

Is Starting Anti-Retroviral Treatment Earlier Cost-effective?

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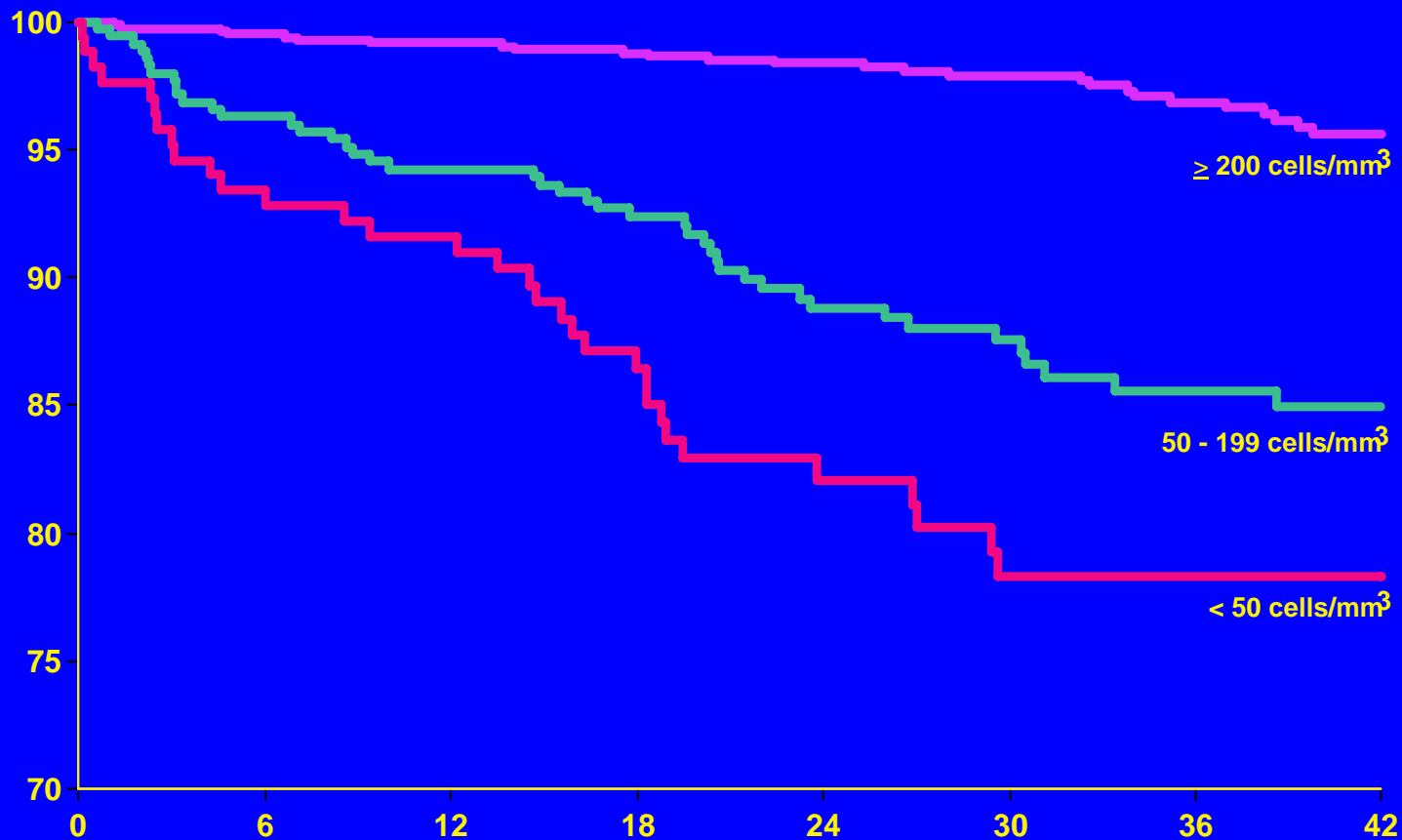
Lisbon, 27th March 2009

Discussions on when to start ART

- Longstanding
- Guidelines provided different advice at different times
- Now US and UK guidelines recommend starting less than 350 cells/mm³
- Cut-off point for previous discussion was start above 200 cells/mm³



Survival on HAART by CD4 count



Hogg et al. JAMA 2001
Wood et al. AIDS 2003

When to Start Antiretroviral Therapy

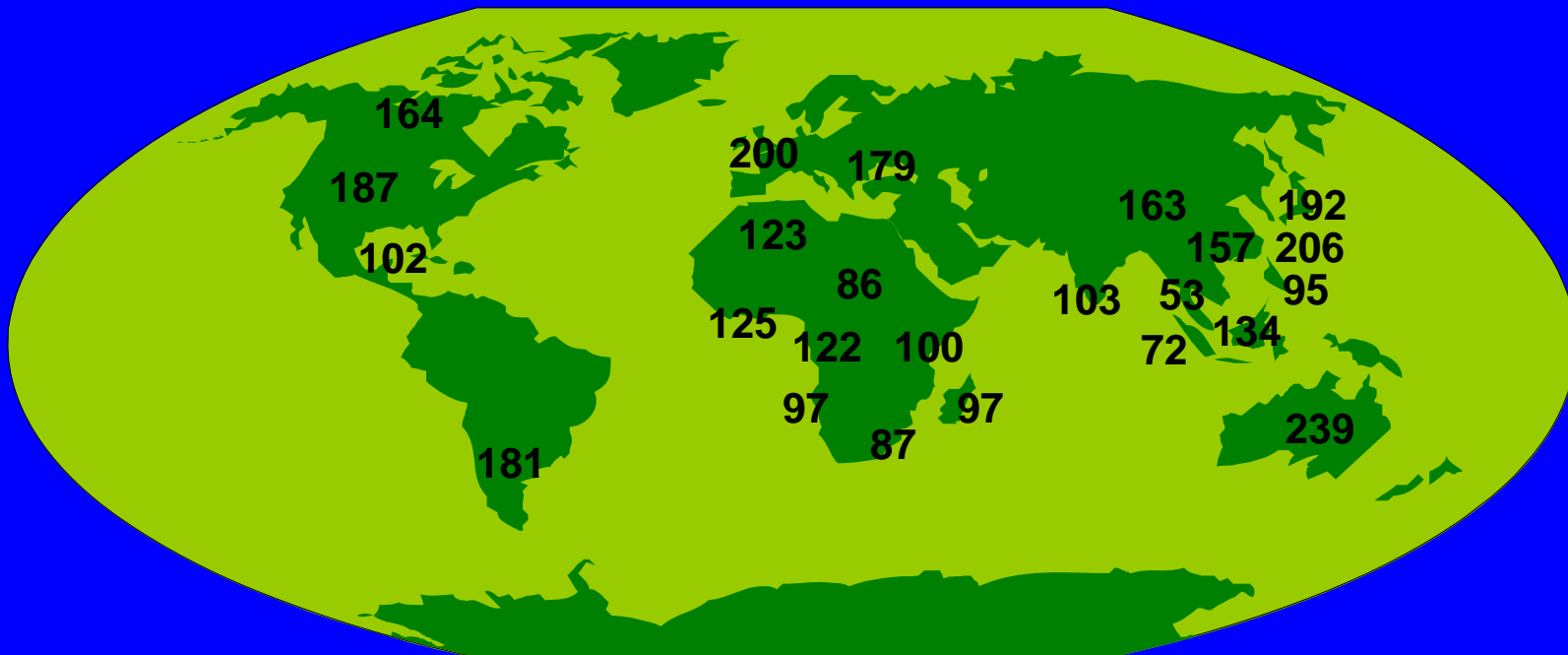
Measure	Recommendation	Comments
Symptomatic HIV disease	Therapy recommended	
Asymptomatic HIV disease		
CD4 <350/ μ L	Therapy recommended	Recommendation strengthened since 2006
CD4 \geq 350/ μ L	Therapy should be considered and decision individualized	<p><u>Correlates of faster HIV disease progression:</u></p> <ul style="list-style-type: none"> • High viral load (>100,000 RNA copies/mL) • Rapidly declining CD4 (>100/μL per year) <p><u>Coexistent conditions influenced by uncontrolled viremia:</u></p> <ul style="list-style-type: none"> • Presence or high risk for, cardiovascular disease • Active HBV or HCV • HIV- nephropathy
<p>Antiretroviral Treatment of Adult HIV Infection 2008 Recommendations of the IAS-USA Hammer SM; Eron JJ, Jr.; Reiss P; Schooley RT; Thompson MA; Walmsley S; Cahn P; Fischl MA; Gatell JM; Hirsch MS; Jacobsen DM; Montaner JSG; Richman DD; Yeni P; Volberding PA. <i>JAMA</i>. 2008; 300 (5) 555-570</p>		<p>Examples</p>

WHO 2006 Guidelines

WHO Clinical Staging	CD4 Testing Not-Available	CD4 Tests Available
1- Asymptomatic	Do not treat	Treat if CD4 count < 200 cells/mm³
2 - Mild symptoms	Do not treat	
3 - Advanced symptoms	Treat	Consider treatment if CD4 < 350 cells/mm³ and start ART before CD4 count drops below 200 cells/mm³
4 - Severe symptoms	Treat	Treat irrespective of CD4 count

When the Real World Starts ART

- Review of data from 2003-2005 from 176 sites in 42 countries (N = 33,008)
- Since 2000, CD4+ cell count at initiation in developed countries stable at approximately 150-200 cells/mm³, increasing in sub-Saharan Africa from 50-100 cells/mm³



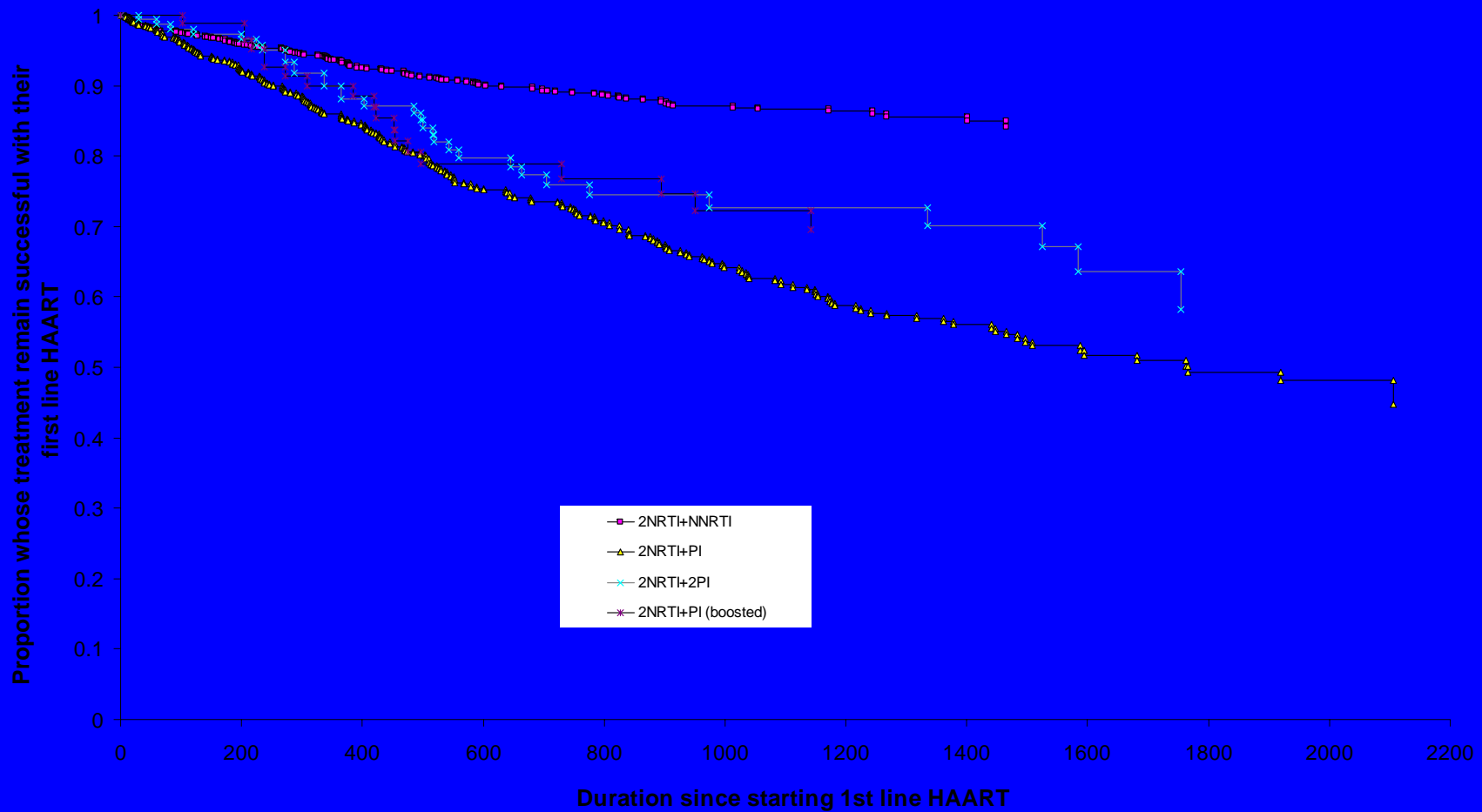
The Cost-effectiveness of different HAART Regimens 1996-2002

- **Comparing 2NRTIs + NNRTI containing regimens with PI comparing regimens for first-, second- and third-line HAART**

Beck EJ, Mandalia S, Youle M et al Treatment Outcome and Cost-effectiveness of different HAART Regimens in the UK 1996-2002. *Int.J.STD & AIDS*, 2008; 19:297-304.



First-line HAART regimens



The Cost-effectiveness per life year gained (LYG) for First Line HAART (2002 prices)

2NRTIs+NNRTI versus 2NRTIs+ PI boosted	US\$19,577 per LYG
2NRTIs+NNRTI versus 2NRTIs + PI	US\$19,659 per LYG
2NRTIs+NNRTI versus 2NRTIs+ 2PI	US\$ 8,571 per LYG

Time-to-Treatment Failure and Cost for People living with HIV starting ART at different CD4 strata (2002 prices)

- **CD4 \leq 100 cells/mm³**
- **CD4 101 – 200 cells/mm³**
- **CD4 201 – 350 cells/mm³**
- **CD4 $>$ 350 cells/mm³**



Median Years from HIV Diagnosis to Starting ART (IQR)

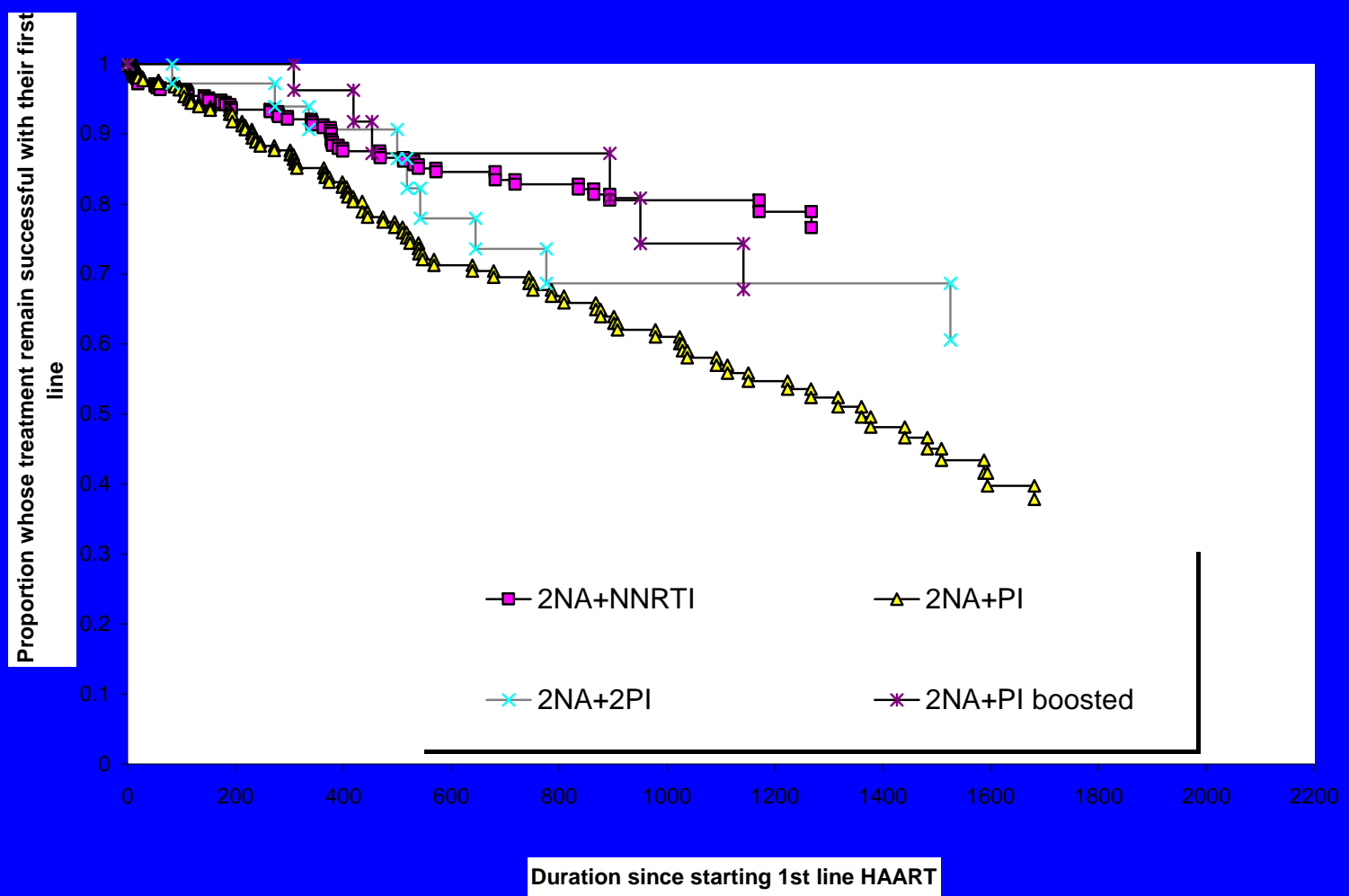
≤100 N=823 Treatment failed=154	101-200 N=725 Treatment failed=77	201-350 N=785 Treatment failed=105	>350 N=280 Treatment failed=44	p-value Kruskal -Wallis test
0.42 (0.09 to 5.63) Range: 0.00 to 16.26	1.86 (0.21 to 6.01) Range: 0.00 to 18.40	2.53 (0.46 to 6.14) Range: 0.00 to 17.98	1.70 (0.37 to 5.10) Range: 0.00 to 17.62	<0.001



Time-Treatment Failure

CD4 \leq 100 cells/mm³

Baseline CD4 count \leq 100 cells/mm³



Estimated Time-Treatment Failure CD4 \leq 100 cells/mm³

\leq 100 CD4 cells/mm ³	2NRTIs + NNRTI	2NRTIs + PI	2NRTIs + PI boosted	2NRTIs + 2PIs
Years (IQR)	6.5 (3.1 to 10.0)	3.3 (1.5 to 5.0)	4.8 (2.5 to 7.0)	4.4 (2.1 to 6.7)

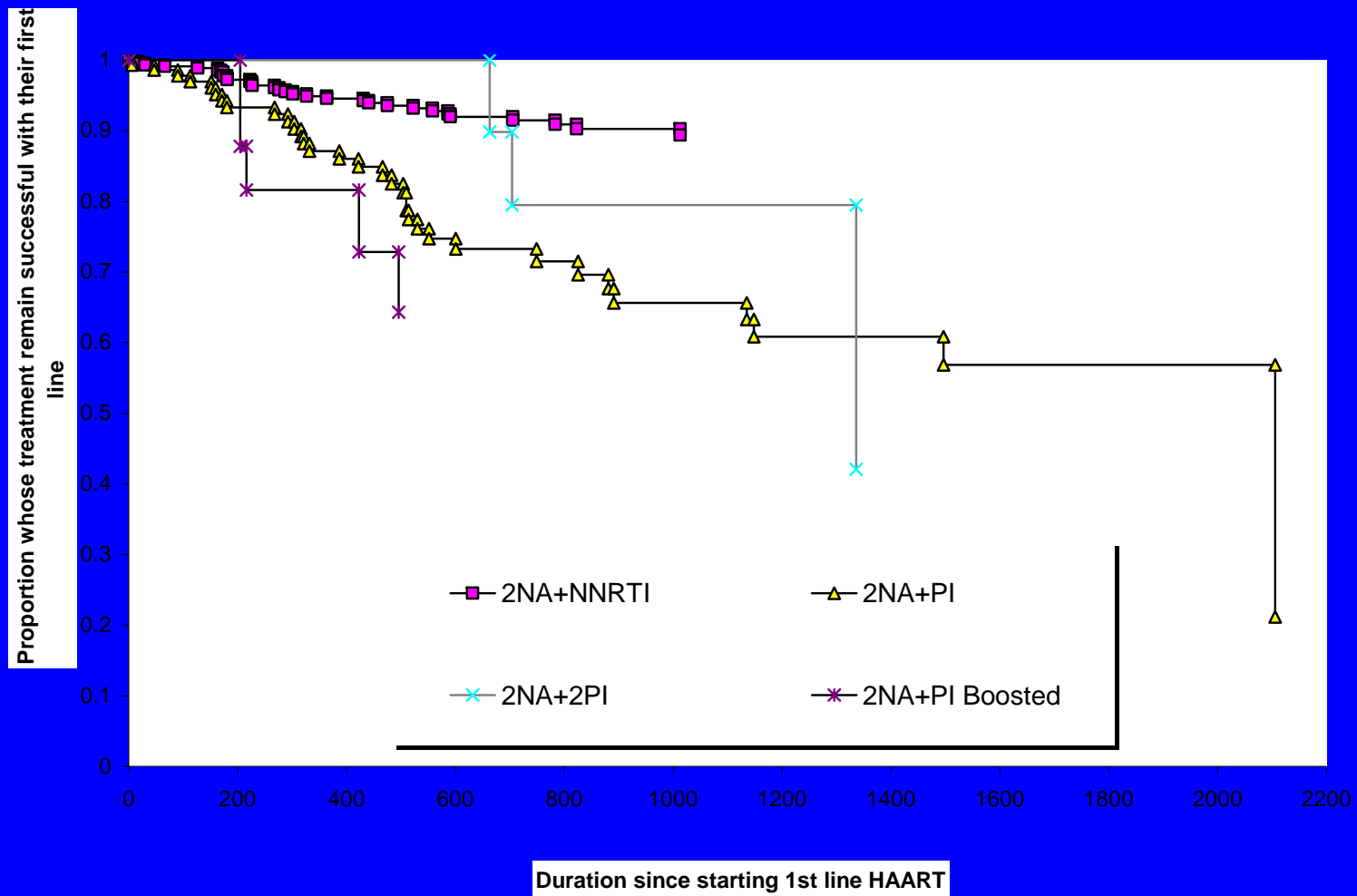
Adjusted for age, gender, baseline VL, baseline CD4 count, baseline CDC stage, stratified by year of starting HAART

Per Patient-Year Cost of different regimens for CD4 \leq 100 cells/mm³ (2002 prices)

2NRTIs+NNRTI	US\$ 22,262
2NRTIs+PIs	US\$ 25,874
2NRTIs+PIboosted	US\$ 23,796
2NRTIs+2PIs	US\$ 30,209

Time-Treatment Failure CD4 101 - 200 cells/mm³

Baseline CD4 count 101 to 200 cells/mm³



Estimated Time-treatment Failure CD4 101 – 200 cells/mm³

	2NRTIs + NNRTI	2NRTIs + PI	2NRTIs + PI boosted	2NRTIs + 2PIs
Years (IQR)	13.6 (6.7 to 20.4)	3.4 (1.7 to 5.1)	2.0 (1.0 to 2.9)	3.9 (2.2 to 5.6)

Adjusted for age, gender, baseline VL, baseline CD4 count, baseline CDC stage, stratified by year of starting HAART

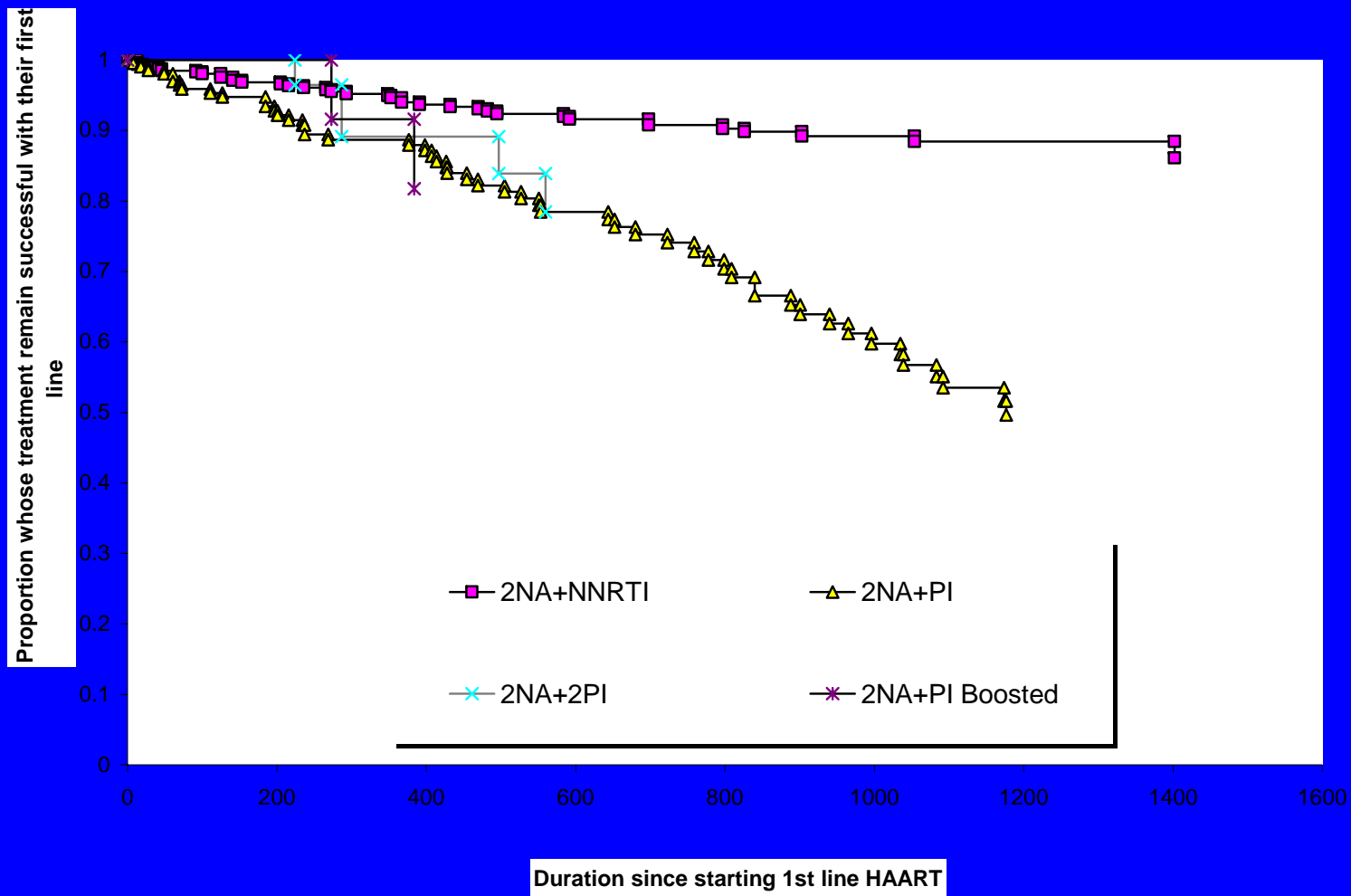
Per Patient-Year Cost of different regimens for CD4 101- 200 cells/mm³ (2002 prices)

2NRTIs+NNRTI	US\$ 21,065
2NRTIs+PIs	US\$ 23,522
2NRTIs+PIboosted	US\$ 23,286
2NRTIs+2PIs	US\$ 30,605



Time-Treatment Failure CD4 201-350 cells/mm³

Baseline CD4 count 201 to 350 cells/mm³



Estimated Time-treatment Failure CD4 201 - 350 cells/mm³

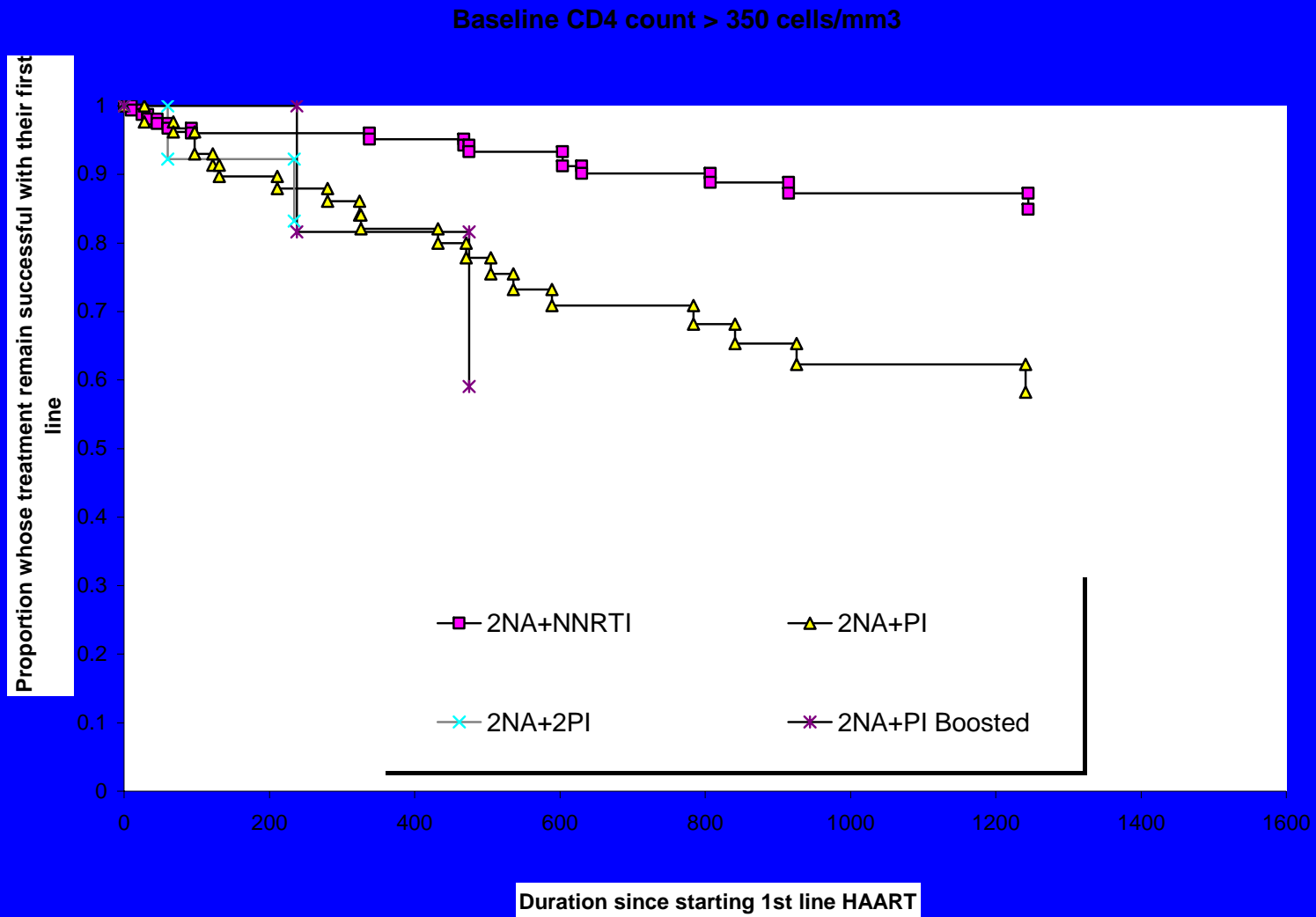
	2NRTIs + NNRTI	2NRTIs + PI	2NRTIs + PI boosted	2NRTIs + 2PIs
Years (IQR)	13.3 (6.5 to 20.2)	3.5 (1.8 to 5.2)	3.5 (1.8 to 5.2)	3.5 (1.8 to 5.2)

Adjusted for age, gender, baseline VL, baseline CD4 count, baseline CDC stage, stratified by year of starting HAART

Per Patient-Year Cost of different regimens for CD4 201-350 cells/mm³ (2002 prices)

2NRTIs+NNRTI	US\$ 20,102
2NRTIs+PIs	US\$ 22,545
2NRTIs+PIboosted	US\$ 22,772
2NRTIs+2PIs	US\$ 29,957

Time-treatment Failure CD4 > 350 cells/mm³





Estimated Time-Treatment Failure CD4 > 350 cells/mm³

	2NRTIs + NNRTI	2NRTIs + PI	2NRTIs + PI boosted	2NRTIs + 2PIs
Years (IQR)	13.3 (6.5 to 20.2)	3.1 (1.4 to 4.9)	1.5 (0.8 to 2.3)	1.9 (0.9 to 2.9)

Adjusted for age, gender, baseline VL, baseline CD4 count, baseline CDC stage, stratified by year of starting HAART

Per Patient-Year Cost of different regimens for CD4 > 350 cells/mm³ (2002 prices)

2NRTIs+NNRTI	US\$ 19,646
2NRTIs+PIs	US\$ 22,550
2NRTIs+PIboosted	US\$ 26,517
2NRTIs+2PIs	US\$ 27,774



Conclusions of CD4 strata-analysis

- **People starting ART with CD4 count less than 100 cells/mm³ fail first-line therapy earlier compared with higher CD4 strata.**
- **Those with a CD4 count \leq 100 cells/mm³ were most likely to be diagnosed late.**
- **Among those with CD4 count $>$ 100 cells/mm³, the 2NRTIs + NNRTI regimen was superior compared with PI based regimens.**
- **2NRTIs + NNRTI less expensive treatment regimen than PI based options**
- **2NRTIs + NNRTI favoured regimen for first-line therapy.**

Annual Cost of 2NRTIs + NNRTI regimens for different CD4 counts (2002 prices)



≤ 100 cell/mm³	US\$ 22,262
101 – 200 cells/mm³	US\$ 21,065
201 – 350 cells/mm³	US\$ 20,102
> 350 cells/mm³	US\$ 19,646

Cost-effectiveness or cost-minimization of 2NNRTI regimens at different CD4 strata (2002 prices)

<p>> 100 cells/mm³ compared with ≤ 100 cell/mm³</p>	<p>US\$ 27,641 per LYG</p>
<p>201- 350 cells/mm³ compared with 100 – 200 cells/mm³</p>	<p>Savings of US\$ 10,562 per year</p>
<p>> 350 cells/mm³ compared with 201- 350 cells/mm³</p>	<p>Savings of US\$ 7581 per year</p>

Conclusion: 2NRTIs + NNRTI

- **Cost-effective regimen for first-line therapy compared with PI regimens**
- **Starting with CD4 counts > 100 cells/mm³ median time to failing first-line therapy is 13 years compared with 6 years if CD4 ≤ 100 cells/mm³**
- **The higher the CD4 count the lower the annual cost of treatment and care**
- **Starting 2NRTIs + NNRTI with CD4 count >100 cells/mm³ is cost-effective compared with ≤ 100 cells/mm³**
- **Starting when > 350 cells/mm³ cost saving compared with starting when CD4 count is between 100 and 350 cells/mm³**
- **These analyses are currently being repeated for the period 1996-2006, as new drugs have come on the market**

Broader conclusions....

- We need to monitor carefully that earlier treatment with ART does not give rise to earlier resistance, aggravate resistance patterns or produce severe longterm adverse events
- Countries need to develop their own HIV information systems to generate their own strategic information as healthcare systems and economies differ between countries
- Analyses on the *effectiveness, efficiency, equity and acceptability* of drug regimens and other interventions need to be performed regularly and monitored over time



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Thank you for your attention