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# **Antiretroviral Treatment lessons from Africa**

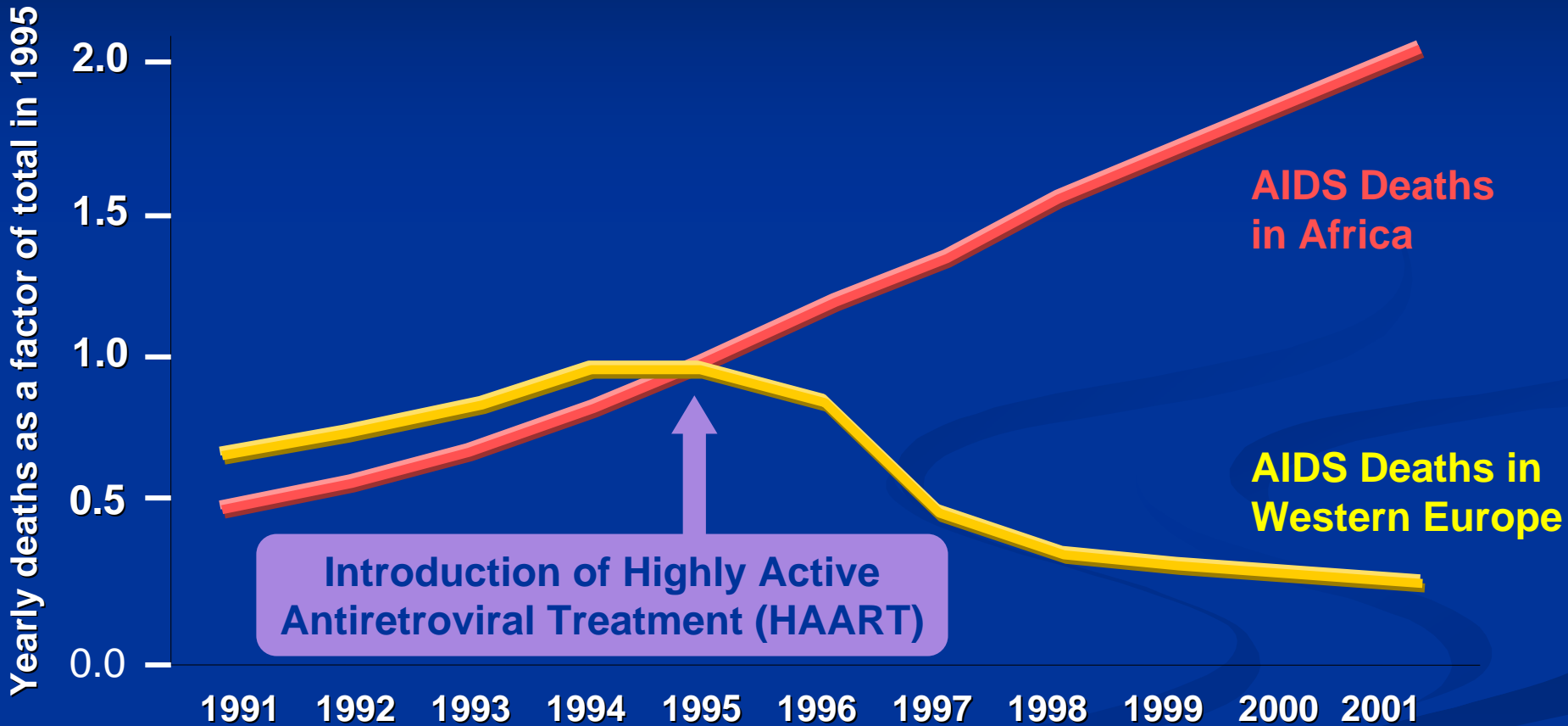
Dr Paula Munderi

DART Trial Team

MRC/UVRI Ugandan research Unit on AIDS

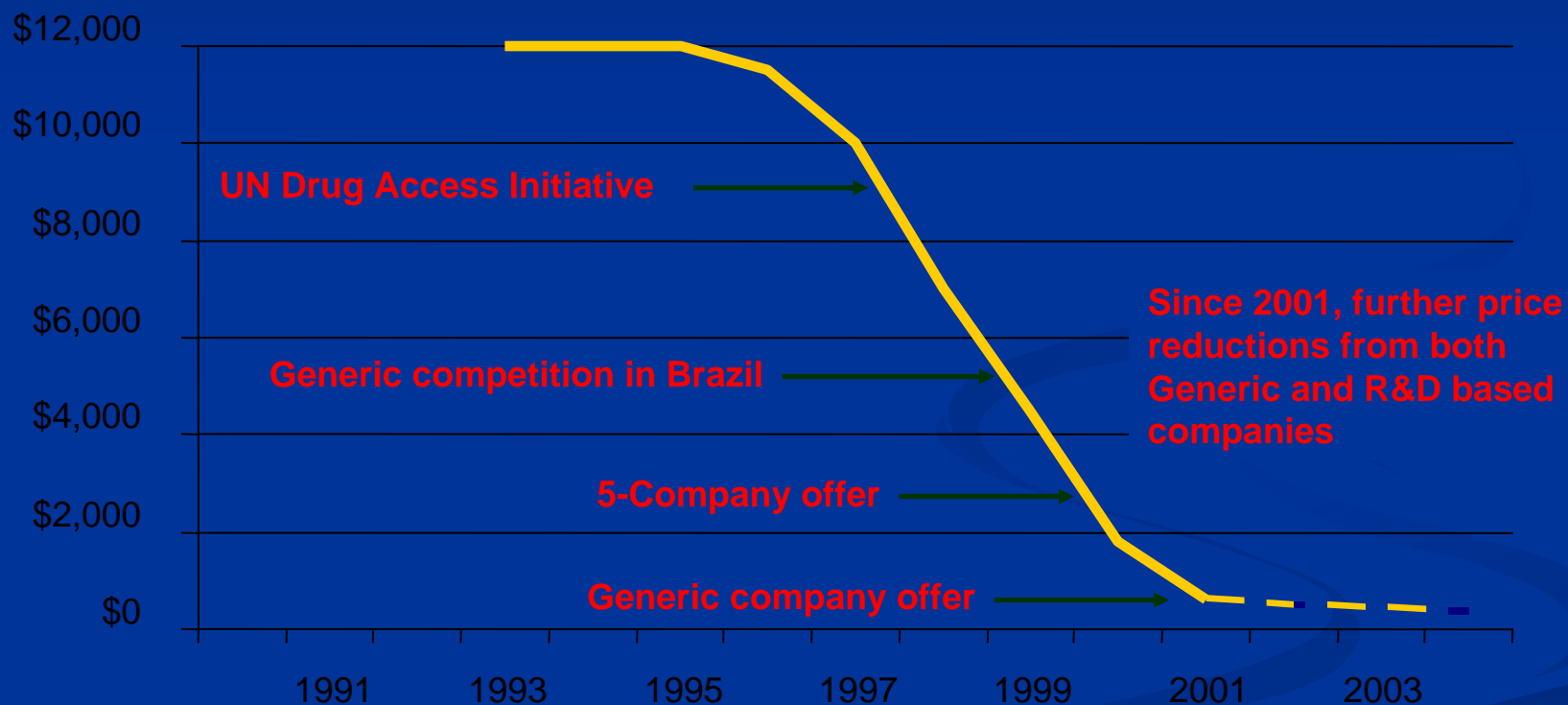
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# Gap in AIDS Treatment

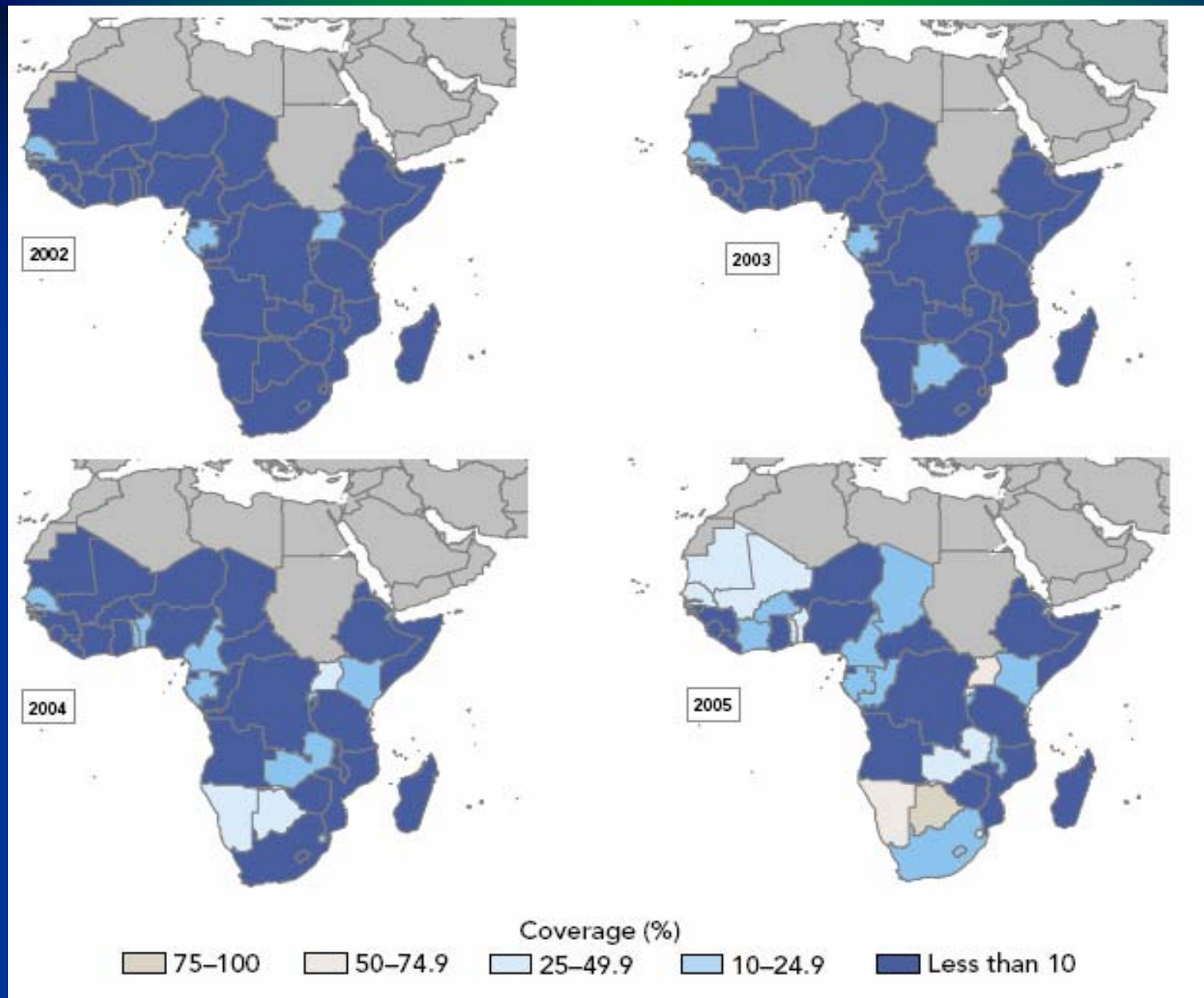


# Annual cost per person for triple therapy (US \$)

*Advocacy, corporate responsiveness, & market forces reduced Antiretroviral prices by 95% in 2 years*



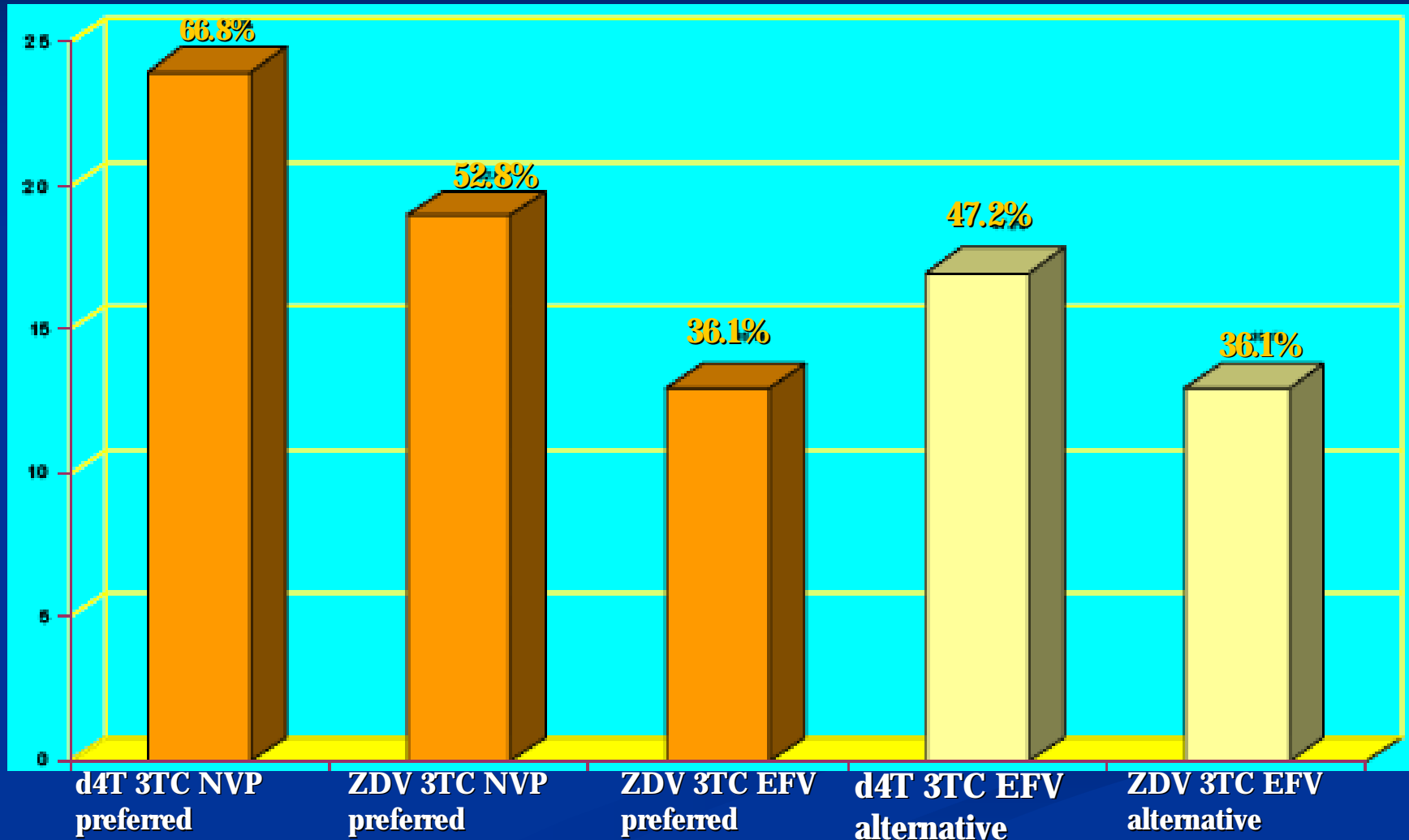
# People on ART as % of those in need



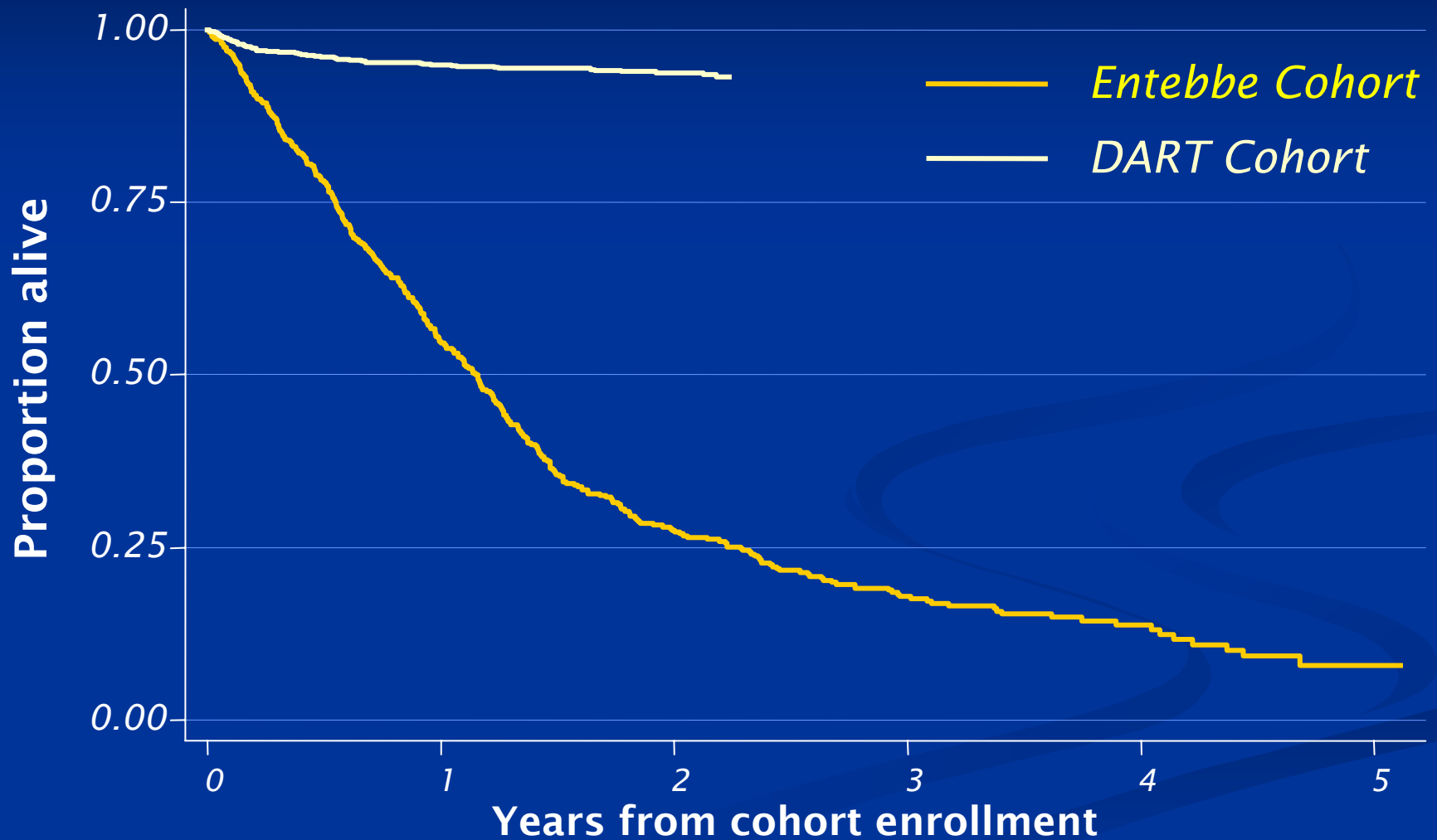
- National treatment programmes had to begin – learning by doing was accepted
- Several issues can be resolved by observational research evaluating programmes as they are implemented.
- Some questions will require more formal trials in a parallel clinical research agenda
- The different profile for treatment
  - Patients more likely to be ARV naïve , advanced disease , female
  - Different co-morbidities which affect treatment decisions – notably TB
  - Different health system resources
  - Limited ARV formulary

# Selection of 1<sup>st</sup> line regimens

## ... Countries following 2003 WHO Guidelines



# Survival benefit of ART

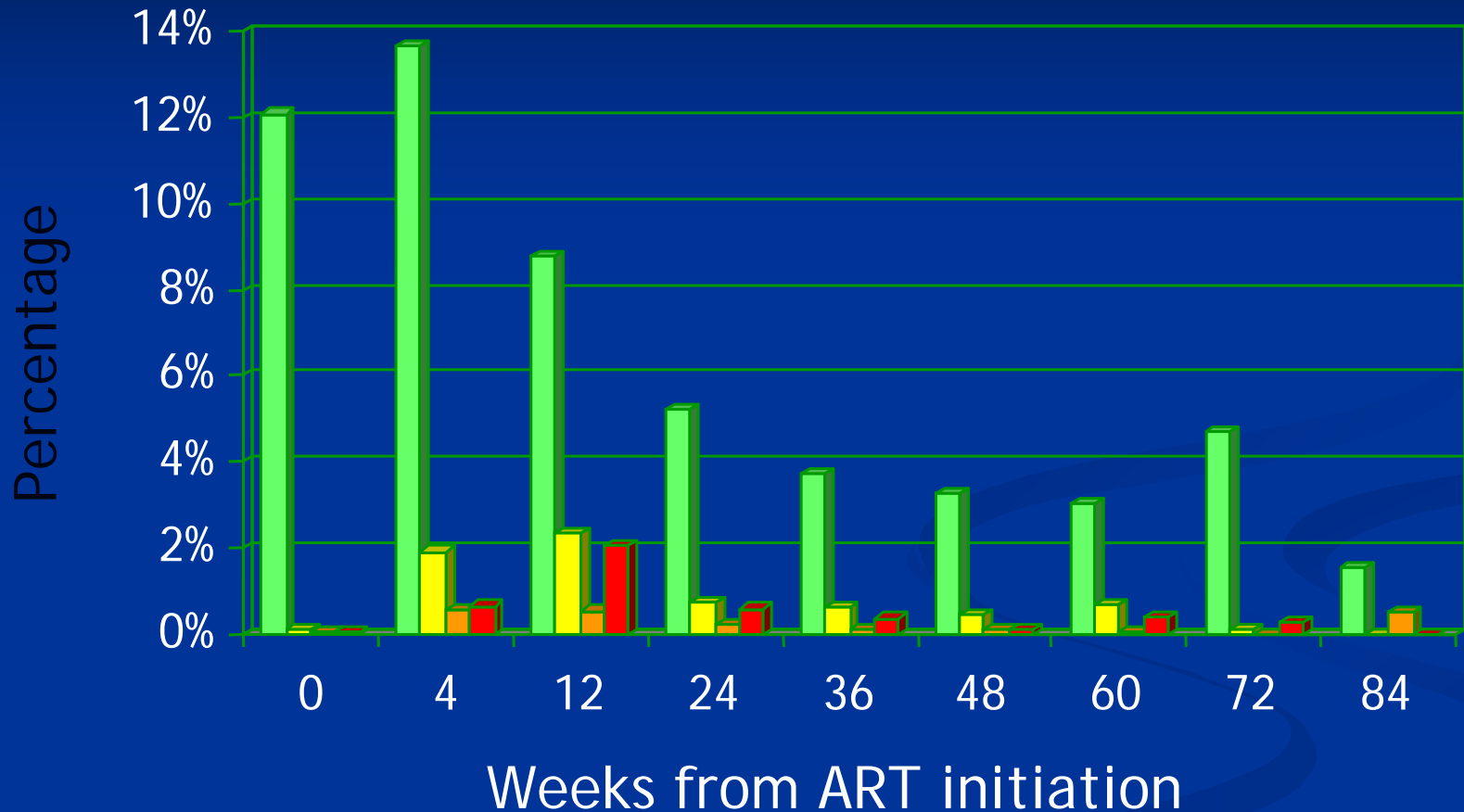


# Managing ART related toxicities

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- Most ART toxicities are
  - Predictable
  - Clinically detectable
  - Can be managed
- The key is patient and provider education

# Prevalence of anaemia at scheduled assessments in DART study population



Grade 1  
8.0 to <9.5

Grade 2  
7.0 to <8.0

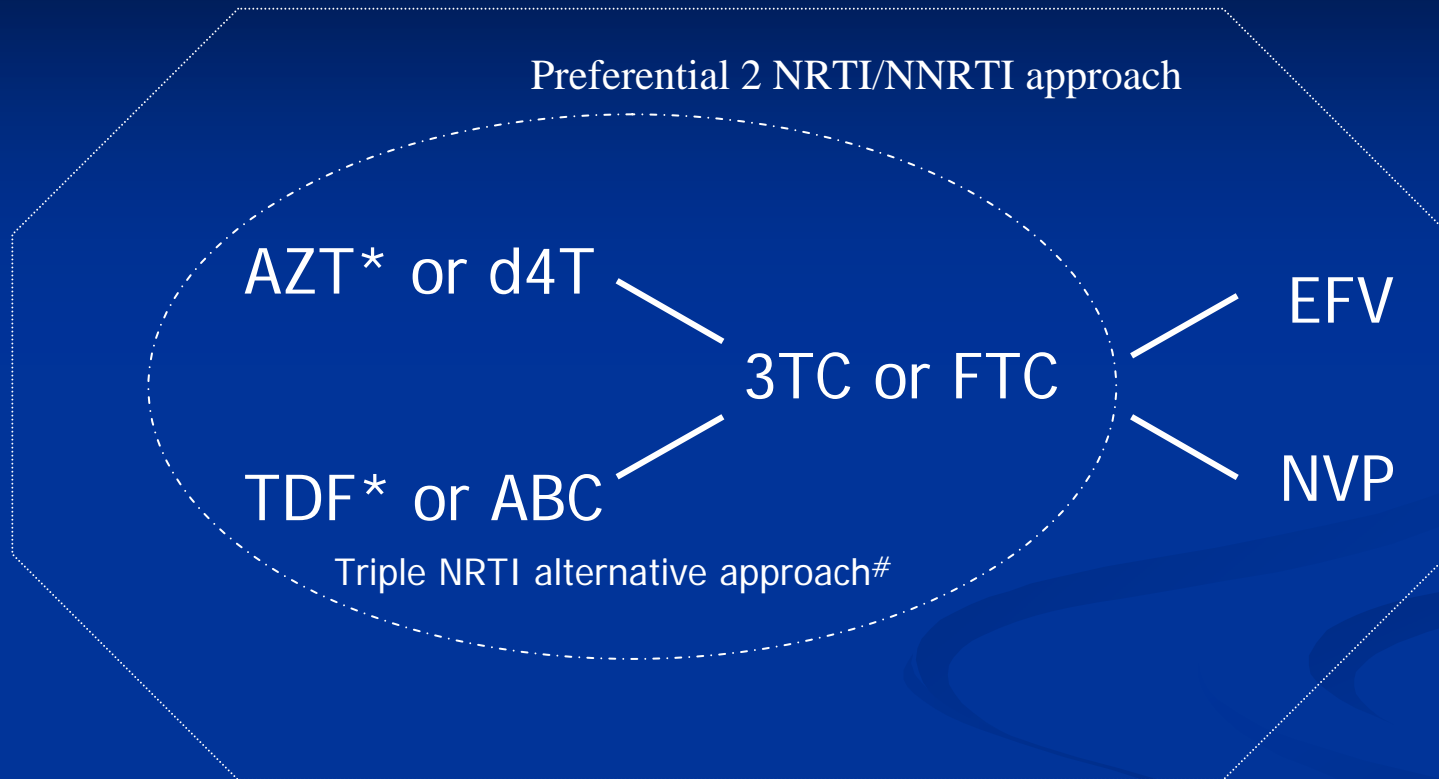
Grade 3  
6.5 to <7.0

Grade 4  
<6.5 g/dl

# Experience with Abacavir - DART population

- In Ugandan patients with low CD4 counts initiating ART with ZDV/3TC/NVP or ZDV/3TC/ABC
  - a trend towards a lower rate of SARs with ABC
  - a lower discontinuation rate with ABC (2% ABC versus 5% with NVP)
  - a lower rate of any grade 4 AE with ABC
- Considerable overlap in clinical manifestations of NVP and ABC reactions. But all ABC - HSR have **fever and a rash.**
- Rate of ABC HSR in this population is 2%
- Ongoing and planned assessment of
  - genetic polymorphisms
  - virological and immunological efficacy

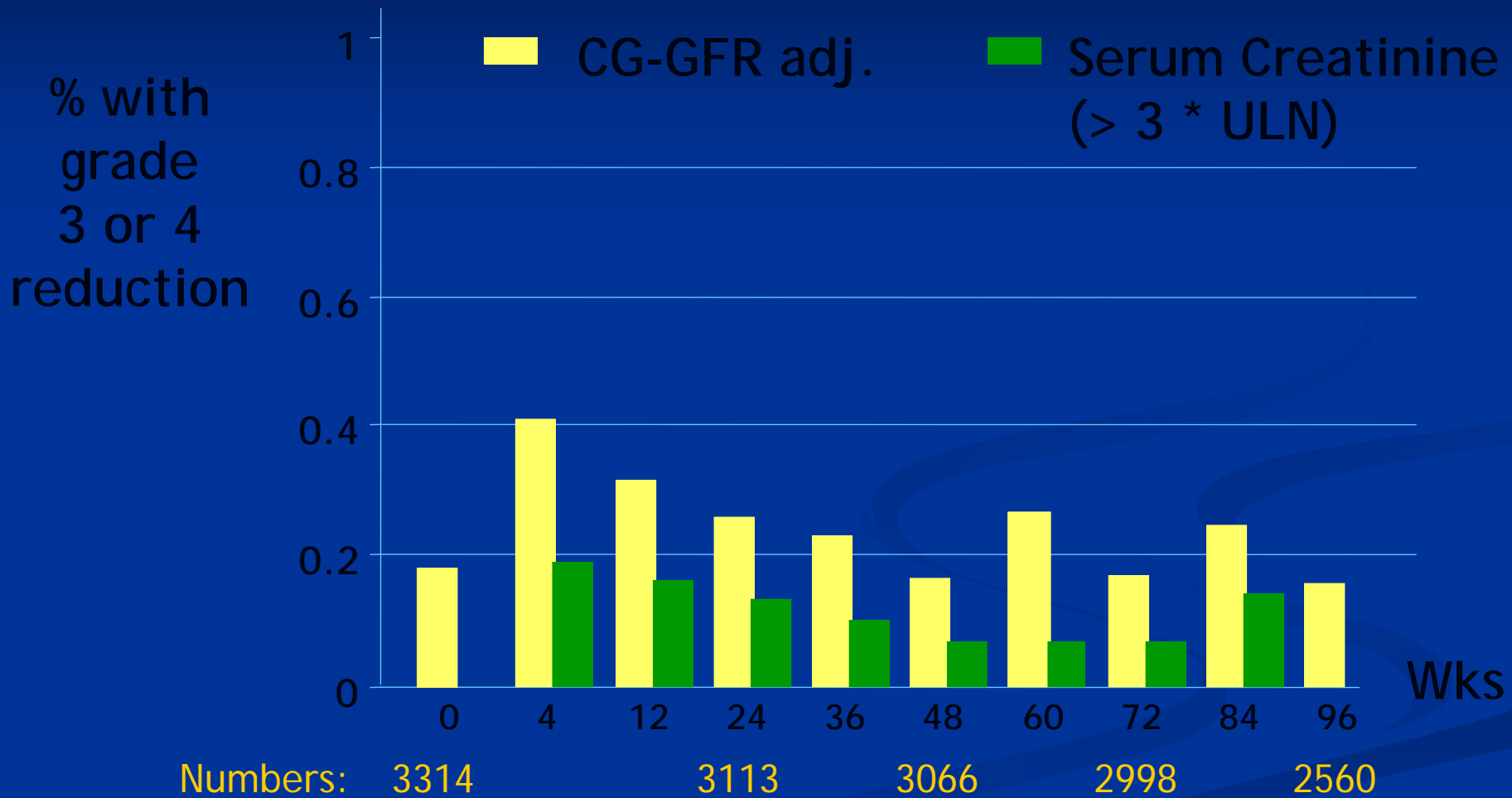
# First Line ARV Drugs in Adults and Adolescents



**\* Preferential NRTI to be combined with 3TC or FTC.**

**# Triple NRTI should be considered as an alternative simplification strategy**

# DART - Prevalence of impaired GFR\* and raised S-Creatinine\*\* (grade 3 or 4)



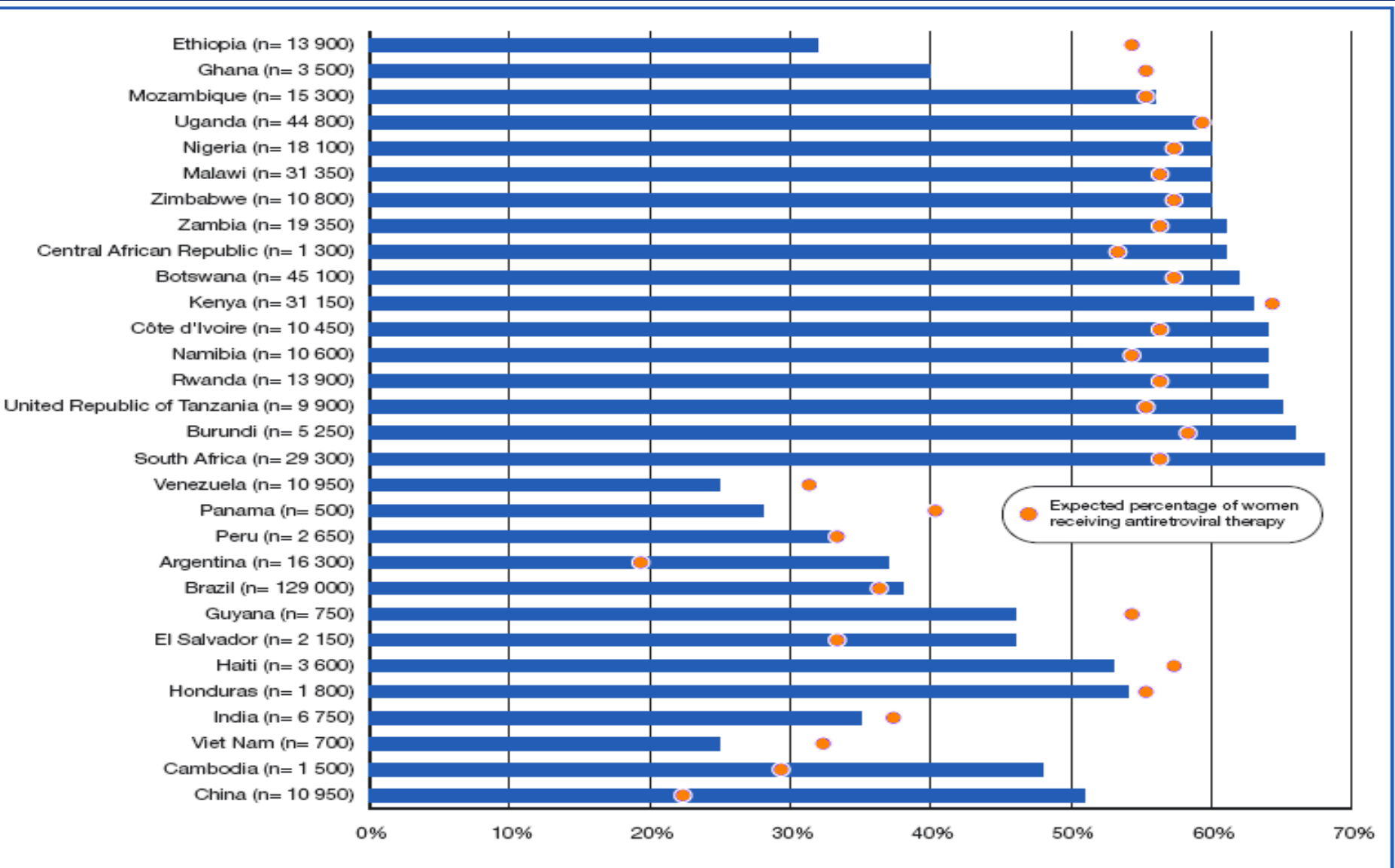
\* National Kidney Foundation; \*\* ACTG criteria

# DART - Incidence of severe GFR reduction

	up to 72 weeks		up to 96 weeks *	
ZDV/3TC/NVP	3 / 247	1.2%	3 / 247	1.2%
ZDV/3TC/NVP	4 / 299	1.3%	4 / 299	1.3%
ZDV/3TC/ABC	3 / 300	1.0%	3 / 300	1.0%
ZDV/3TC/TDF	33 / 2468	1.3%	40 / 2468	1.6%
Overall	43 / 3314	1.3%	50 / 3314	1.5%
	$p = 0.98$		$p = 0.93$	

\* Proportion of participants with complete follow-up to 96 weeks larger in these 2 groups (~85%) .

# Percentage of women among all adults receiving antiretroviral therapy, 2005



# Women in treatment

- Targeted prevention
- Incident pregnancies
- Specific reproductive health services
- Reproductive choice



# AIDS , 25 years and counting .....

***They called it the "slim disease."***

***Its victims became ill, lost weight and died.  
No one knew why.***

***The year was 1982.....***

***John Hopkins Public Health Magazine***



***Slim disease: A new disease in Uganda and its association with HTLV-III infection .*** Serwadda D, et al. Lancet. 1985 Oct 19;2(8460):849-52.

# Causes of Death – shifting patterns

	<b>Pre-ART Cohort</b>		<b>DART Cohort</b>	
	<b>Deaths (rate/100PY)</b>		<b>Deaths (rate/100PY)</b>	
<b><u>Specific HIV related causes</u></b>	<b>118</b>	<b>(17.9)</b>	<b>27</b>	<b>(1.5)</b>
<b>Cryptococcus</b>	<b>64</b>	<b>(9.7)</b>	<b>4</b>	<b>(0.2)</b>
Cryptosporidium	18	(2.7)	2	(0.1)
<b>Tuberculosis</b>	<b>16</b>	<b>(2.4)</b>	<b>10</b>	<b>(0.5)</b>
HIV-related malignancy	11	(1.7)	6	(0.3)
Bacteraemia	3	(0.5)	5	(0.3)
CMV	4	(0.6)	0	(0)
Severe anaemia	2	(0.3)	0	(0)
<b><u>Syndrome likely HIV related</u></b>	<b>176</b>	<b>(26.7)</b>	<b>18</b>	<b>(1.0)</b>
<b>Wasting (+/- diarrhoea)</b>	<b>111</b>	<b>(16.9)</b>	<b>1</b>	<b>(0.1)</b>
Febrile event	48	(7.3)	12	(0.7)
Neurological event	17	(2.6)	5	(0.3)
<b>Cause not HIV-related</b>	<b>4</b>	<b>(0.6)</b>	<b>6</b>	<b>(0.3)</b>
<b>Unknown cause</b>	<b>82</b>	<b>(12.6)</b>	<b>11</b>	<b>(0.6)</b>
<b>Total deaths</b>	<b>380</b>	<b>(57.7)</b>	<b>62</b>	<b>(0.3)</b>

# Clinical work load – DART Entebbe

**Number of patients screened 2650**

**Number of patients enrolled 1020**

