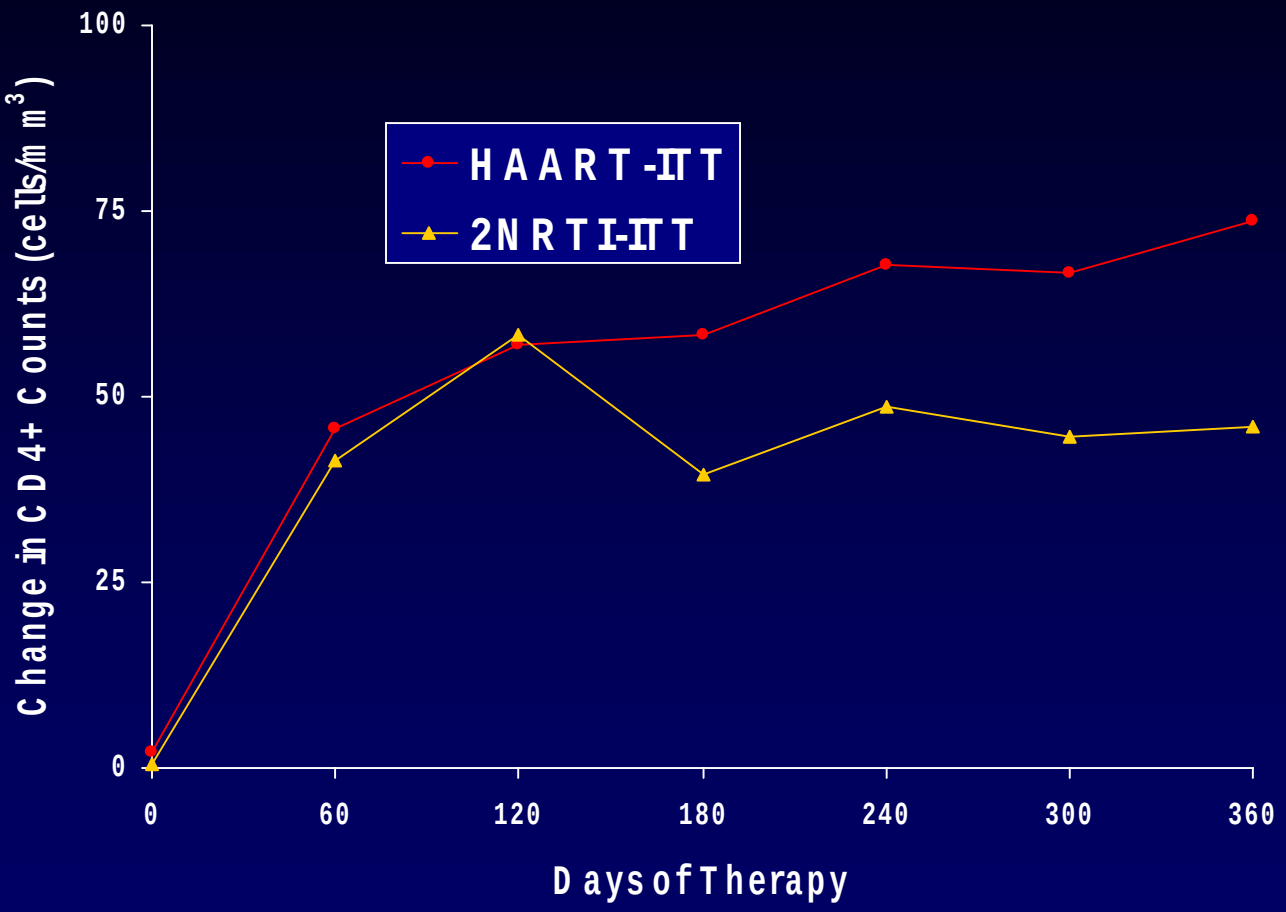
Characteristics of Patients on Antiretroviral Therapy, UNAIDS/MOH Drug Access Initiative August 1998-July 2000

	Côte d'Ivoire	Uganda
Patients (N)	**757**	**912**
Percent initiated with 2NRTI	**38%**	**45%**
Median baseline CD4+/mm^2	**107**	**73**
Baseline viral load (log copies/ml)	**5.6**	**5.3**

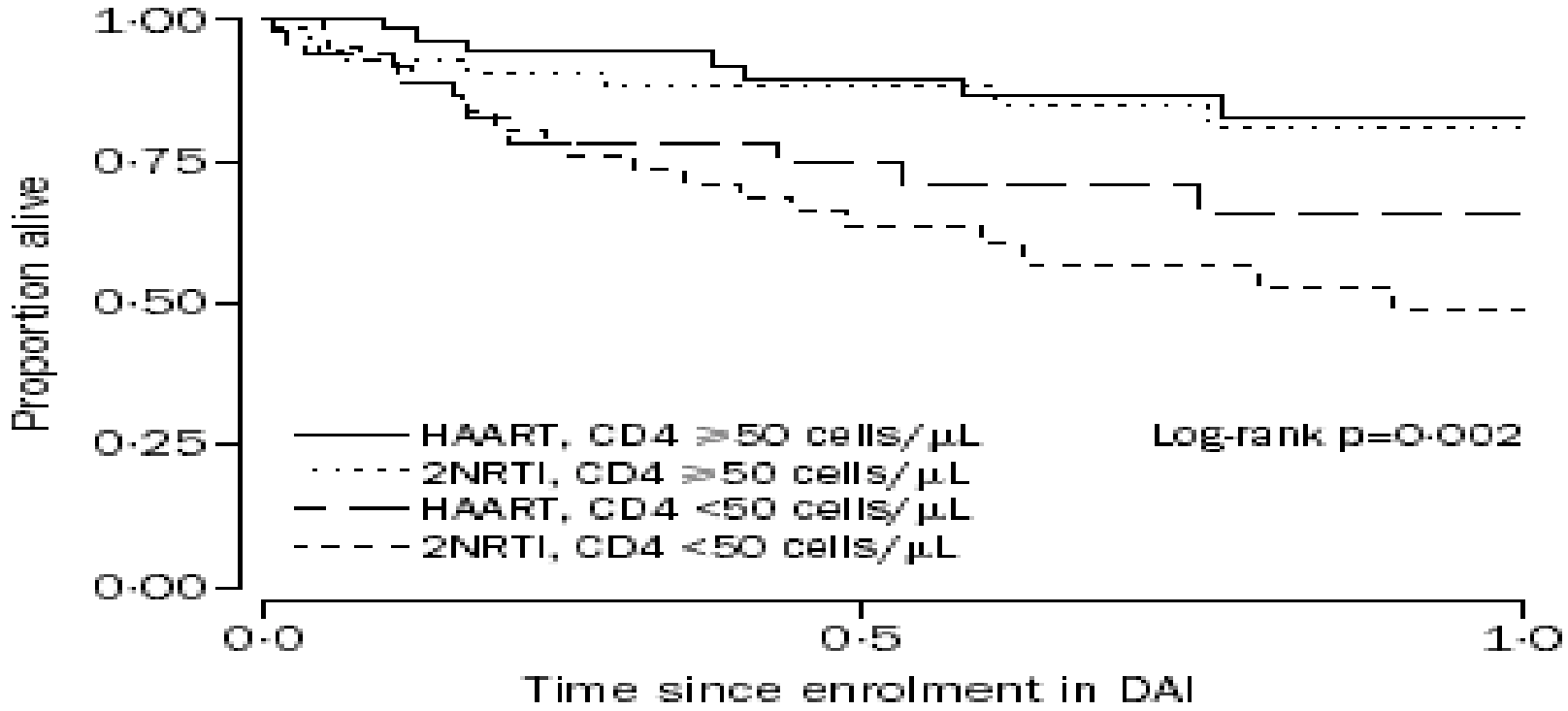
Undetectable Viral Load (<400 copies/ml)
Uganda and Cote d'Ivoire, 1998-2000



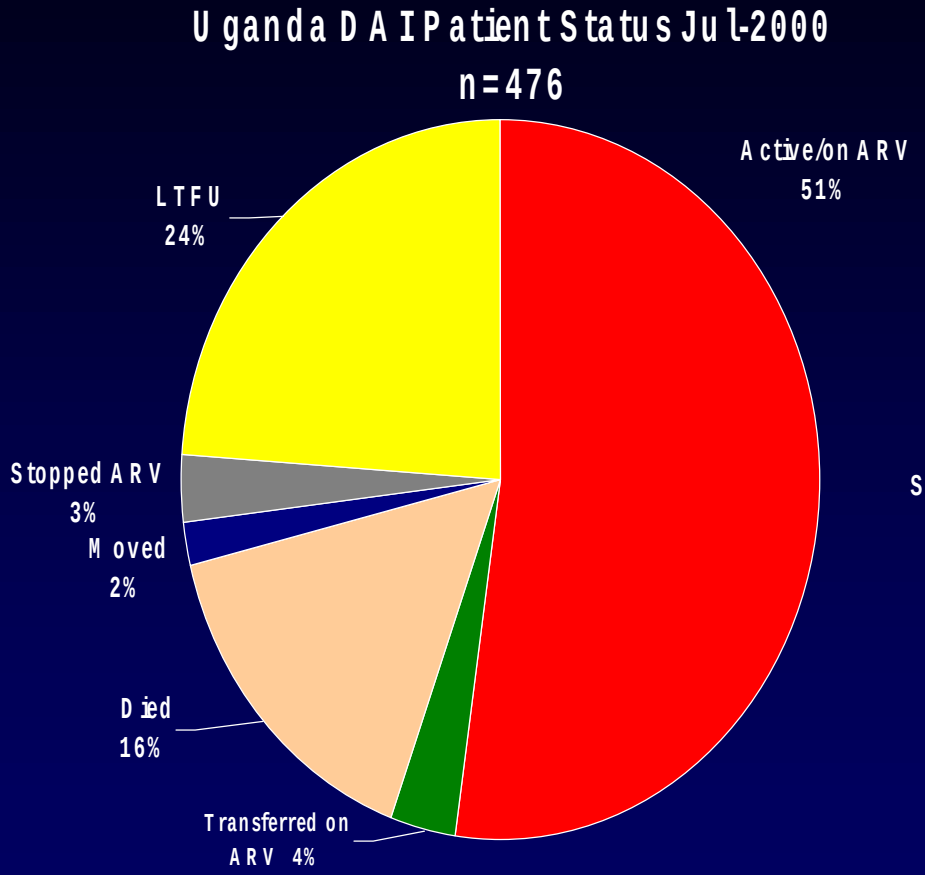
Change from Baseline CD4+
Uganda Drug Access Initiative, 1998-2000

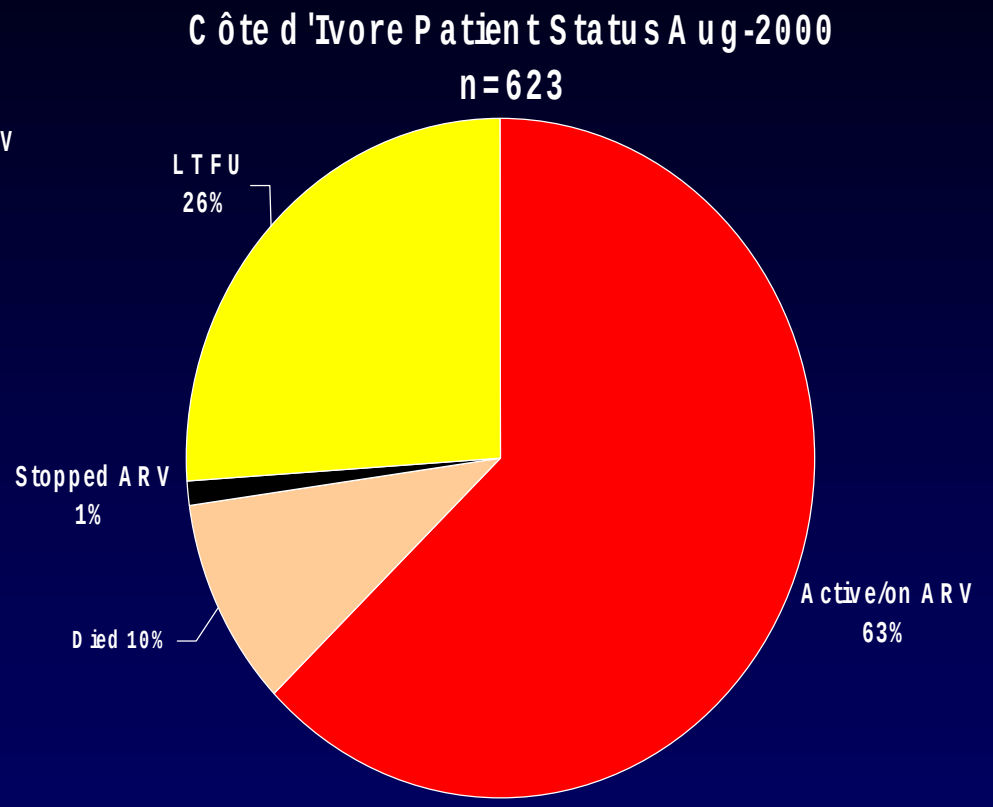


Kaplan-Meier Survival Analysis
Uganda UNAIDS/MOH Drug Access Initiative



Patient Status at End of Pilot Period of DAI





Phenotypic Resistance Uganda Drug Access Initiative

Resistance to NNRTI, first specimen tested

≥ 90 days after initiation of therapy (median, 251 days)

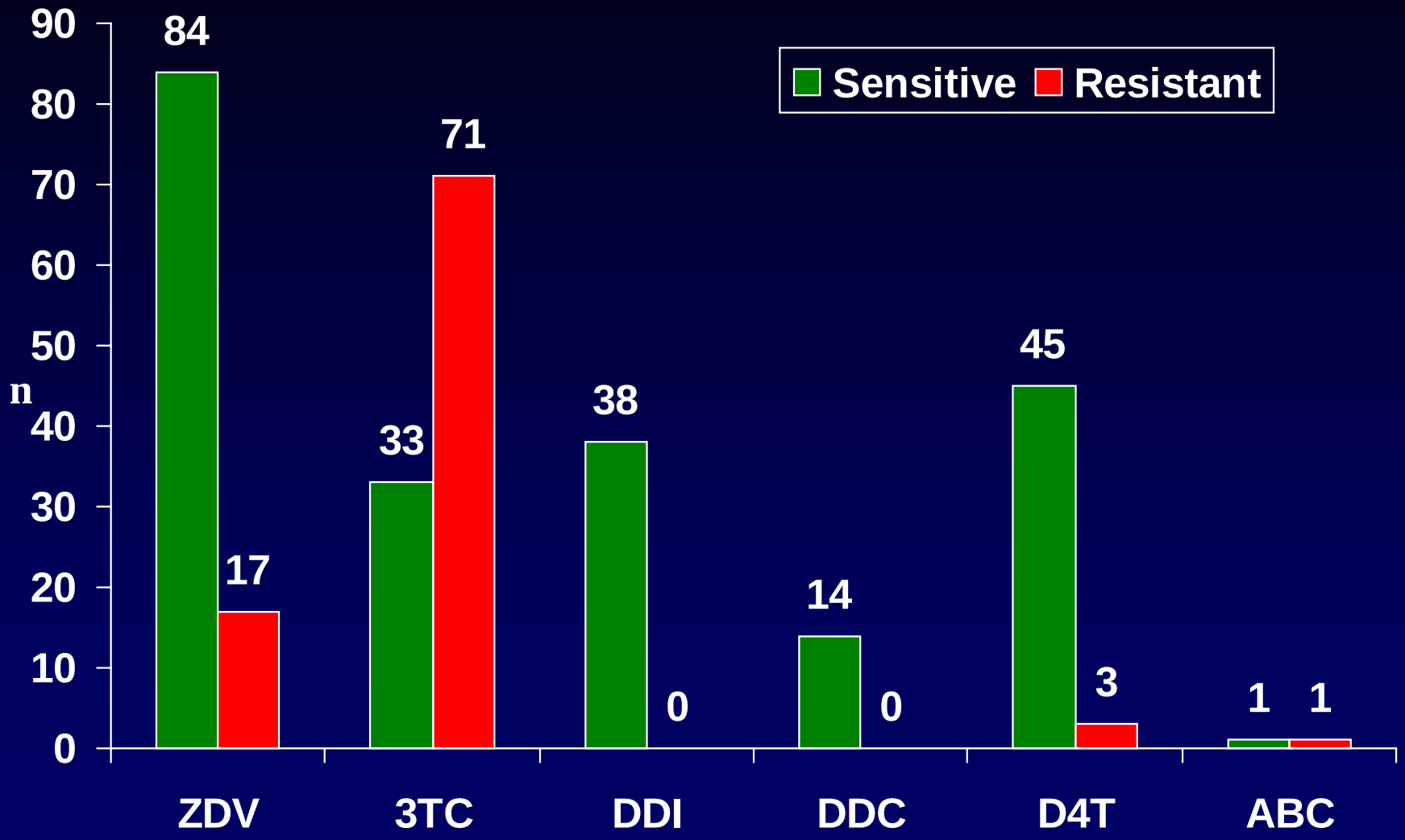
- **Overall: 52% (47/82) resistant**
- **Of those with resistance, 90% (42/47) were to 3TC**

Resistance by initial regimen:

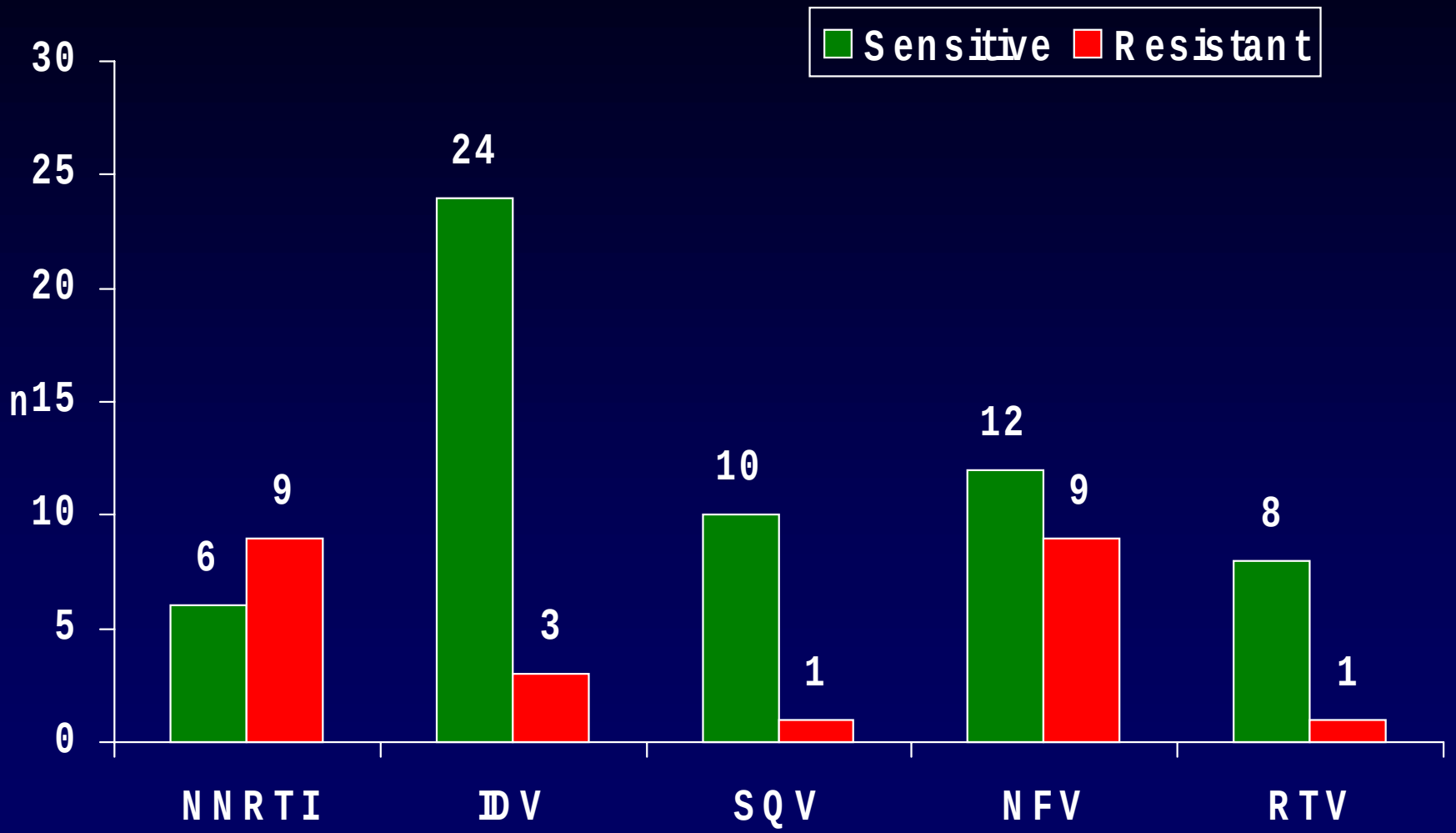
- **Patients on HAART: 40% (18/45)**
- **Patients on 2NRTI: 78% (29/37) p<.01**

Phenotypic Resistance to Nucleoside RTI

Jun 1999 - Jul 2000



Phenotypic Resistance to NNRTI and Protease Inhibitors (Jun 1999 - Jul 2000)



Genotypic Markers of Resistance to Nucleoside RTI

Drug	*mutation*	*N*	*%*
Lamivudine ***(n=77 spec)***			
	M184V, V/M	72	94%
	M184I	2	3%
	None	3	4%

UNAIDS/MOH DAI Côte d'Ivoire and Uganda: Summary

- Demonstrated AIDS patients can be managed successfully with ARVs in resource-restricted settings
- Self-reported drug adherence good
- CD4, viral load, survival similar to U.S. clinic populations
- Patterns of drug resistance similar to U. S. populations
- Approximately 65% of patients remained alive and in care at 1 year
- Identified need to access patients earlier in the course of their disease and improve continuity of care

Development of Simplified, Standardized Algorithms for Treatment and Monitoring

- Patient management was individualized
- Highly-trained physicians
- Complicated regimens and sequencing
- Limited practicality for broad access
- World Health Organization drafted simplified, standardized treatment algorithms*
- Streamline training and drug procurement

*http://www.who.int/HIV_AIDS/HIV_AIDS_Care/ARV_Draft_April_2002.pdf

Scaling Up HAART in SSA: When to Start?

CD4 Testing Available

- WHO stage IV irrespective of CD4 cell count
- WHO stage I, II or III[a] with CD4 count< 200

CD4 Testing Not Available

- WHO Stage IV irrespective of TLC
- WHO Stage II or III[c] with TLC less than 1200/mm^3

WHO 2002 Guidelines foe Scaling Up HAART in SSA: A Public Health Approach

Scaling Up HAART in SSA: Approved ARVs on WHO's List

NsRTIs	NtRTI	NNRTIs	Pis
Zidovudine (ZDV) Didanozine (DDI) Stavudine (D4T) Lamuvidine (3TC) Abacavir (ABC)	Tenofovir disoproxil fumarate (TDF)	Nevirapine (NVP) Efavirenz (EFV)	Saquinavir (SQV) Ritonavir (RTV) Indinavir (IDV) Nelfinavir (NFV) Lopinavir/ritonavir (LPV/r)

Scaling Up HAART in SSA: First Line Regimens

- **2NRTI + 1NNRTI**

  ZDV/3TC or D4T/3TC or D4T/DDI or ZDV/DDI

  +NVP or EFV

- **2NRTI + 1NRTI**

  ZDV/3TC/ABC

- **2NRTI + PI or PI/r**

  ZDV/3TC + LPV/r or SQV/r or NFV or IDV/r

WHO 2002 Guidelines foe Scaling Up HAART in SSA: A Public Health Approach

Scaling Up HAART in SSA: Second-Line Regimens

First-Line Regimens	Second-Line Regimen for Rx failure	Alternative regimens for Rx failure
ZDV/3TC/EFV or ZDV/3TC/NVP	D4T/DDI/PI-r	PI-r/ABC/DDI NFV/ABC/DDI or D4T/DDI/NFV
ZDV/3TC/ABC	D4T/DDI/EFV or D4T/DDI/NVP	D4T/DDI/RTV
ZDV/3TC/PI-r or ZDV/3TC/NFV	D4T/DDI/EFV or D4T/DDI/NVP	ABC/DDI/or ABC/DDI/NVP

Scaling Up HAART in SSA: Special Considerations

Pregnancy

- Substitute NVP for EFV
- Avoid D4T/DDI→Lactic Acidosis
- ABC & LPV/r safety data limited

Children

- 1st line: ZDV/3TC/NVP or EFV (>3y)
- ZDV/3TC/ABC if TB Rx
- 2nd line: D4T/DDI + PI (NLF and LPV/r: supportive safety data)

Scaling Up HAART in SSA: Tuberculosis co-infection

Situation	Recommendation
Pulmonary TB and CD4 < 50 or Extra Pulmonary TB	Start TB Rx. + AZT/3TC/ABC AZT/3TC/EFV ZDV/3TC/SQVr
Pulmonary TB and CD4 50-200 or TLC <1200	Start TB Rx. Delay HAART until 2 months of TB Rx (as above)
Pulmonary TB and CD4>200 or TLC >1200	Start TB Rx. HAART if WHO stage 4

Pharmacokinetic Interactions Between EFV and RIF in HIV-Infected Patients with Tuberculosis. Lopez-Cortes, et al. Clin Pharm 2002;41:681-690

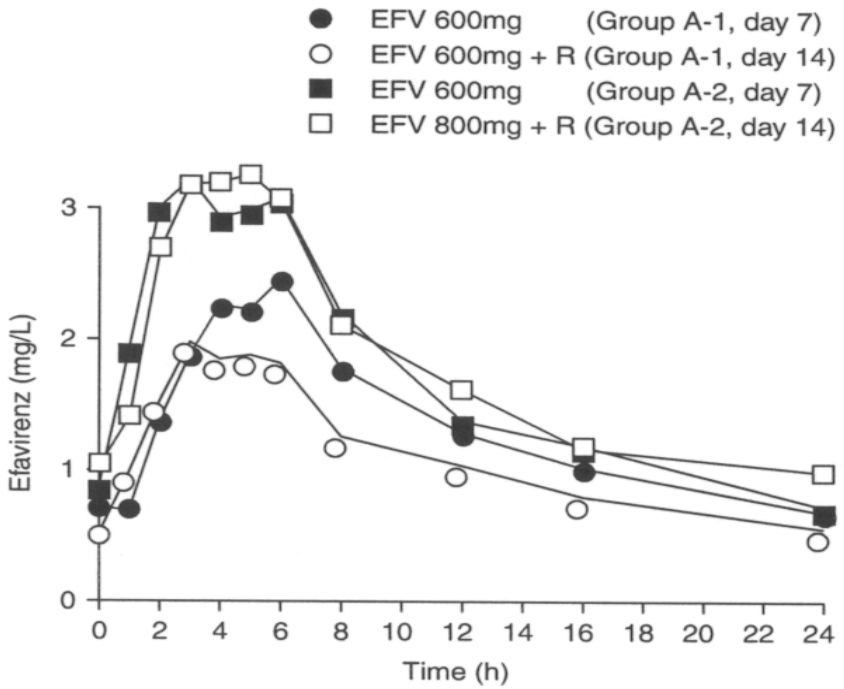


Fig. 2. Median plasma efavirenz (EFV) concentration-time profiles alone (day 7) and in combination with rifampicin (R) [day 14]. One patient from group A-2 was excluded because of very abnormal efavirenz plasma concentrations on day 14.

Scaling up HAART in SSA: Recommended Diagnostic and monitoring Testing

- **Baseline Medical History and PE**: TB, Current or planned pregnancy, Medications …
- **FUP**: One month post HAART initiation then every 3-4 months
- **Clinical Monitoring**: symptoms (weight, change in frequency and severity of HIV associated symptoms (fevers. diarrhea, candidiasis, etc.)
- **Absolute minimum tests**: HIV testing and Hemoglobin level
- **Basic tests tests**: WBC and differential/TLC, LFTs, U&C, Glucose, Pregnancy test
- **Desirable tests**: bilirubin, amylase, serum lipid and CD4
- **Optional test**: Viral load

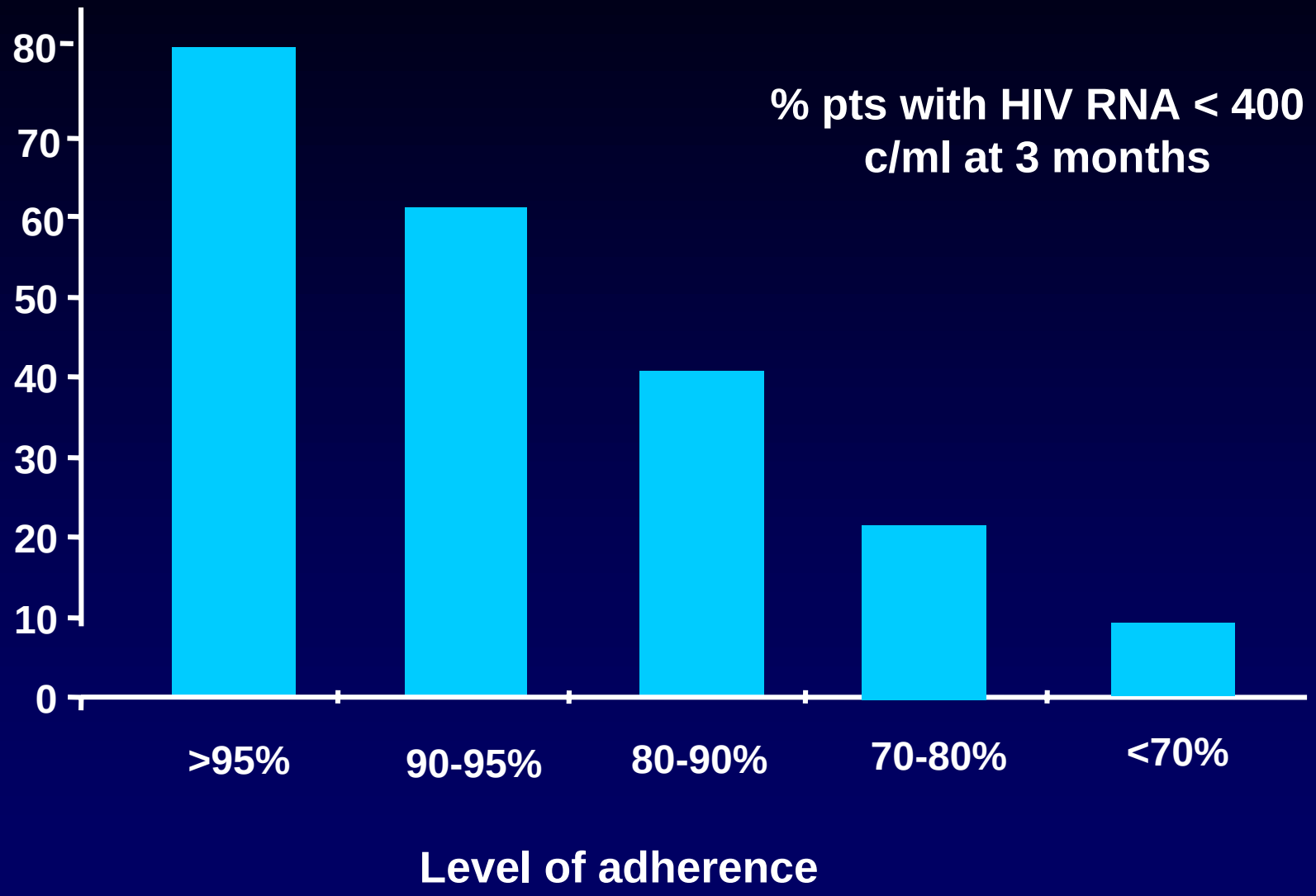
Research Priorities in ARV Monitoring Evaluation of Low Cost Diagnostics

- Evaluate low-cost diagnostics for viral load and CD4+
  - Blood stabilizers for transport of specimens
  - Taqman-based viral load
  - Reagent-sparing CD4+, panleucogating
  - Heat denatured boosted p24 antigen
  - Cavidi - reverse transcriptase
  - Dynabeads
  - Microchip based CD4 count technology

Research Priorities for Scaling Up Access to Antiretroviral Therapy

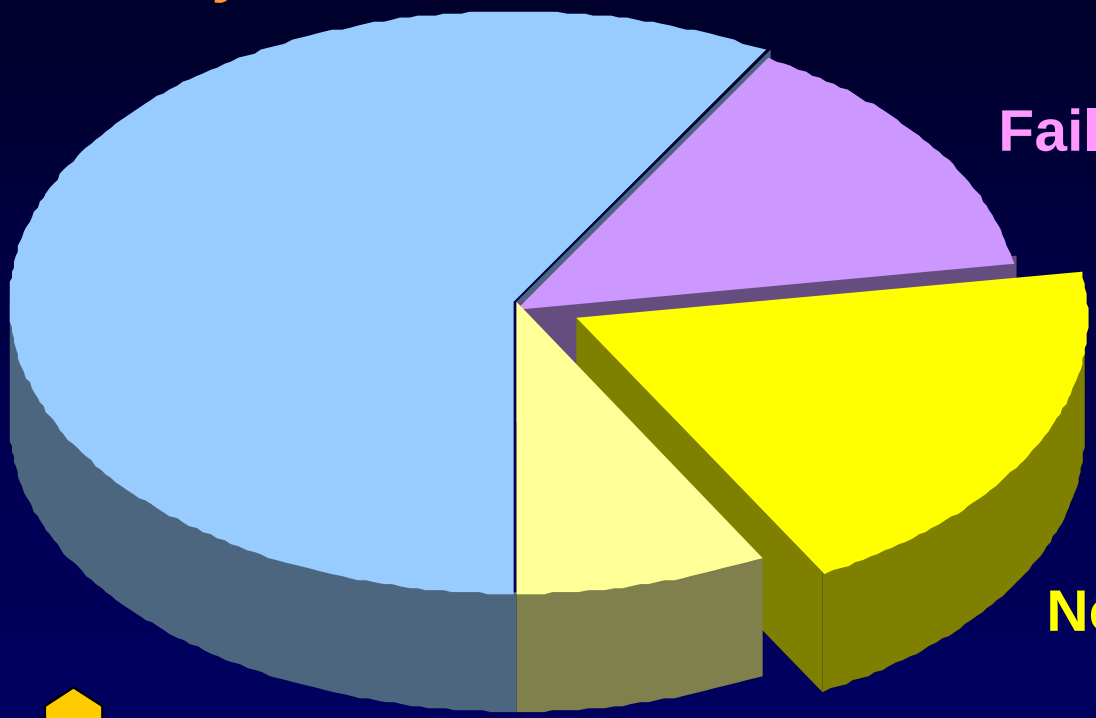
- Need to identify strategies to improve adherence and continuity of care
  - Improve understanding of chronic disease management
  - Community involvement
  - Role of families, partner notification
  - Patient support systems

ART Adherence and Viral Suppression



Paterson D, Swindells S, Mohr J. et al. 6th CROI, 2001, Chicago, 1999, Ab.# 92

Main reasons for discontinuation of HAART in naive patients (n=862)



Italian Cohort Naive Antiretroviral

Monforte *et al*. *AIDS* 2000;14:499-507

Knowledge, Attitude, Beliefs & Practices (KABP) about ART, Soweto, South Africa

Design:

- Cross-sectional study
- August to October 2002

Setting:

- Chris Hani Baragwanath Hospital, HIV Adult Clinic

Research Questions:

- What are expectations and assumptions about ART in setting where these drugs are scarce?
- Are there likely to be barriers to ART adherence?

Nachega J., Lehman D., Hlatshwayo D., *et al*. 10th CROI 2003. Boston, Th Or #169

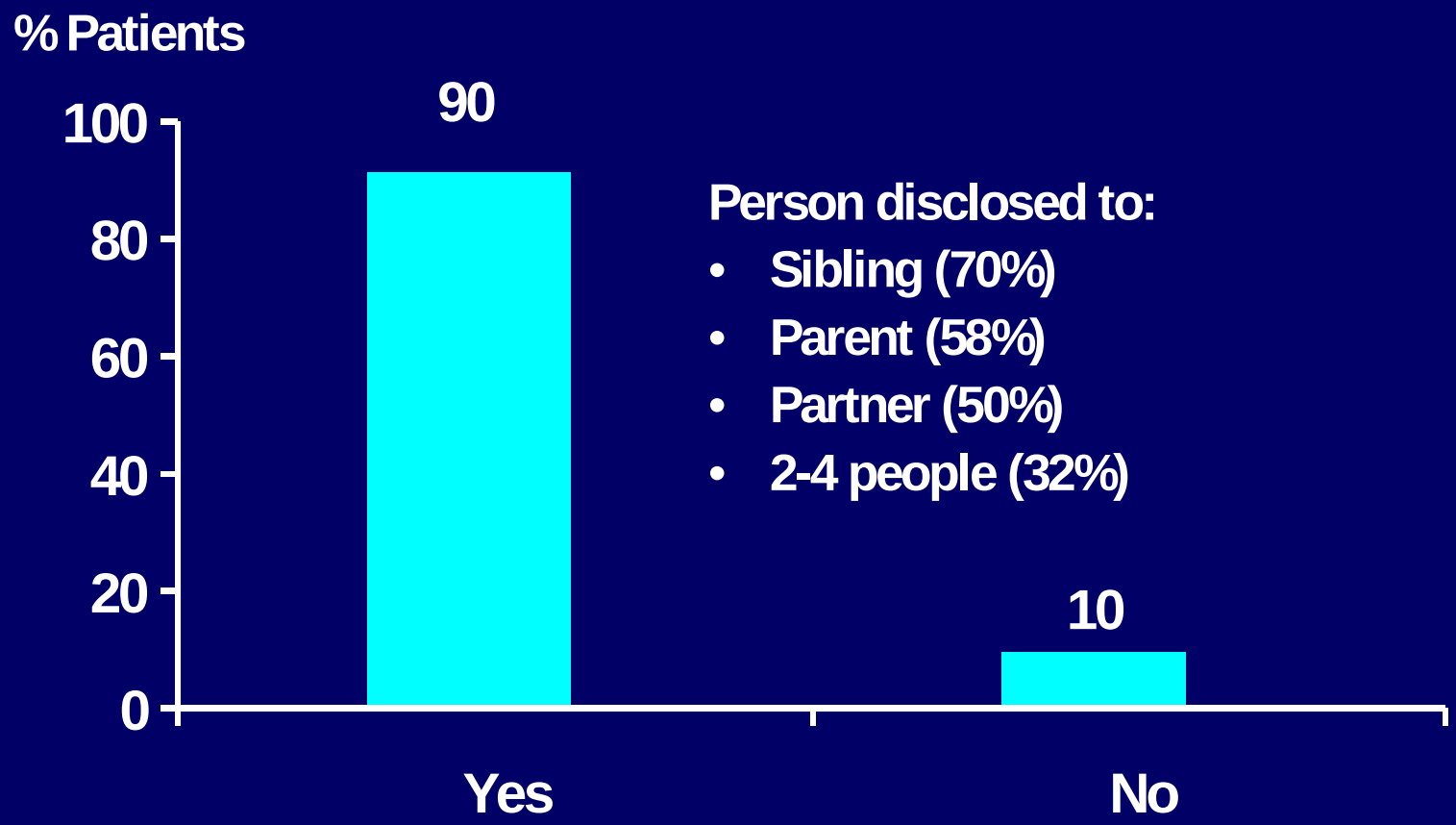
KABP ART, Soweto, South Africa

Results:

- N= 105
- Mean age: 34yrs; SD: 9; Range: 18-62
- 99% Black African; 72% women
- 65% unemployed
- 70% education lower than a high school diploma
- 90% with electricity; 64% with running water

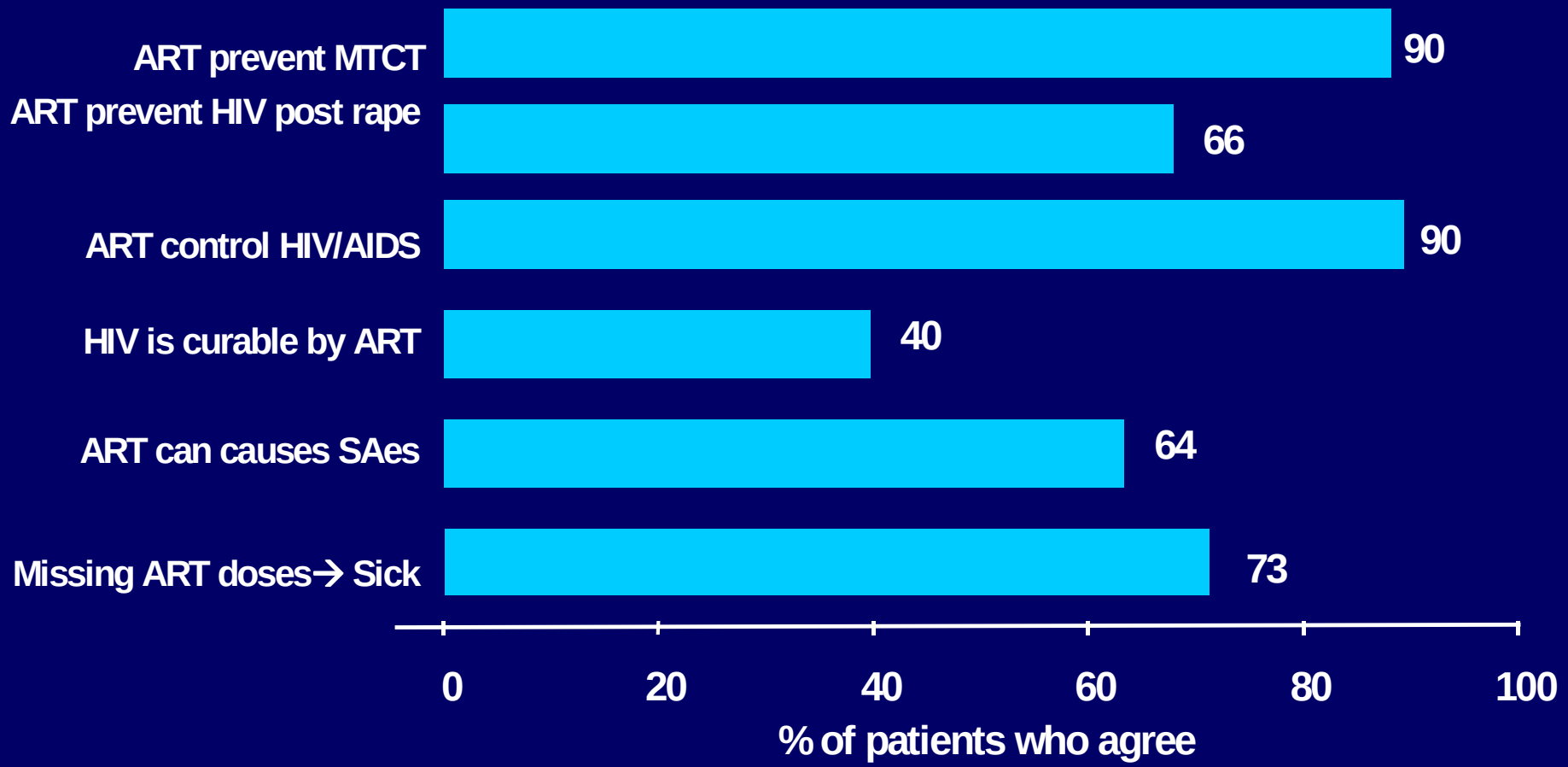
Nachega J., Lehman D., Hlatshwayo D., *et al*. 10th CROI 2003. Boston, Th Or #169

“Have you told anyone that you are HIV positive?” (N=105)



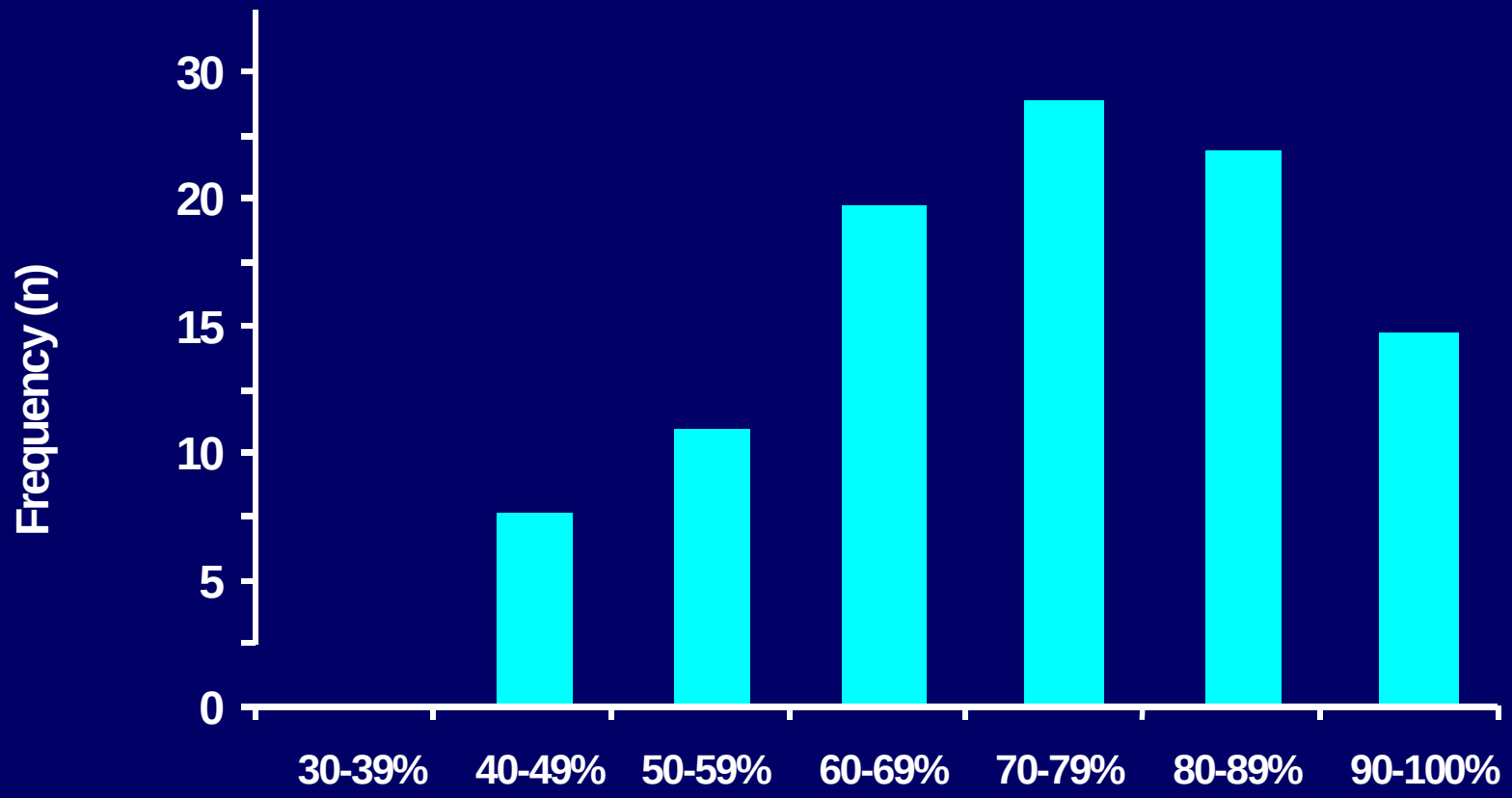
Nachega J., Lehman D., Hlatshwayo D., *et al*. 10th CROI 2003. Boston, Th Or #169

KABP ART Soweto, South Africa: Patient's perception benefit of ART



Nachega J., Lehman D., Hlatshwayo D., *et al*. 10th CROI 2003. Boston, Th Or #169

KABP ART, Soweto, South Africa: % ART Knowledge Score



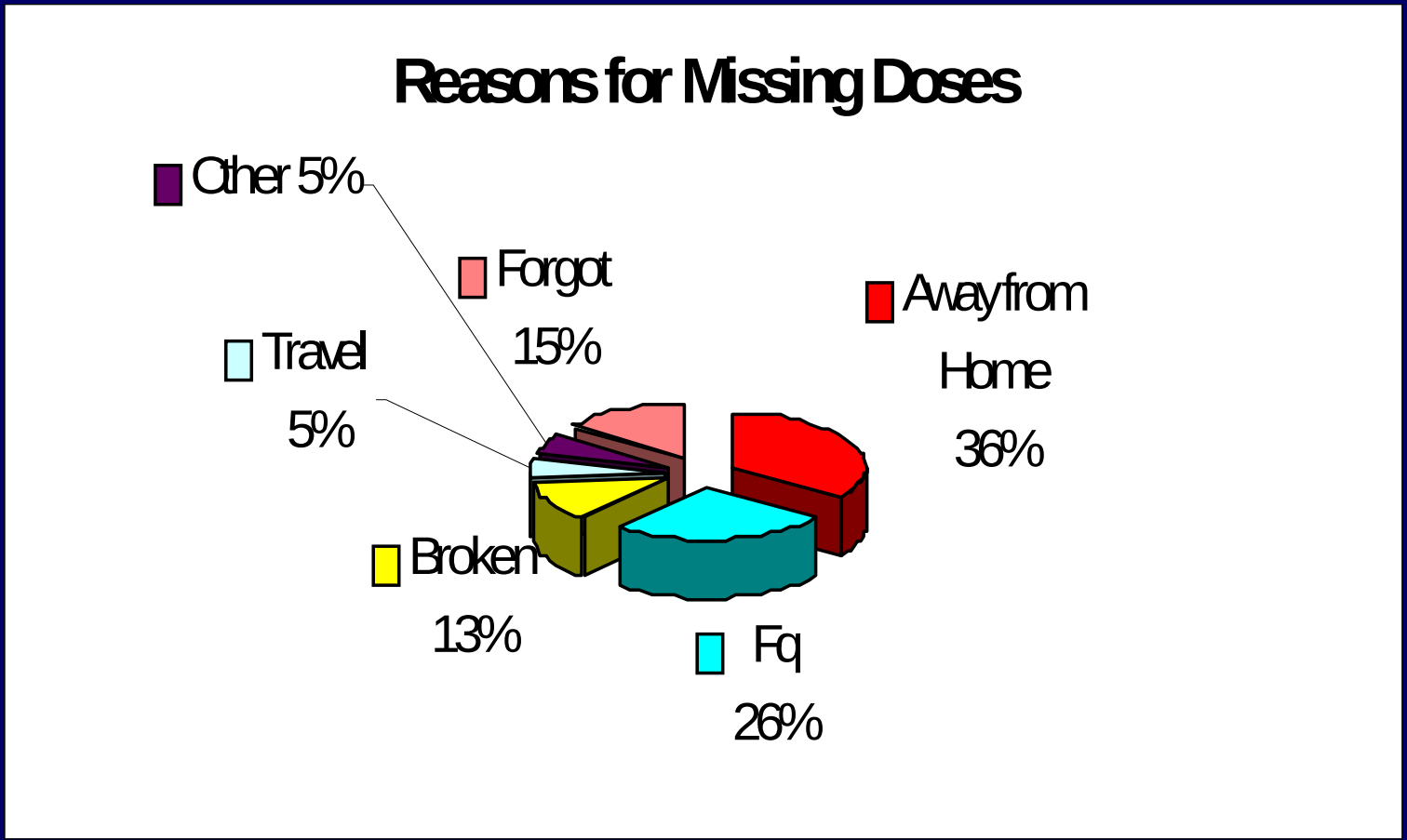
Nachega J., Lehman D., Hlatshwayo D., *et al*. 10th CROI 2003. Boston, Th Or #169

Beliefs in HIV cure by HAART: Bivariate Logistic Regression Model

	AOR	*95% CI*	*P-Value*
Age	1.1	1.0, 1.17	0.004
Gender	1.7	0.53, 5.5	0.37
Education (high/low)	0.29	0.07, 1.3	0.09
Length known HIV+	0.9	0.76, 1.1	0.19
ART Use (yes/no)	0.53	0.13, 2.2	0.38
Married (yes/no)	1.69	0.5,5.7	0.4
SES Score	0.59	0.35, 1.0	0.051

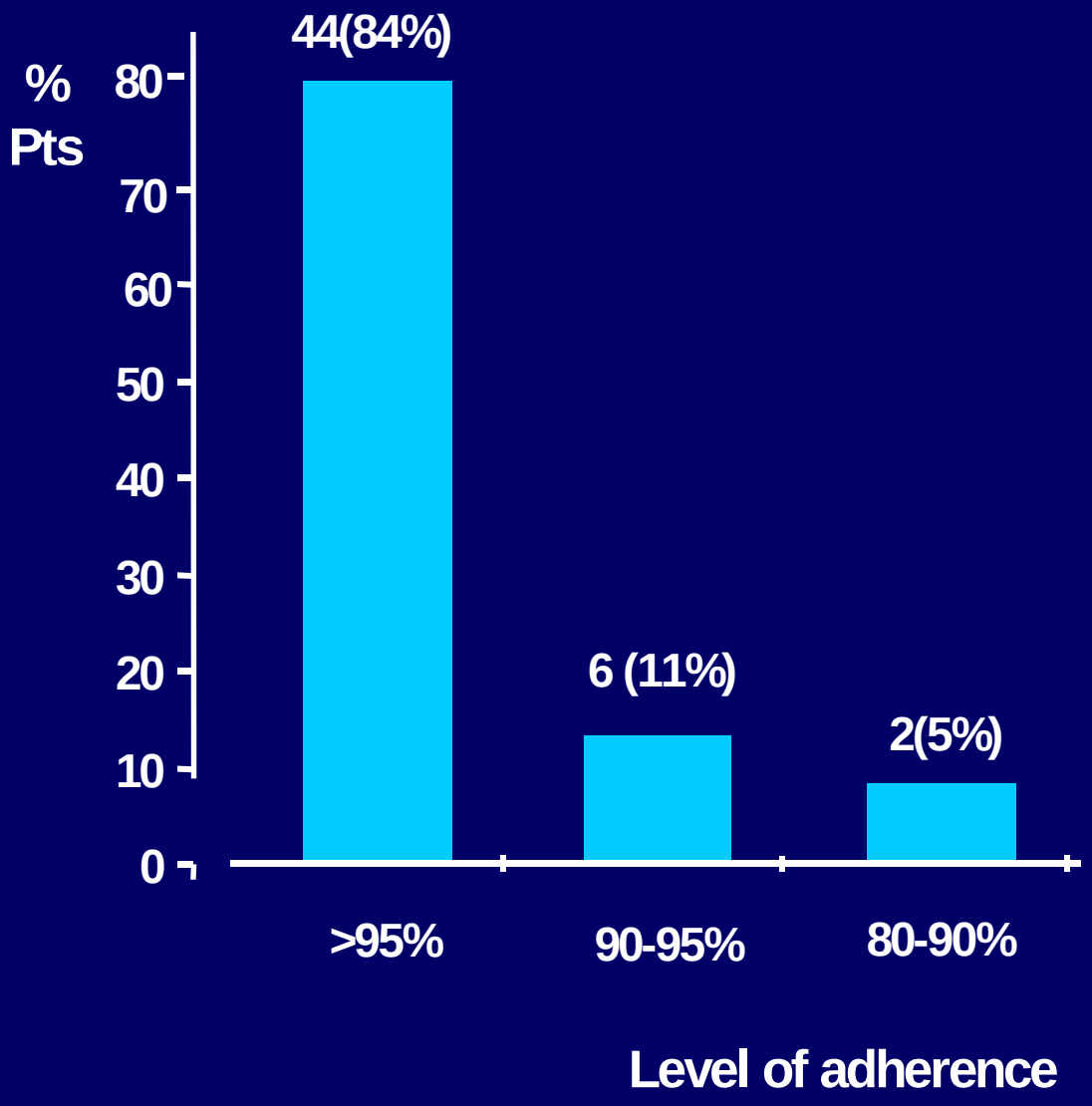
Nachega J., Lehman D., Hlatshwayo D., *et al*. 10th CROI 2003. Boston, Th Or #169

ART Adherence, Soweto, South Africa



Nachega J., Lehman D., Hlatshwayo D., *et al*. 10th CROI 2003. Boston, Th Or #169

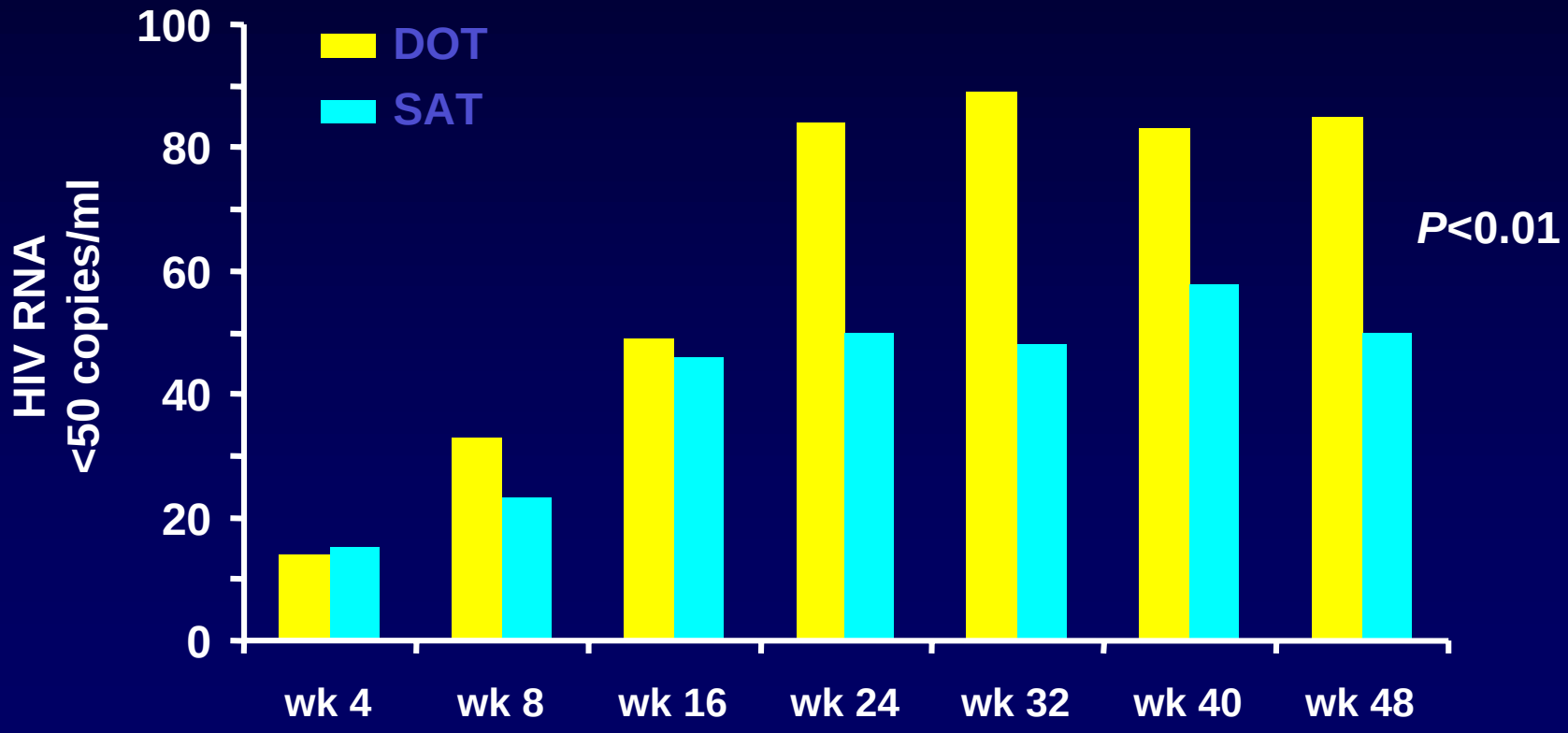
Monthly Self-Report Adherence (N=52)



Nachega J., Lehman D., Hlatshwayo D., *et al*. 10th CROI 2003. Boston, Th Or #169

Directly observed therapy (DOT) and RNA decline

Prisoners in 4 clinical trials by DOT or self-administration (SAT)



Fischl M *et al*. 7th CROI 2000. San Francisco: Poster 71

Alternative Methods for measuring CD4+ Lymphocytes in Peripheral Blood: Dynabeads Assay

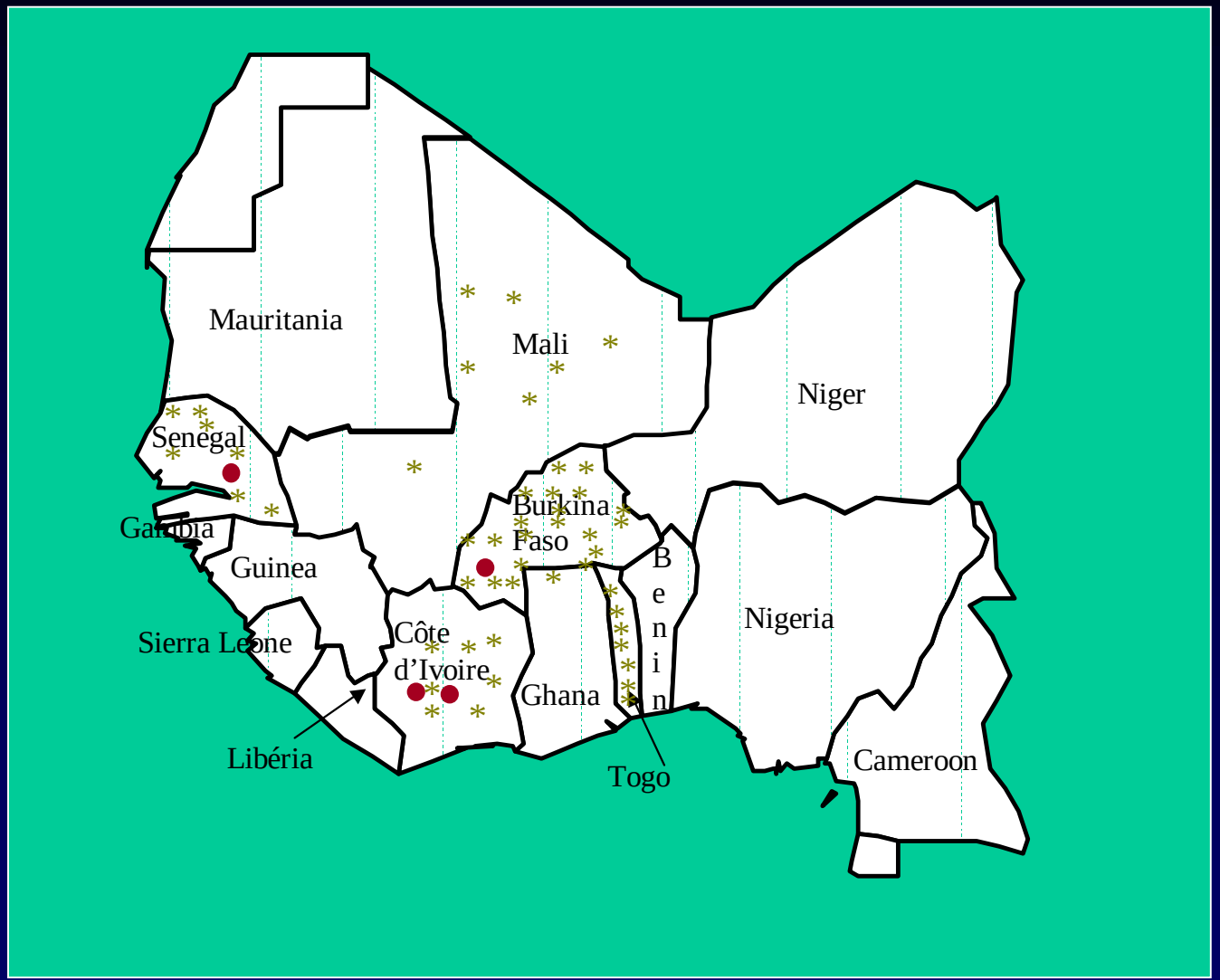
- **Use anti-CD4 monoclonal antibody coated magnetic beads**
- **Validated by a multi-center study conducted in Senegal, Burkina, Togo, Ivory Coast and Mali**
- **Coefficient of correlation as compare to FC was 0.89**
- **Ability to consistently measure CD4 at clinically relevant thresholds was 95%**

Diabouga S. et al. Barcelona AIDS 2002: Abstract # 1342

Compared costs (in USD) of Flow Cytometry *versus* Dynabeads Method

	Flow Cytometry	Dynabeads Method
Instrument	40 000	10 000
Annual Maintenance	8 000	0
One CD4 test	11.5	2.7
Hematology/test	2.6	0
Accessories	ND	ND
Reagent Availability	X	XXXX

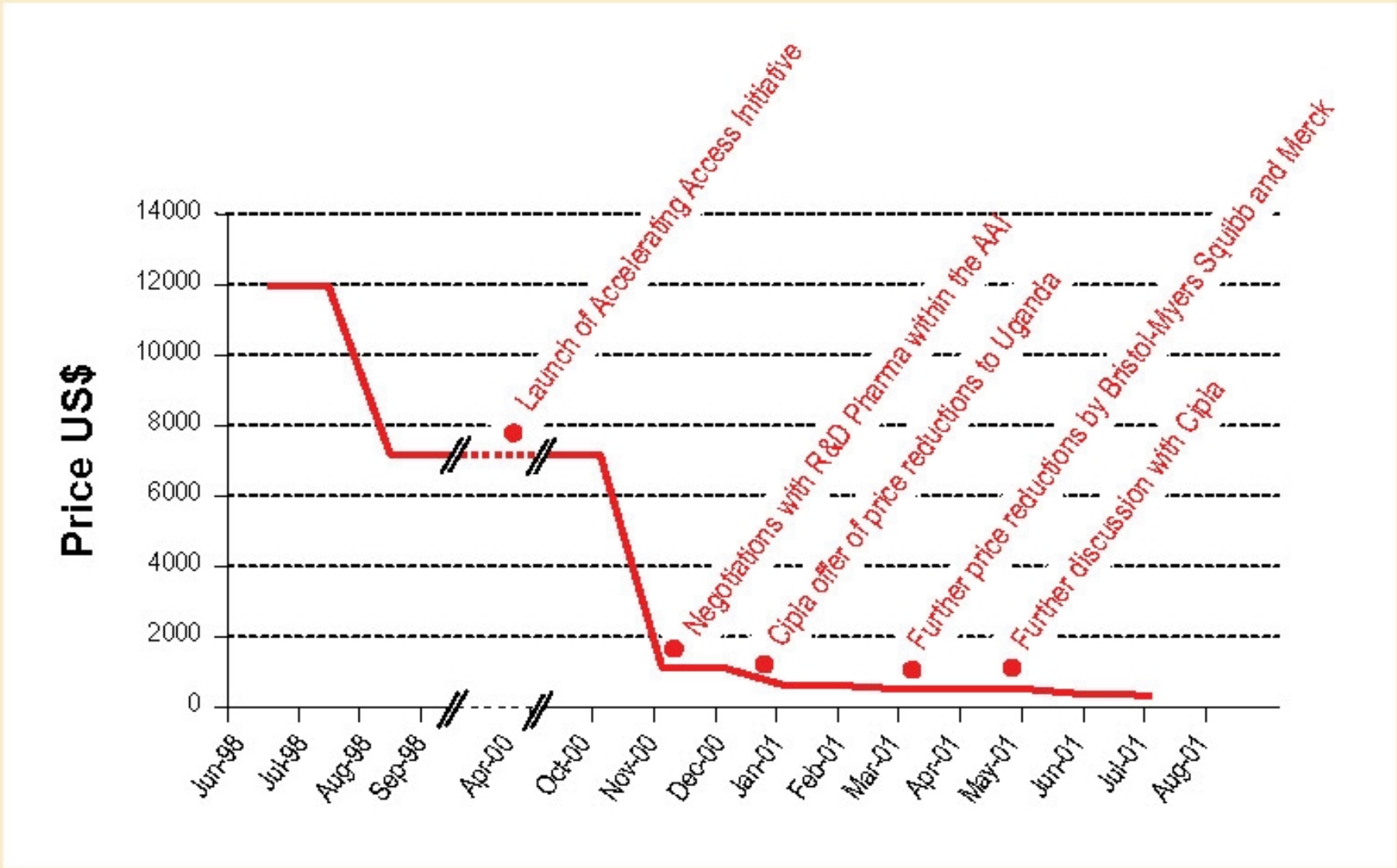
West African Sites where Dynabeads^{R} technique (*) was implemented



Scaling up HAART in SSA: Procurement and Financing

- Discount and marketplace competition
- Generic products from India (Cipla), Brazil etc.
- International AID as GRANT not LOAN
- UN Global HIV/AIDS Prevention and Treatment Fund

Prices (US$/year) of a first-line antiretroviral regimen in Uganda: 1998-2001



Key Predictors of Successful ARV Programs: Attention to Systems for Delivery of AIDS Care, Not Just AIDS Drugs

- Use maximally suppressive regimens
- Ensure patient adherence and continuity of care
- Uninterrupted supply of drugs
- Effective training of health care providers
- Attention to patient education, social support, family treatment
- Prevention as an integral part of treatment
- Program evaluation will be key

Providing ART using TB structures

TB control policy	ART counterpart
Government commitment	Package of HIV care Integrate with NTC
Passive case-finding	Rx symptomatic HIV
Standardised short-course R_x	Standardised ART regimens
Regular drug supply	Use TB network
Monitoring system	Register

Lancet 2001;358:410

Scaling Up HAART in SSA: Need for Clinical Trials to Define the "Best Practice"

- Which HAART regimens are the best tolerated?
- Which symptomatic signs or inexpensive lab tests most reliably predict when HAART should be initiated?
- Does therapeutic outcome of HAART depend on DOT? What type of DOT?
- What level of adherence can be achieved according to different HAART regimens?

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