



PROBABILITY OF AIDS AND NON-AIDS-RELATED MORTALITY OF EARLY-TREATED CHILDREN LIVING WITH HIV-1

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Conflict of interest disclosure



I have no relevant financial relationship with ineligible companies to disclose

Background

Early antiretroviral therapy (ART) initiation in children

Low HIV reservoir

Payne et al, AIDS Res Ther 2021
Ajibola et al, CID, 2021

Good immunological outcomes

EPIICAL

The HIV CLINICAL & EXPERIMENTAL PLATFORM

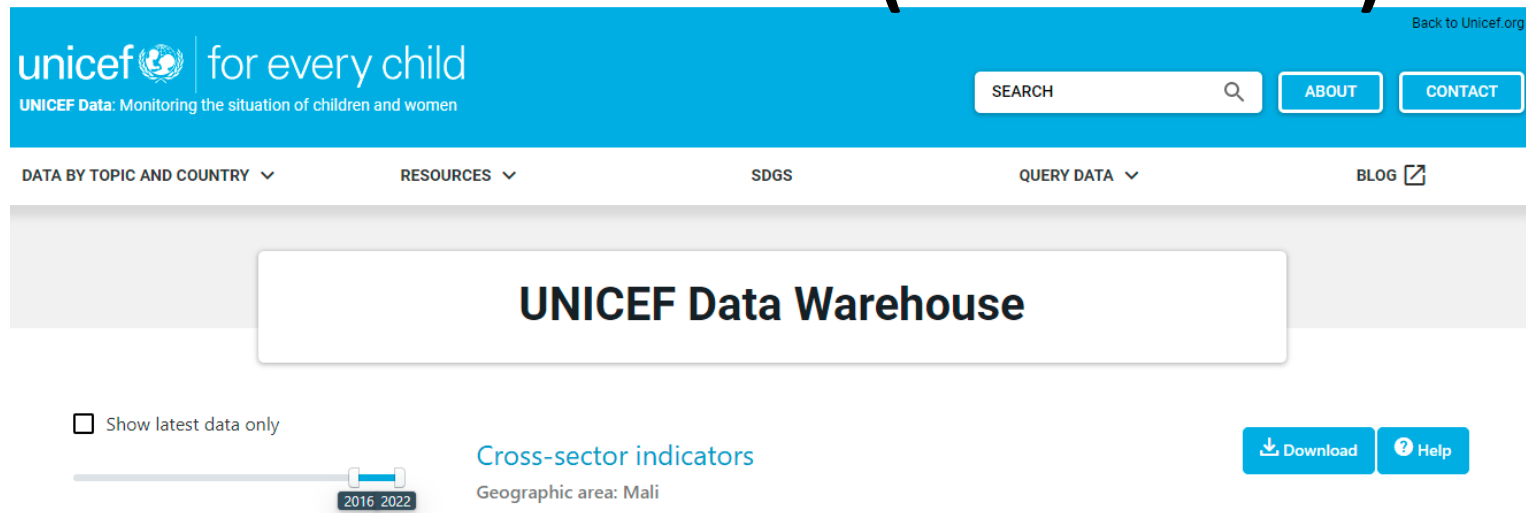
Early treated Perinatally HIV Infected individuals:
Improving Children's Actual Life

Consortium
Aim: to select promising HIV therapeutic strategies candidates

Early-treated perinatally HIV-positive children

Background

Baseline mortality rate < 2 years (UNICEF 2019):



unicef | for every child
UNICEF Data: Monitoring the situation of children and women

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UNICEF Data Warehouse

Cross-sector indicators
Geographic area: Mali

Show latest data only

2016 2022

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- **Mali: 6/100** live births
- **Mozambique: 5,5/100** LB
- **South Africa: 2,7/100** LB

Total proportional baseline: **3,8/100** LB

Background

Are the CD4% a powerful mortality predictor in children living with HIV?

CD4% monitoring is the best for predicting HIV/AIDS mortality

Chekole, SAGE Open Med, 2022

Arage, SAGE Open Med, 2019

Steiniche, Trop Med Int Health, 2018

Gebre-medhin et al. BMC Public Health 2013

CD4% monitoring is not the best for predicting HIV/AIDS mortality

Mutanga et al. BMC Public Health, 2019

Njom Nlend et al, Med Mal infect, 2017

Shanbangu et al, Afr J AIDS Res, 2017

Aim 1

To describe the proportion of AIDS-related mortality in a cohort of early treated children born with HIV

Aim 2

To assess factors related to AIDS and non-AIDS related mortality

Methods

- EARTH-EPIICAL Cohort: 2 rural and 4 urban sites in Mozambique, Mali, and South Africa (SA)



- Infants with HIV who started ART in the first 3 months of life
- Follow-up to 4 years

Methods

AIDS related death: Death in a child with prior or current diagnosis of a disease defining WHO clinical stage III or IV or with severe immunosuppression according to CDC thresholds

Stage ^a	Aged <1 Year		Aged 1 Year to <6 Years		Aged ≥6 Years	
	Cells/mm ³	%	Cells/mm ³	%	Cells/mm ³	%
1	≥1,500	≥34	≥1,000	≥30	≥500	≥26
2	750–1,499	26–33	500–999	22–29	200–499	14–25
3	<750	<26	<500	<22	<200	<14

^a The stage is based primarily on the CD4 count; the CD4 count takes precedence over the CD4 percentage, and the percentage is considered only when the count is missing. If a Stage 3–defining condition has been diagnosed (see Table 6), then the stage is 3, regardless of CD4 test results.

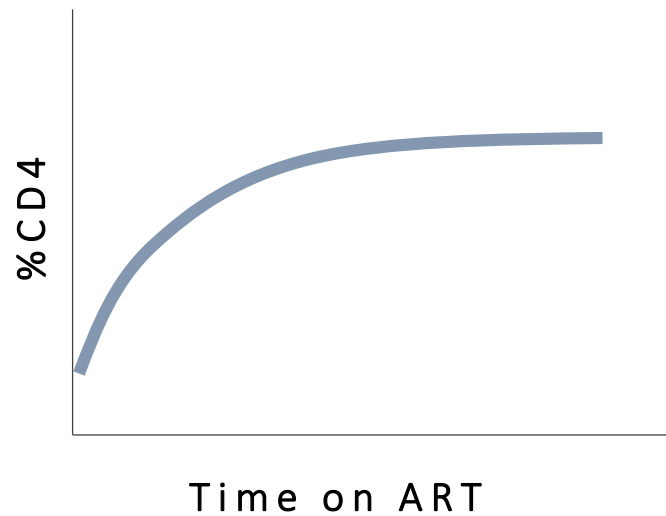
Key: CD4 = CD4 T lymphocyte

Source: Centers for Disease Control and Prevention. Revised surveillance case definition for HIV infection—United States, 2014. *MMWR* 2014;63 (No. RR-3):1-10.

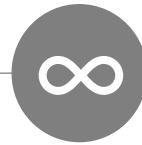
Methods

TWO-STAGE MODELLING JOINT MODELS

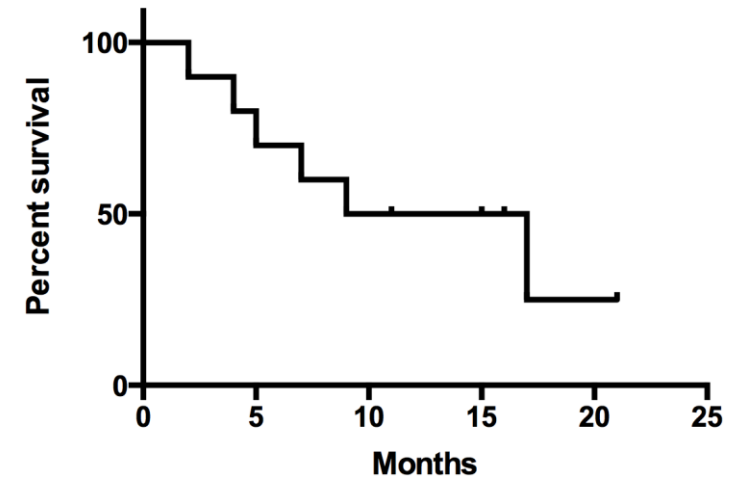
MODEL THE %CD4 DURING THE
TIME OF FOLLOW-UP



The association between CD4 and time on ART
adjusted by confounders



MODEL THE SURVIVAL PROBABILITY IN
THE PRESENCE OF COMPETING RISK



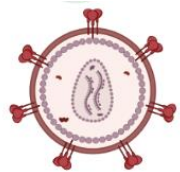
The survival probability adjusted by confounders **AND**
the longitudinal CD4 trajectories in time

Results



212 enrolled in EARTH

Median time of follow-up
17 [6.8;27.5] months



Median VL = 5.21 logs (3.8 to 6)



Median ART = 34 [26;74] days

< 3 months

1 year

2 years



3TC+ABC+LPV/r
or
3TC+AZT+ LPV/r } 83%



Suboptimal adherence (<90%): 56%

212

173

84

Results



212 enrolled in EARTH

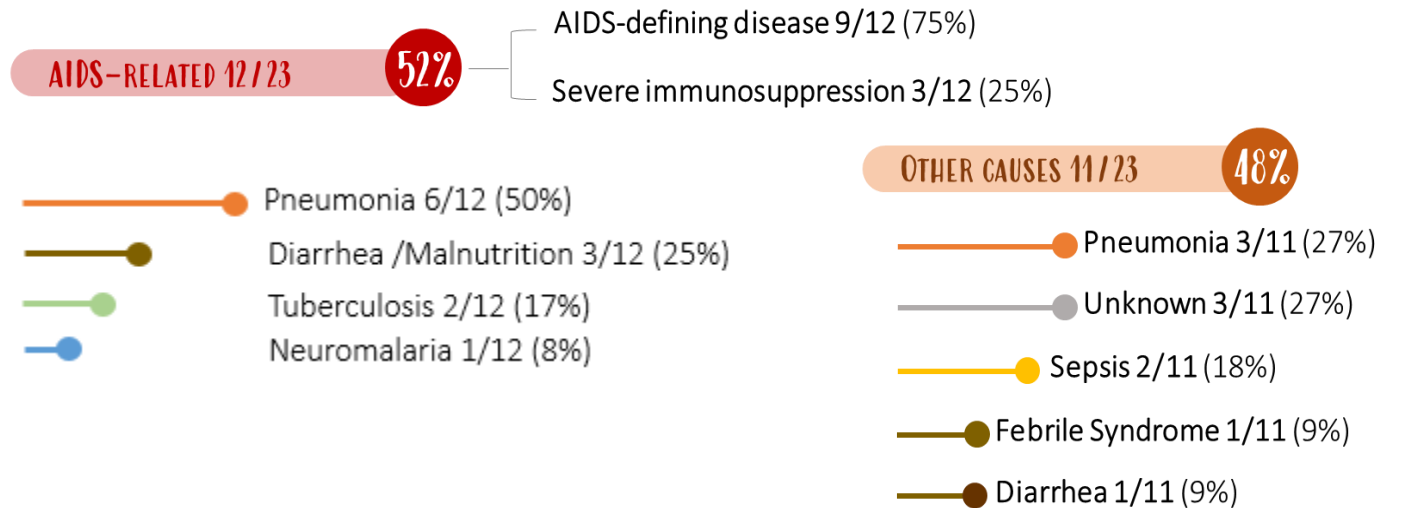
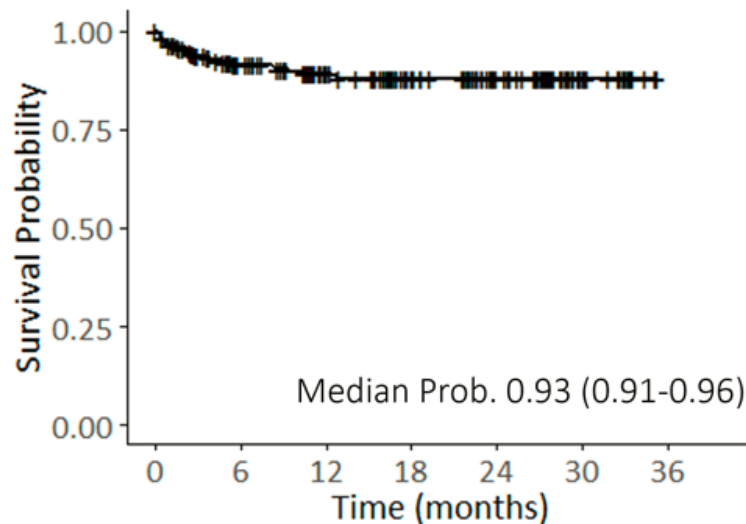


23 patients (10.8%) died

At a median of 2.5 [0.6;6.8] months
74% in the first 6 months

➤ Probability of death:

- at 1 year = 11% (CI95%,6 to 15)
- at 2 years = 12% (CI95%,7 to 17)



Results

Excess of mortality compared to baseline mortality = **7%**

Due to **AIDS-related causes** = **5.7%**

Due to **non-AIDS related causes** = **1.4%**

	South Africa n=123 Baseline 2,7/100 LB			Mozambique n=79 5,5/100 LB			Mali n=10 6/100 LB			All n=212 3,8/100 LB		
	Deaths	%	Excess	Deaths	%	Excess	Deaths	%	Excess	Deaths	%	Excess
All	7	5,7	3%	14	17,7	12.2%	2	20	14%	23	10,8	7%
No AIDS	3	2,4	-0.3%	8	10,1	4.6%	0	0,0	0%	11	5,2	1,4%
AIDS	4	3.3	3.3%	6	7,6	7.6%	2	20,0	14%	12	5,7	5.7%

Results

	Estimate (95% CI)	p-value
Longitudinal model		
Time on ART	-0.008 (-0.01-(-0.004))	2.1·10 ⁻⁴
ART regimen		
3TC+ABC/AZT+NVP	5.29 (0.36-8.24)	0.007
3TC+AZT+LPVr	-3.84 (-8.0-0.70)	0.063
Survival model		
<u>Baseline Viral load</u>	AIDS-related cause, 1.47 (0.87-3.74)	0.290
	<u>Other cause, 4.34 (1.84-20.7)</u>	<u>0.026</u>
Baseline Weight-for-age	AIDS-related cause, 1.22 (0.78-1.71)	0.353
	Other cause, 1.07 (0.70-2.12)	0.792
Age at diagnosis	AIDS-related cause, 1.01 (0.99-1.01)	0.411
	Other cause, 0.99 (0.95-1.00)	0.276
<u>Association CD4</u>		
	<u>AIDS-related cause, 0.9 (0.86-0.98)</u>	<u>0.046</u>
	<u>Other cause, 1.09 (1.02-1.15)</u>	<u>0.003</u>

Conclusion



- Despite early treatment, excess of AIDS- and non-AIDS-related mortality remains high in children living with HIV-1 in Sub-Saharan Africa
- Differentiating AIDS and non-AIDS related mortality in children with HIV may allow us to understand better the risk factors associated with mortality
- CD4 percentage changes over time, and it impacts the probability of death
- Infants with high baseline VL and low CD4% require specific attention.

Aknowledgements

Patients and families
EPIICAL Consortium
EARTH Cohort



Penta
Child Health Research

