

OUTCOMES OF INFANTS STARTING ANTIRETROVIRAL THERAPY IN SOUTHERN AFRICA, 2004-2012

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Background

- 1) HIV infected infants – an extremely high risk population
 - Without ART provision it is estimated that up to 30% of HIV positive infants will die before reaching one year of age and 50% by the age of two years. (Newell et al, 2004)
- 2) 2010 WHO ART infant ART initiation guidelines
 - immediate initiation for all children under the age of 24 months
- 3) Children with Human Immune Deficiency Virus Early Antiretroviral Therapy Trial (CHER) provided evidence of a reduction in mortality and HIV progression associated with early ART initiation
- 4) Limited evidence pertaining to the outcomes of infants starting ART in routine care settings of Southern Africa

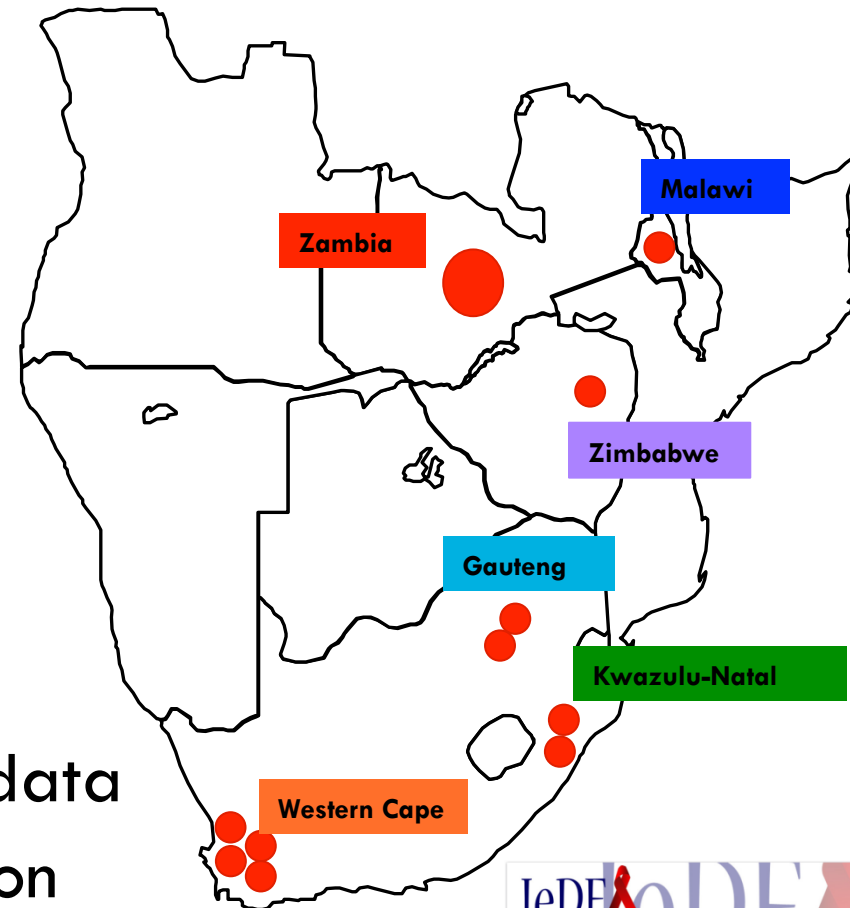
Objective

To examine the baseline characteristics and outcomes of infants starting first line ART in routine care sites within Southern Africa.



Methodology

- Prospectively collected routine data
- Site inclusion: infant ART initiation before and after 1 January 2010
- Participant inclusion:
 - HIV infected (recorded PCR diagnosis)
 - ART naïve (except for PMTCT exposure)
 - First line ART (≥ 3 antiretroviral drugs)
 - Recorded date prior to 1st birthday
- Outcomes:
 - Mortality, loss to follow-up, transfer-out
 - Virological suppression
- Missing baseline characteristics data modeled using multiple imputation



RESULTS

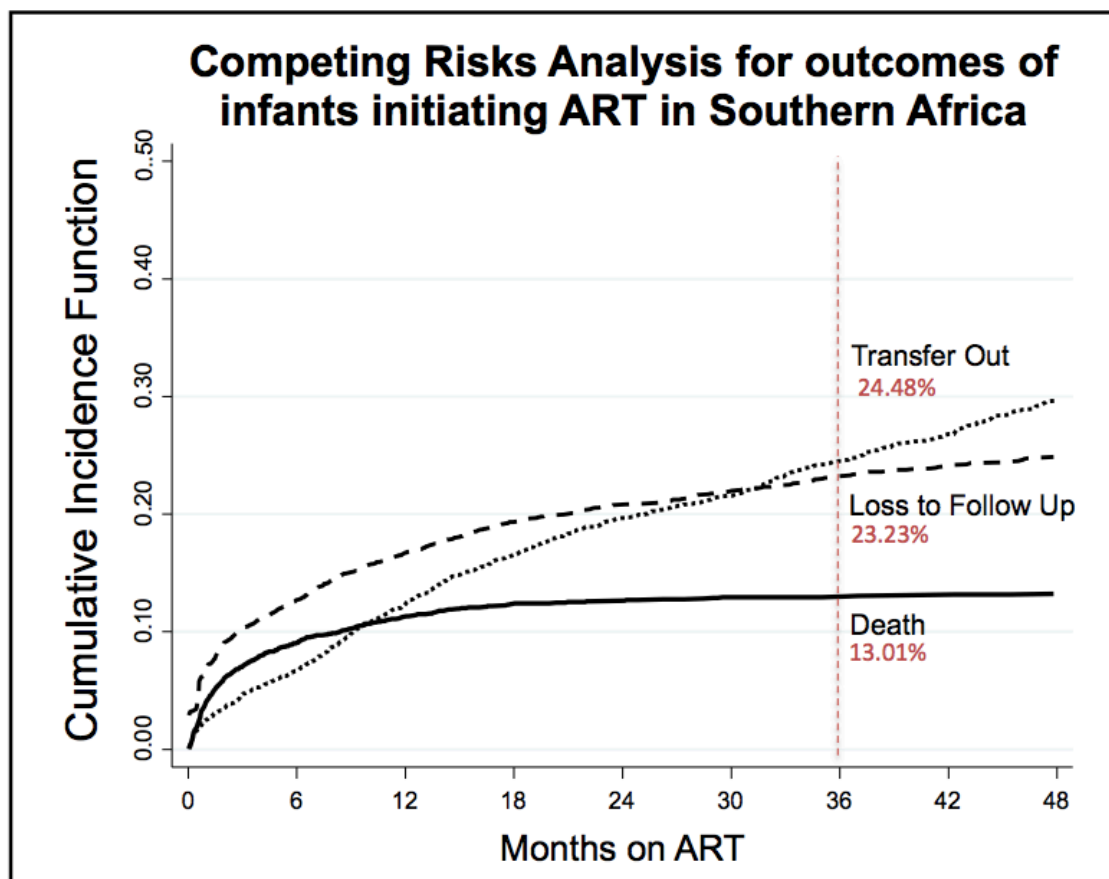
Baseline Characteristics

(n=4945)

Characteristic at ART initiation	Overall	2004 - 2009	2010 - 2012	p value
Age (months), median	5.9	6.1	5.4	0.0000
WHO stage 3 or 4, %	76.5%	81.2%	63.4%	0.0000
CD4 Percentage, median	18.5	18	20.7	0.0000
Severe Immunosuppression, %	87.2%	89.2%	81.3%	0.0000
WAZ category ≤ -3 , %	41.8%	44.5%	34.2%	0.0000
First ART Drug, %				
Stavudine	69.7%			
Zidovudine	15.2%			
Abacavir	14.9%			
Protease inhibitor as 3 rd drug, %	68.1%			
PMTCT exposed, %	57.9%			

Mortality, Loss to Follow-up and Transfer Out

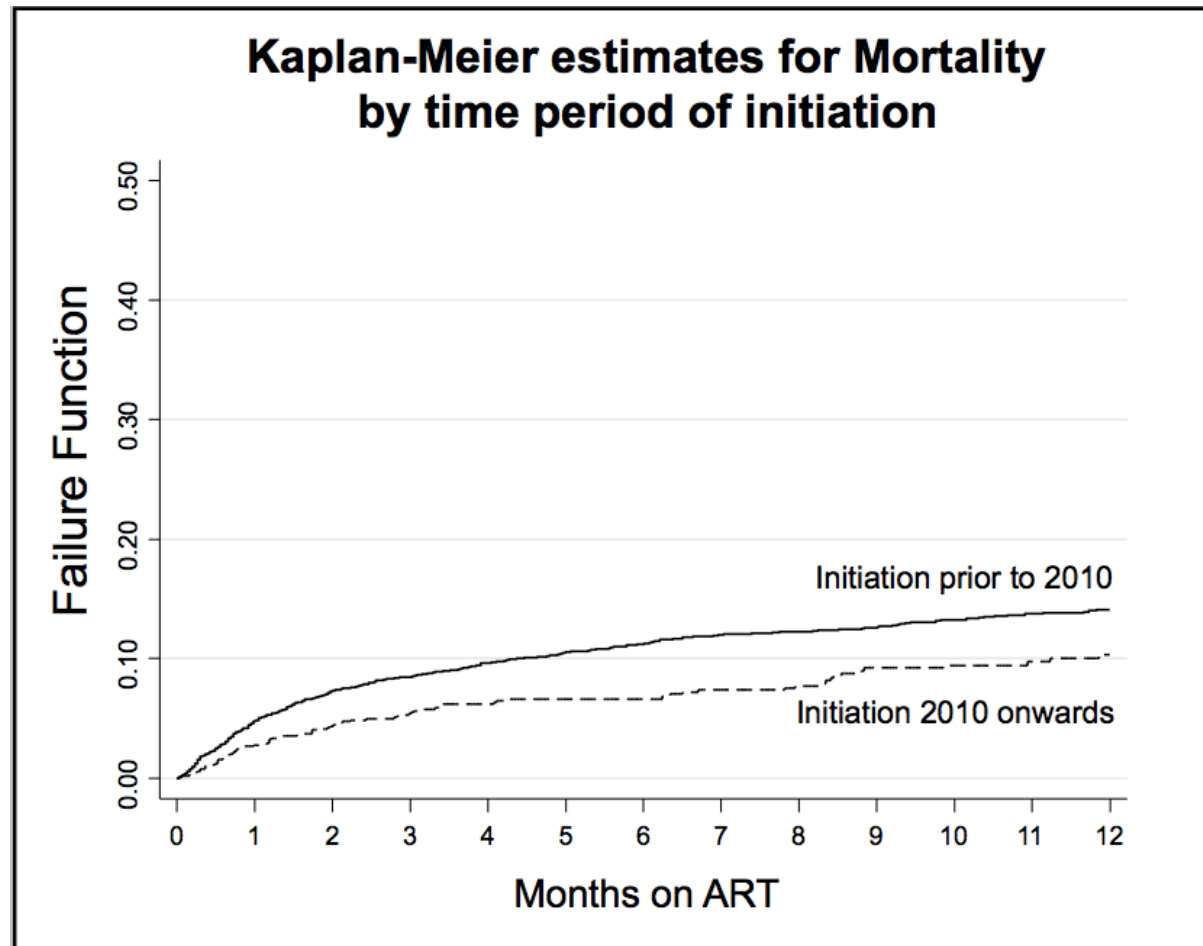
Estimates from Survival Analysis for outcomes Mortality, Loss to Follow-up and Transfer out in infants initiating ART in Southern Africa 2004-2012



Alive and in care at 36 months **39.4%**

Mortality by time period of initiation

Estimates from Survival Analysis for outcome Mortality

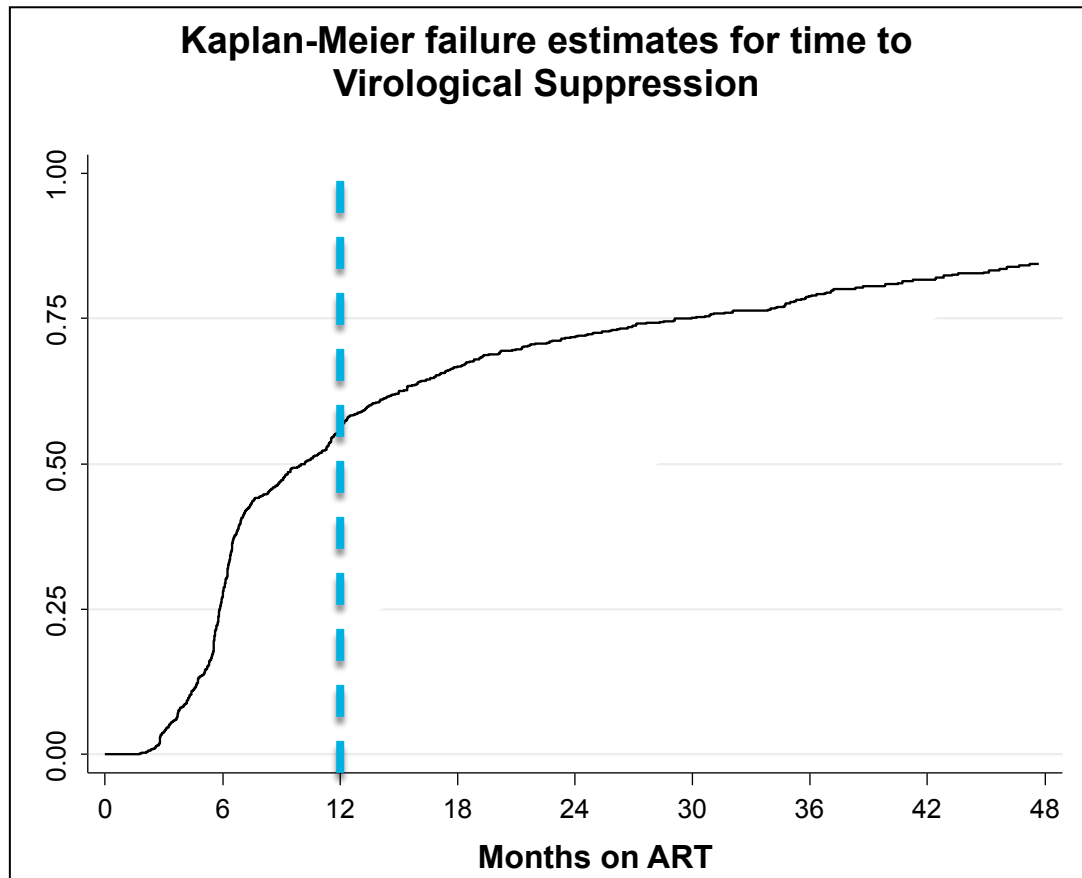


Predictors of Mortality

Variable		Multivariate Cox Regression			Model Selection		
		HR	P value	95% CI	HR	95% CI	VI
Age at initiation	< 3 months		<i>reference</i>		<i>reference</i>		
	3 - 6 months	0.87	0.268	0.68-1.11	-	-	0.22
	6 -12 months	0.84	0.161	0.66-1.07	-	-	-
Non-severe Immune suppression			<i>reference</i>		<i>reference</i>		
Severe Immune suppression (WHO 2006)		2.19	0.000	1.44-3.33	2.15	1.42-3.27	1
WHO stage 1 or 2			<i>reference</i>		<i>reference</i>		
WHO stage 3 or 4		1.36	0.023	1.04-1.78	1.35	1.04-1.77	0.87
Mild or Moderate Anaemia			<i>reference</i>		<i>reference</i>		
Severe Anaemia (DAIDS 2009)		1.34	0.062	0.98-1.82	1.29	0.82-2.05	0.79
WAZ category	> -2		<i>reference</i>		<i>reference</i>		
	-2 to -3	1.29	0.063	0.99-1.71	1.29	0.99-1.71	1
	< -3	2.23	0.000	1.78-2.80	2.22	1.78-2.79	-
ART initiation before 2010			<i>reference</i>		<i>reference</i>		
ART Initiated from start of 2010		0.75	0.015	0.59-0.94	0.75	0.59-0.95	0.88

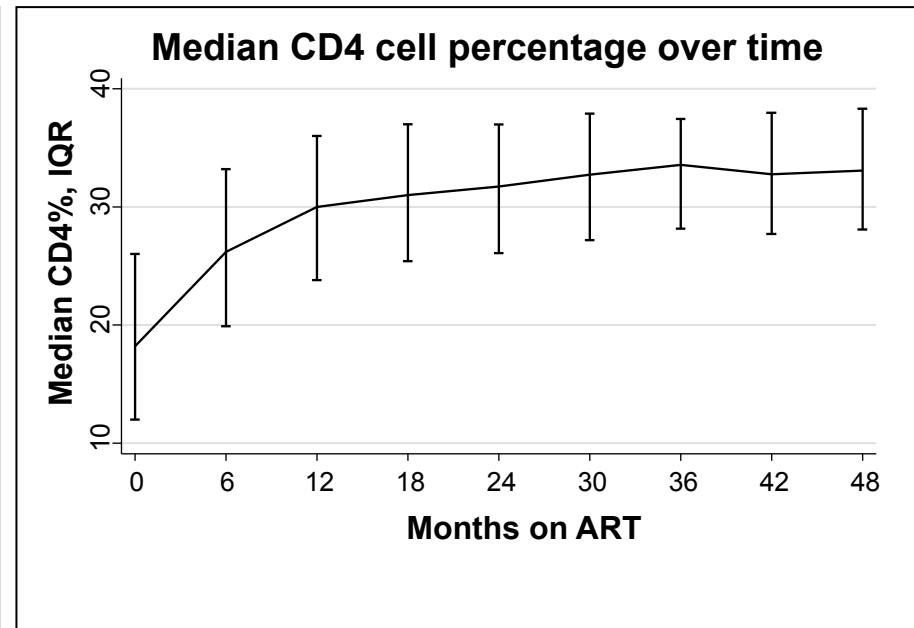
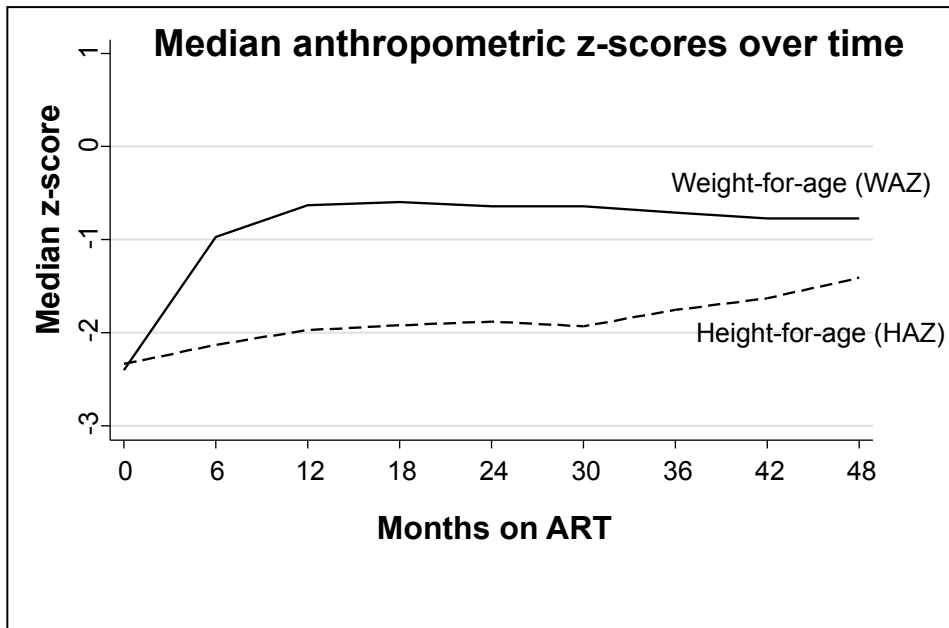
Virological Suppression (n=1364)

Virological Suppression in a subset of South African infants with a baseline and ≥ 1 other virological measure



Anthropometric and Immunologic response

Response over time on ART for infants remaining in care for a minimum of 12 months



Conclusion

- Very different picture to CHER trial
- Infants continue to initiate ART too late with advanced disease and at older ages
→ high mortality and suboptimal outcomes.
- BUT, a notable improvement from the start of 2010 both in characteristics at ART start and outcomes
→ suggests WHO 2010 guidelines did lead to prompter ART initiation with improved outcomes beyond an improvement in baseline disease characteristics.

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References

- Newell M-L, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *The Lancet*. 2004;364(9441):1236-43.
- World Health Organisation (2010). "Antiretroviral Therapy For HIV Infection in Infants and Children: Towards Universal Access. Recommendations for a public health approach. 2010 revision."
- Violari A, C. M., Gibb DM, Babiker AG, Steyn J, Madhi SA, Jean- and M. J. s. Philippe P (2008). "Early antiretroviral therapy and mortality among HIV-infected infants." *N Engl J Med* 359(21): 2233-2244.

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