

Lessons from Southern African treatment programmes

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International Epidemiological Databases to Evaluate AIDS (leDEA) Collaboration

Acknowledgements and data sources

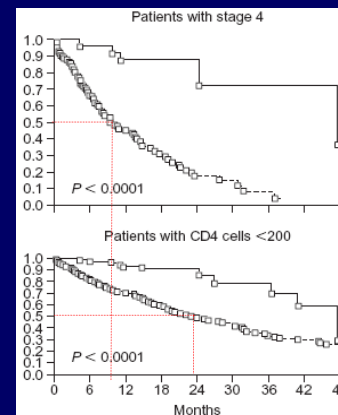
- Focus on routine clinical monitoring of programmes
 - Does not cover models of care, or health system issues for which there are many lessons
- Individual cohorts
 - Khayelitsha, Gugulethu
- Western Cape provincial programme
- Free state provincial programme
- Inter-regional comparisons
 - Egger, CROI 2007

Outline

- What is the benefit?
- How do we make sense of early on-programme mortality?
- How well is the service being delivered?
- What have we learnt to inform programme design?
 - First-line regimens
 - Loss to follow-up

What is the benefit?

Natural history after CD4 count < 200 or AIDS cells/ μ l



Post et al, QJM 1996: 20% of those with CD4 < 50 cells/ μ l survived at 24 months

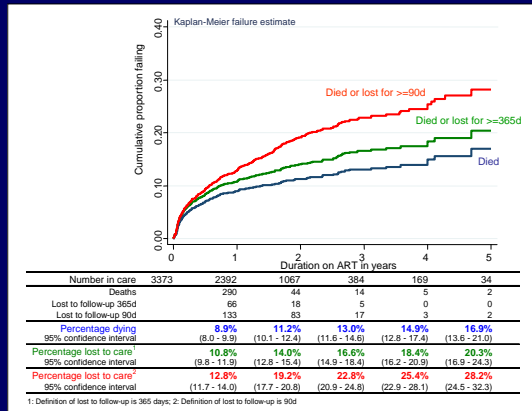
Cleary* combined these to estimate

Average: 2.9 years
Median: Less than 2 years

* Cost Effectiveness and Resource Allocation 2007

What is the benefit?

5-year outcomes of adult patients starting ART in Khayelitsha

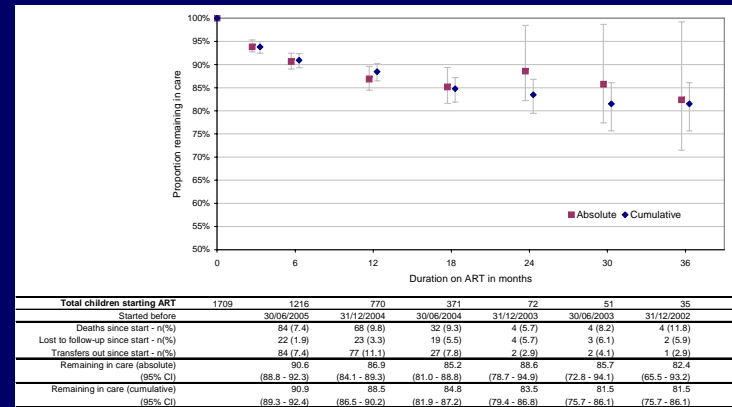


Van Cutsem. CROI 2007

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What is the benefit?

4-year outcomes of paediatric patients starting ART in the Western Cape



Cloete. 3rd South African AIDS Conference 2007

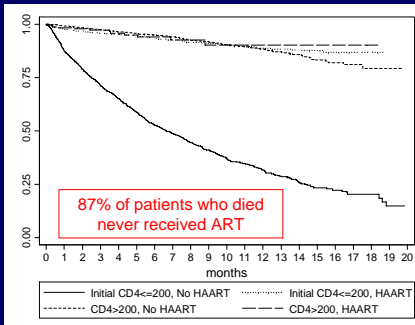
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What is the benefit?

Pre-ART mortality completely overwhelms on-ART outcomes



Free State programme survival



Fairall, Bachmann et al, Archives of Internal Medicine, in press

Gugulethu cohort

Mortality
Pre-ART: 33/100 py
Early ART: 19/100py
Late ART 3/100py

46% of patients who died never received ART

Lawn et al, 2006; CID 43:770-6

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What is the benefit?

Summary

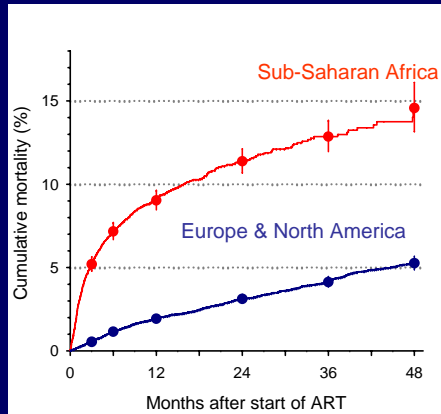


- Compared to natural history, substantial benefit:
 - 7 out of 10 adults and 8 out of 10 children who started ART are still in care at 5 and 3 years respectively
- Majority of deaths in patients known to the services occur prior to starting ART
 - Never let it be said that the demand for ART is not there
- Nevertheless, early evidence of population-level impact
 - Laubsher R, Bradshaw D, Bourne D, Dorrington R. Rapid Surveillance Of AIDS Mortality In South Africa (437). 3rd South African AIDS Conference 2007.

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Understanding early mortality on ART

Comparing African cohorts with Europe and North America

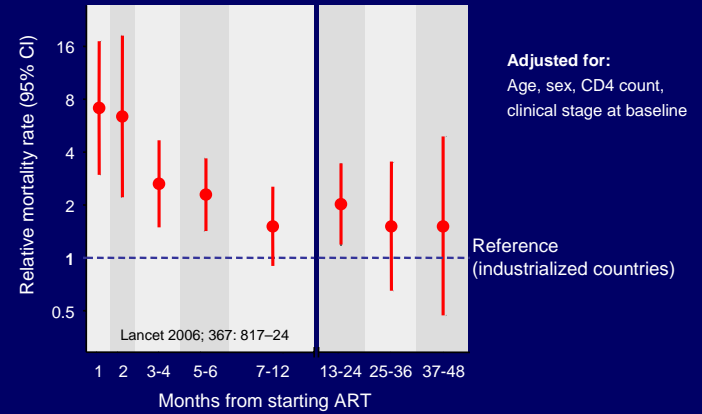


Egger, CROI 2007

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Understanding early mortality on ART

Relative rates by duration on ART comparing regions

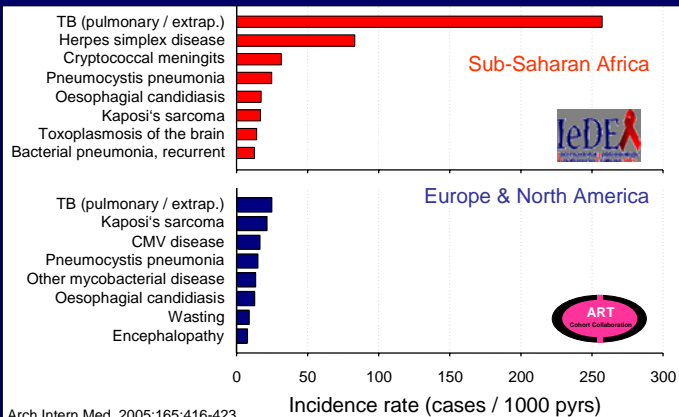


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Understanding early mortality on ART

Comparing co-morbidity burden between regions



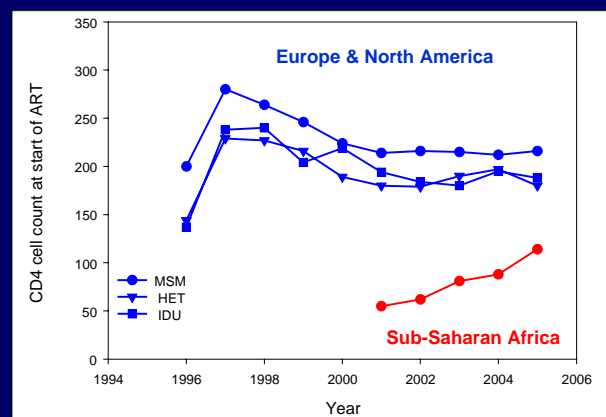
Arch Intern Med. 2005;165:416-423

Egger, CROI 2007

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Understanding early mortality on ART

Differing access to care as an explanation for differences in early mortality



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Understanding early mortality on ART

Changing meaning of clinical parameters as access improves

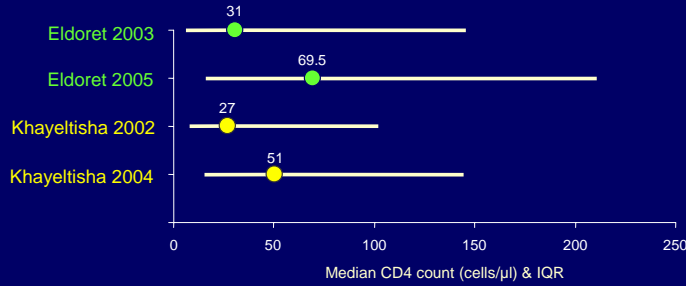
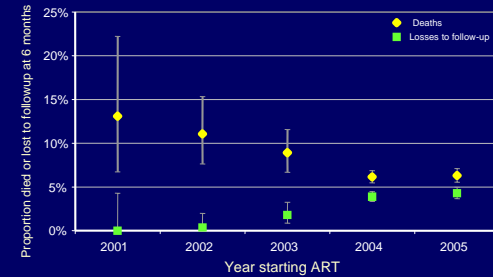


Figure: CD4 count at ART initiation in stage IV, by year and cohort

Boulee, 3rd South African AIDS Conference 2007

Understanding early mortality on ART

Declining early mortality in the Western Cape

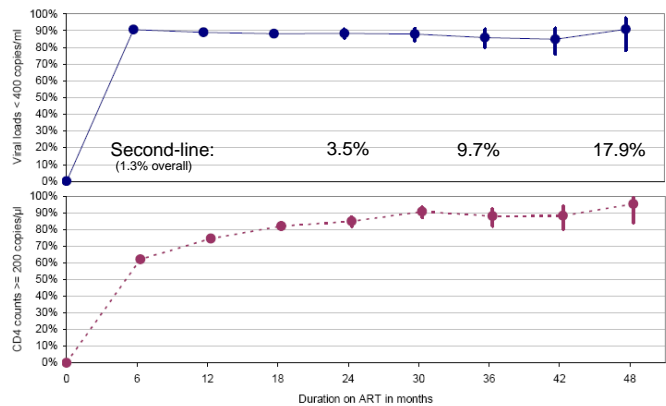


	n	80	248	524	4041	7694
CD4 < 50 cells/µl	51.3%	50.4%	36.8%	24.4%	19.7%	
95% CI	(39.8 - 62.6)	(44.0 - 56.8)	(32.7 - 41.1)	(23.1 - 25.8)	(18.8 - 20.6)	
Mortality	13.1%	11.1%	8.9%	6.1%	6.3%	
95% CI	(6.7 - 22.2)	(7.6 - 15.3)	(6.7 - 11.6)	(5.5 - 6.9)	(5.6 - 7.1)	
Loss to follow-up	0.0%	0.4%	1.8%	3.9%	4.3%	
95% CI	(0.0 - 4.3)	(0.0 - 2.0)	(0.9 - 3.3)	(3.4 - 4.5)	(3.7 - 5.0)	

Cloete, 3rd South African AIDS Conference 2007

How well is the service being delivered?

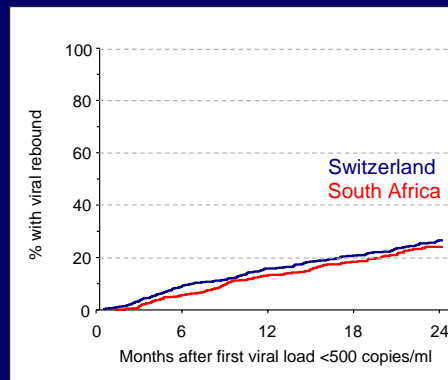
Laboratory outcomes by duration on ART – Western Cape



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How well is the service being delivered?

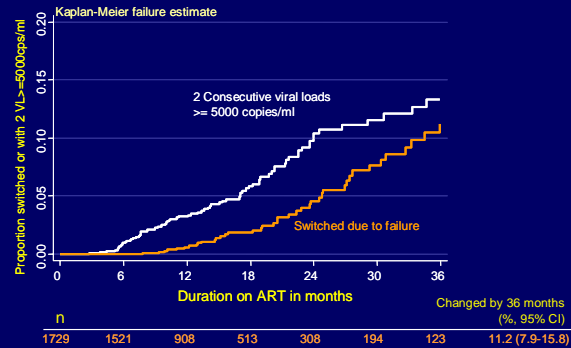
Time to rebound no worse than Switzerland



Egger, CROI 2007

How well is the service being delivered?

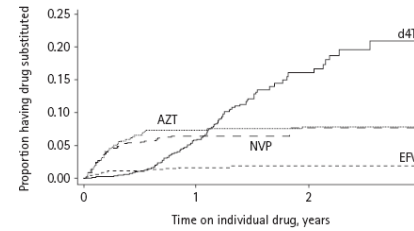
Delays in starting patients on second-line



Boule. CROI 2006

Informing programme design

Tolerability of first-line regimens

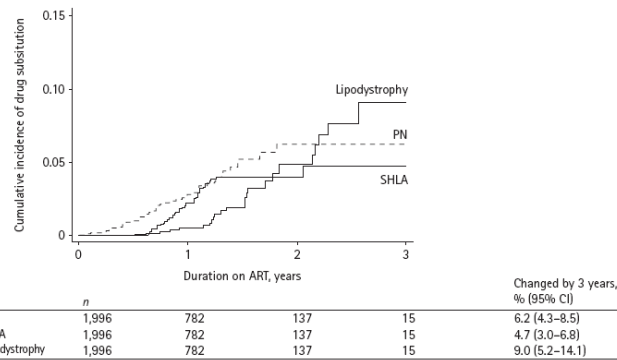


	n	676	469	295	126	Changed by 36 months, % (95% CI)
AZT	676	469	295	126	7.8 (5.9-10.3)	
EFV	1,613	858	334	74	1.9 (1.3-2.8)	
NVP	1,062	376	75	44	7.6 (5.3-10.9)	
d4T	1,996	782	137	15	20.8 (16.2-26.5)	

Antiviral Therapy 12:753-760

Informing programme design

Stavudine adverse events



Antiviral Therapy 12:753-760

Informing programme design

Risk factors for stavudine-related adverse events



Table 4. Multivariate models of associations with toxicity-related regimen modifications in patients on stavudine, by specific toxicity

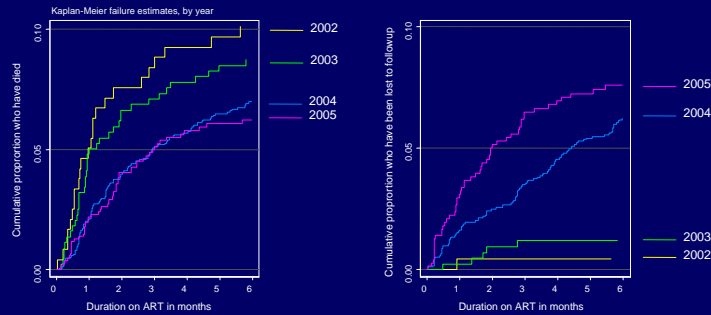
Association	Lipodystrophy			Hyperlactataemia/lactic acidosis			Peripheral neuropathy		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Female gender	10.0	1.3-74.5	0.025	10.7	1.5-79.0	0.02	-	-	-
Weight									
<60 kg	1.0	-	-	1.0	-	-	-	-	-
60-74.9 kg	0.6	0.2-1.9	0.017	5.7	1.5-21.0	<0.001	-	-	-
≥75 kg	4.1	1.6-10.5	-	36.1	10.6-122.8	-	-	-	-
Nyanga district	3.5	0.9-12.8	0.062	0.4	0.2-0.9	0.026	-	-	-
Weight gain first 3 months ≥5 kg	-	-	-	3.1	1.5-6.2	0.002	-	-	-
Age per 10-year increase	-	-	-	-	-	-	1.4	1.0-1.9	0.034
WHO stage per increment	-	-	-	-	-	-	1.6	1.0-2.5	0.040

CI, confidence interval; HR, hazard ratio; WHO, World Health Organization.

Antiviral Therapy 12:753-760

Losses to follow-up

Opposite trends across 2 large regional cohorts



Known deaths*

* Based on 3,531 patients in two cohorts

Losses to follow-up (> 6 months)**

** Based on 3,219 patients in two cohorts

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Summary



- Substantial benefit demonstrated for those accessing ART programmes
- Lack of access a key contributor to ongoing HIV-related mortality
- Pre-ART mortality is substantial even in patients enrolled in care
- High early mortality compared to rich countries due to combination of disease burden and lack of access
- Virological outcomes are good for those retained in care. The clinical impact of delays in starting second-line therapy is unknown.
- Identifiable risk factors for most pressing adverse-events can inform clinical practice with existing drug regimens
- Retention in care should be the ultimate goal – evidence of programme saturation with increasing loss to follow-up as scale-up has progressed

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