

Antiretroviral treatment outcomes and their predictors in a large cohort of HIV-infected children in Sub-Saharan Africa.

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Challenges to ART access for children in Sub-Saharan Africa

- Lack of sufficient diagnostic tools and of pediatric formulations of antiretrovirals and other therapeutics.
- Mortality is particularly high in the initial years of life.
- Background of other co-morbid conditions already carrying significant morbidity and mortality:
 - malnutrition
 - respiratory and diarrheal infections
 - Malaria
 - TB

The DREAM (Drug Resource Enhancement against AIDS and Malnutrition) program

- Held by the Community of Sant'Egidio in 10 African countries
- Supports care and treatment of HIV-infected adults, mothers and children through a comprehensive approach.
- Public ART sites are supported by the program
 - health care personnel training and empowerment,
 - nutritional support to adult and pediatric patients,
 - laboratory support for diagnostics and monitoring,
 - education and training of peers for patients support.
 - Electronic health records are uniform throughout the program: data included in real time

Study aims

- To analyse the response to antiretroviral therapy (ART) of vertically infected HIV-1 positive children in Sub-Saharan African treatment sites supported by DREAM (VL, CD4, weight/growth parameters)
- to analyse the morbidity and the mortality of children undergoing ART
- To analyse the patients retention into the program
- to analyse the predictors of mortality and loss to follow up

Methods

- Cohort study of ART-naive children (age ≤ 14 years) starting ART in 17 DREAM-supported public sites
 - in Mozambique, Malawi and Guinea Conakry,
- Data collected from the electronic health records: baseline:
 - demographics and hemoglobin (Hb) levels;
 - CD4 percentage, plasma HIV RNA (VL, bDNA), age-adjusted weight z-score (WAZ), height z-score (HAZ) and weight for height z-score (WHZ) according to the WHO/NCHS growth standards
- 6 and 12 months on ART:
 - WAZ, HAZ and WHZ
- Last follow-up:
 - CD4 percentage, plasma HIV RNA (VL, bDNA),

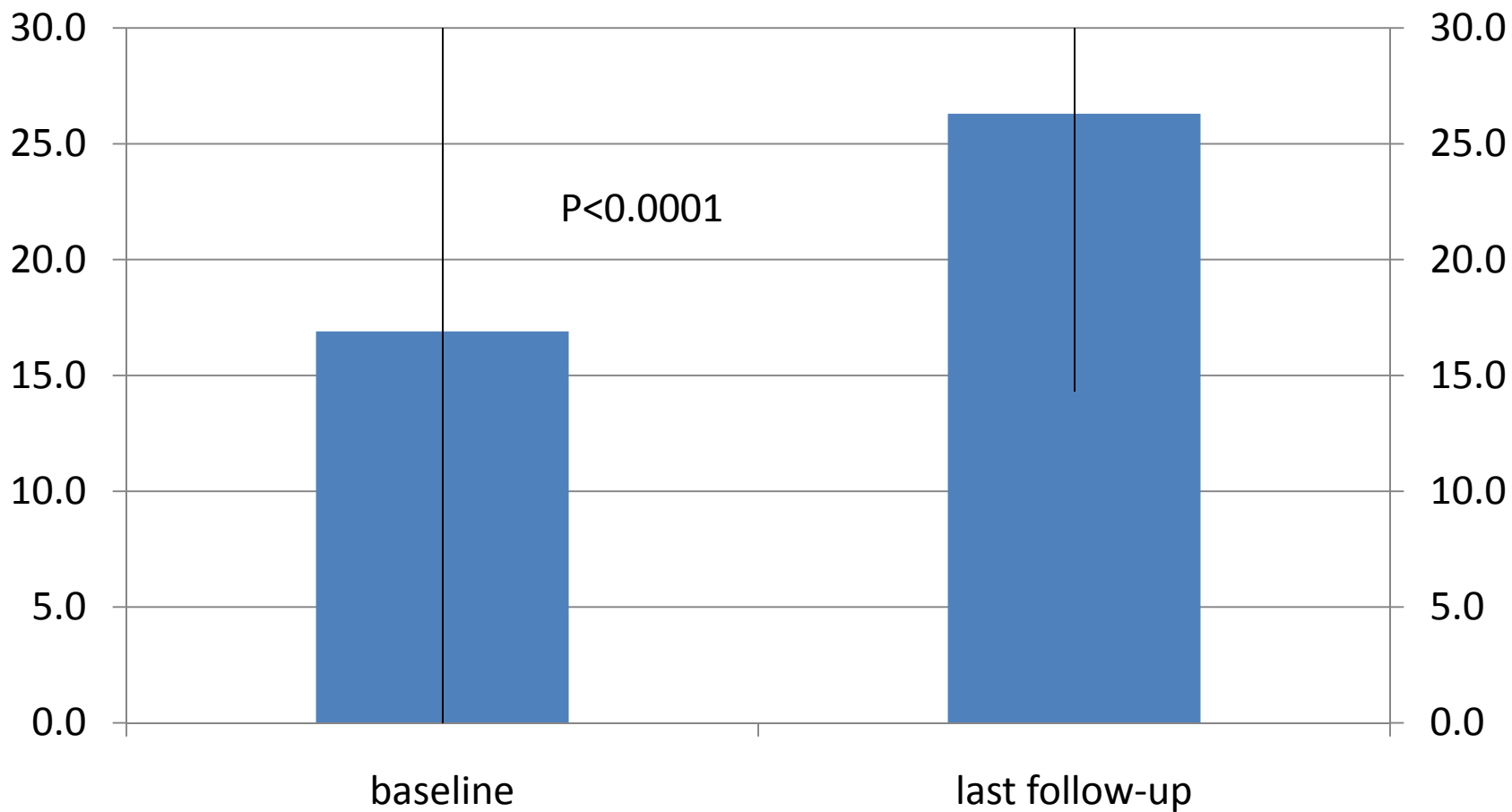
Methods -2

- Dates death
 - direct ascertainment or family investigation using a home care team
- Dates “lost to follow up”
 - >3 months not showing at the clinical or pharmacy appointment and death not ascertained, unless returned later.
- Predictors of time-to-death and time-to-loss to follow up (LTFU) were analyzed by univariable and multivariable Cox’s regression models.

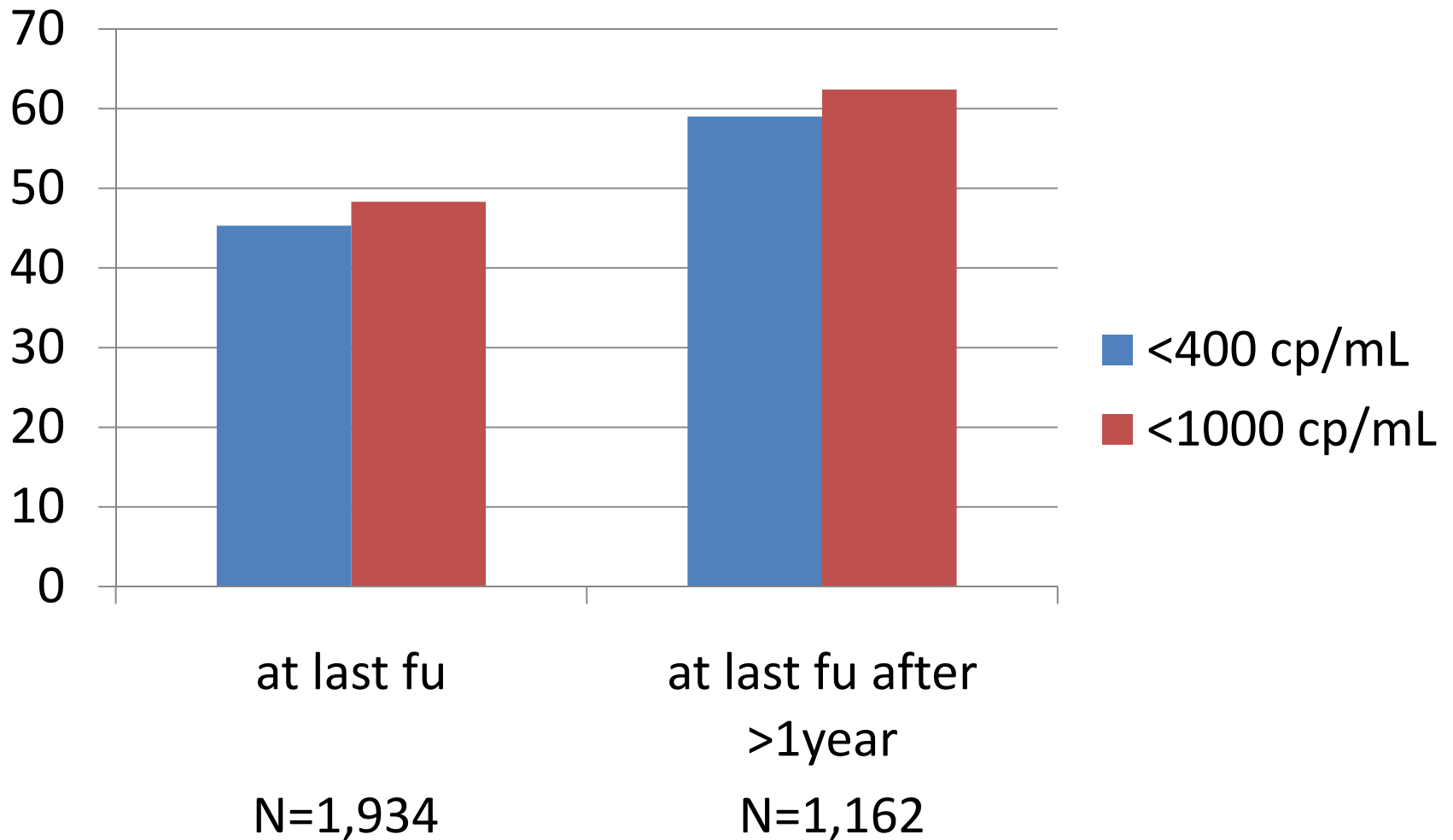
Baseline patients characteristics (n=2,215)

Variable	Median (IQR) or %
Males (%)	52.3%
Age, years	4 (2-8)
CD4% (n=2,055)	15.3 (9.9, 21.3)
HIV RNA, log ₁₀ cp/mL (n=1,922)	4.97 (4.39, 5.50)
age-adjusted weight z-score (2,055)	-2.16 (-3.02, -1.28)
age-adjusted height z-score (2,051)	-2.58 (-3.65, -1.55)
Weight for height z-score (1,782)	-0.74 (-1.70, +0.18)
hemoglobin (g/dL) (n=2,148)	9.5 (8.3-10.6)
ART used	d4T/ZDV+3TC+NVP (97%)

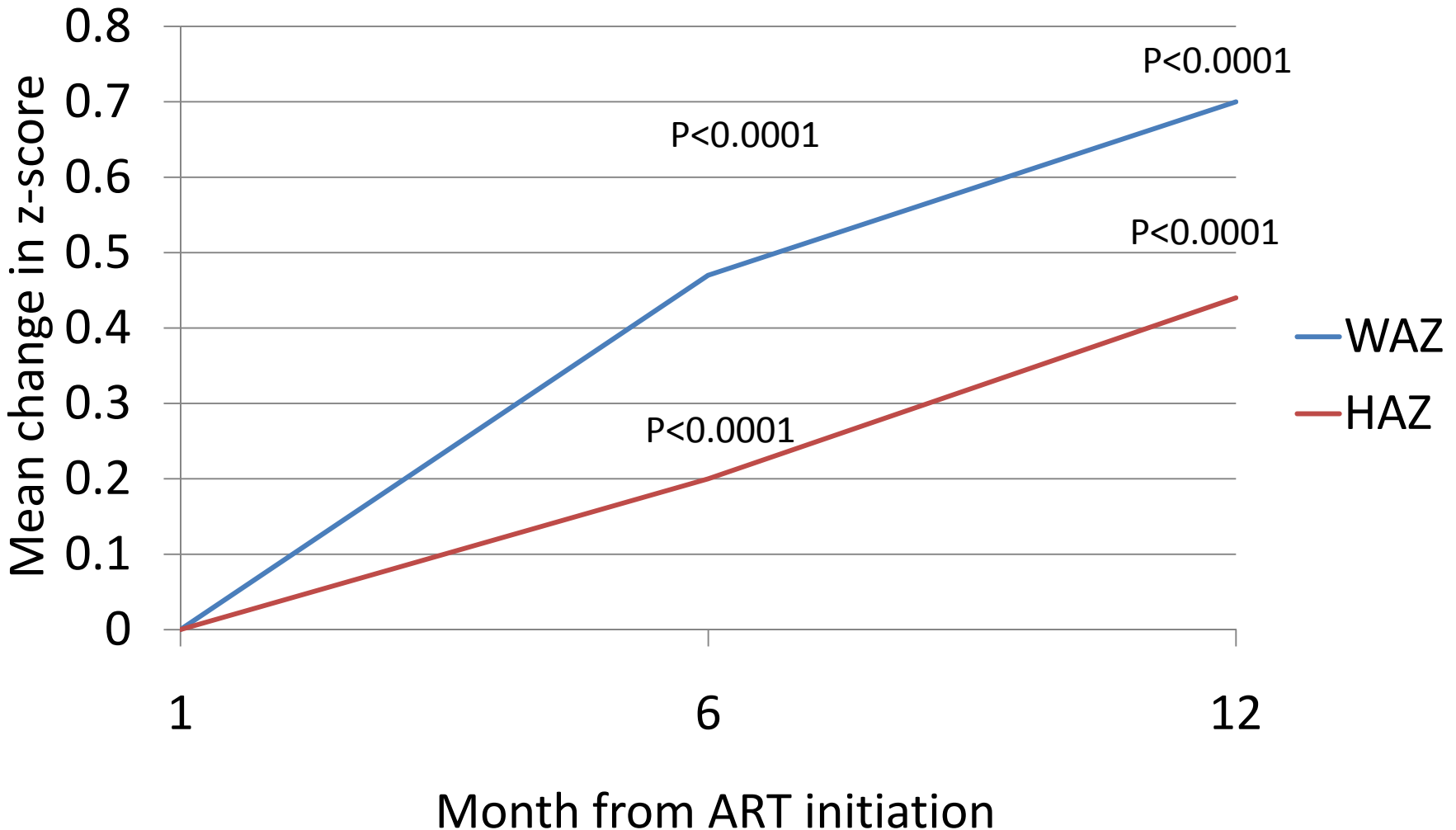
Mean CD4 percentage at baseline and last f/u (n=2,030)



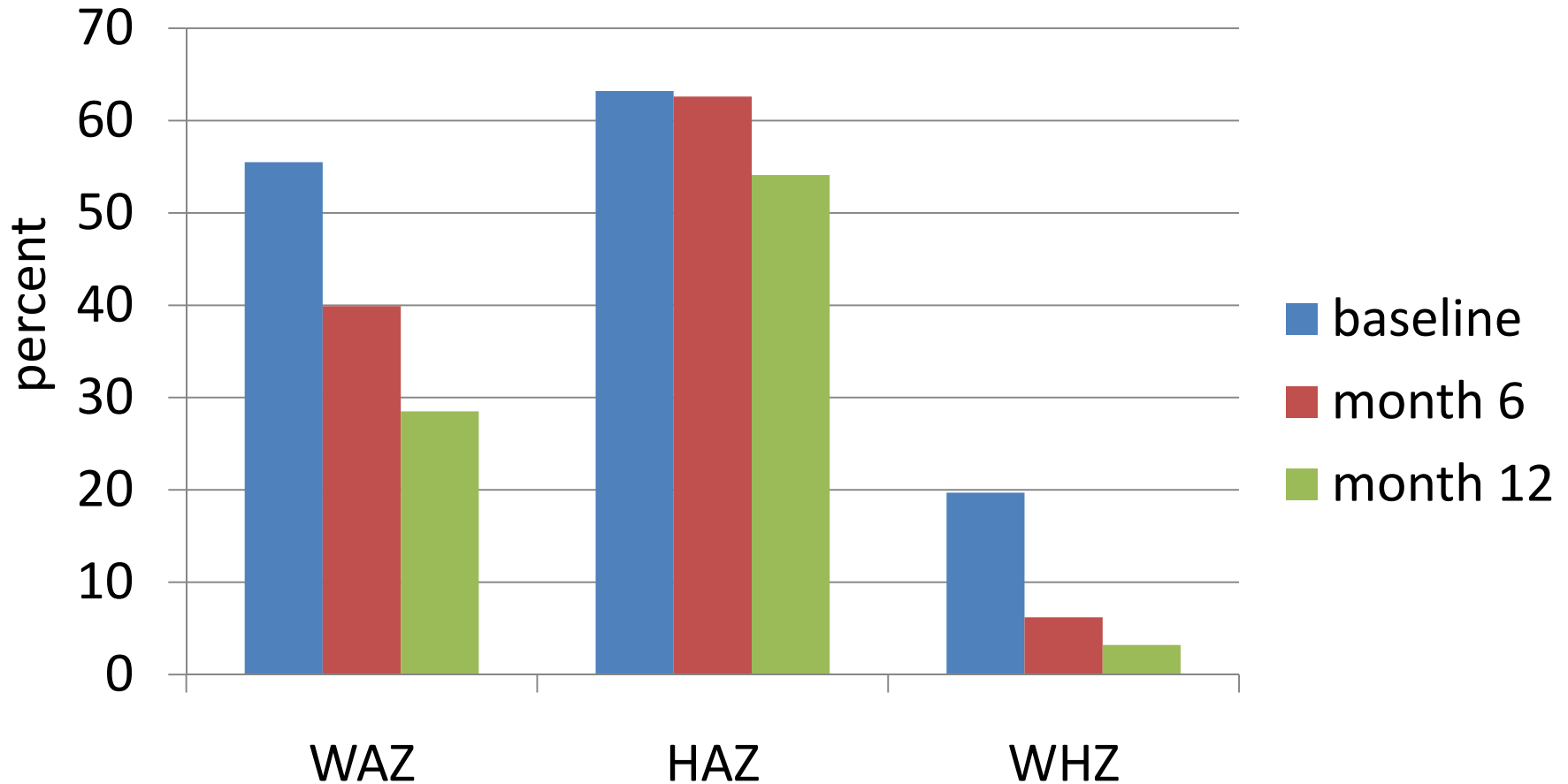
Percentage with VL response at last f/u



Mean change in nutritional and growth measures during ART



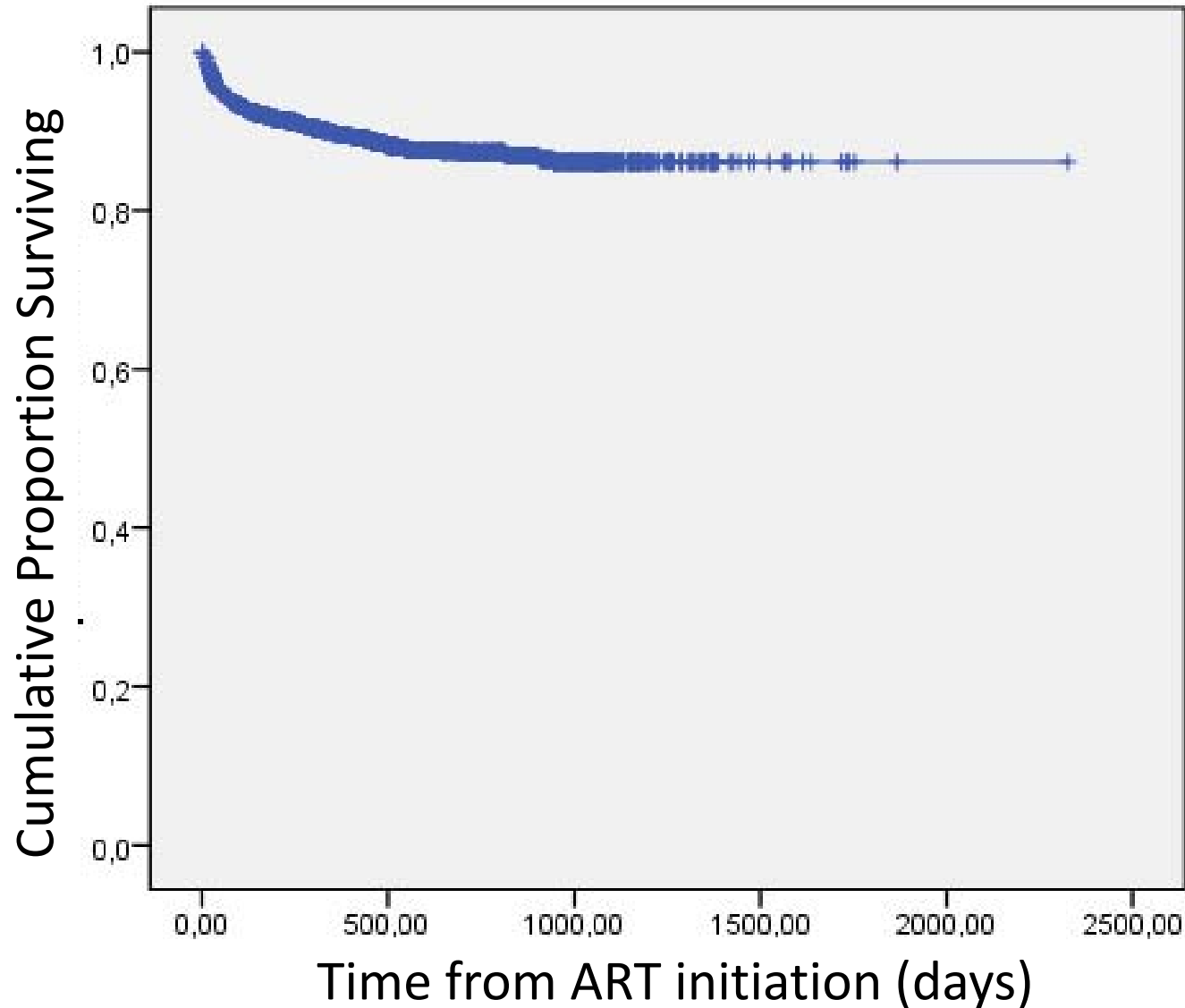
Percent with nutrition and growth z-scores < -2 (moderate/ severe deficits) during ART



Clinical events during follow-up

- 1,410 children (63.7%) developed at least one clinical event: distribution of first event:
 - gastrointestinal infection 673 (30.4%)
 - malaria 476 (21.5%)
 - tuberculosis 158 (7.1%)
 - Pneumonia 102 (4.6%)
- 897 (40.5% of the overall population; 63.6% of those experiencing a first event) experienced concomitant or subsequent events.

Kaplan Meier plot of patients survival (n=238 deaths)

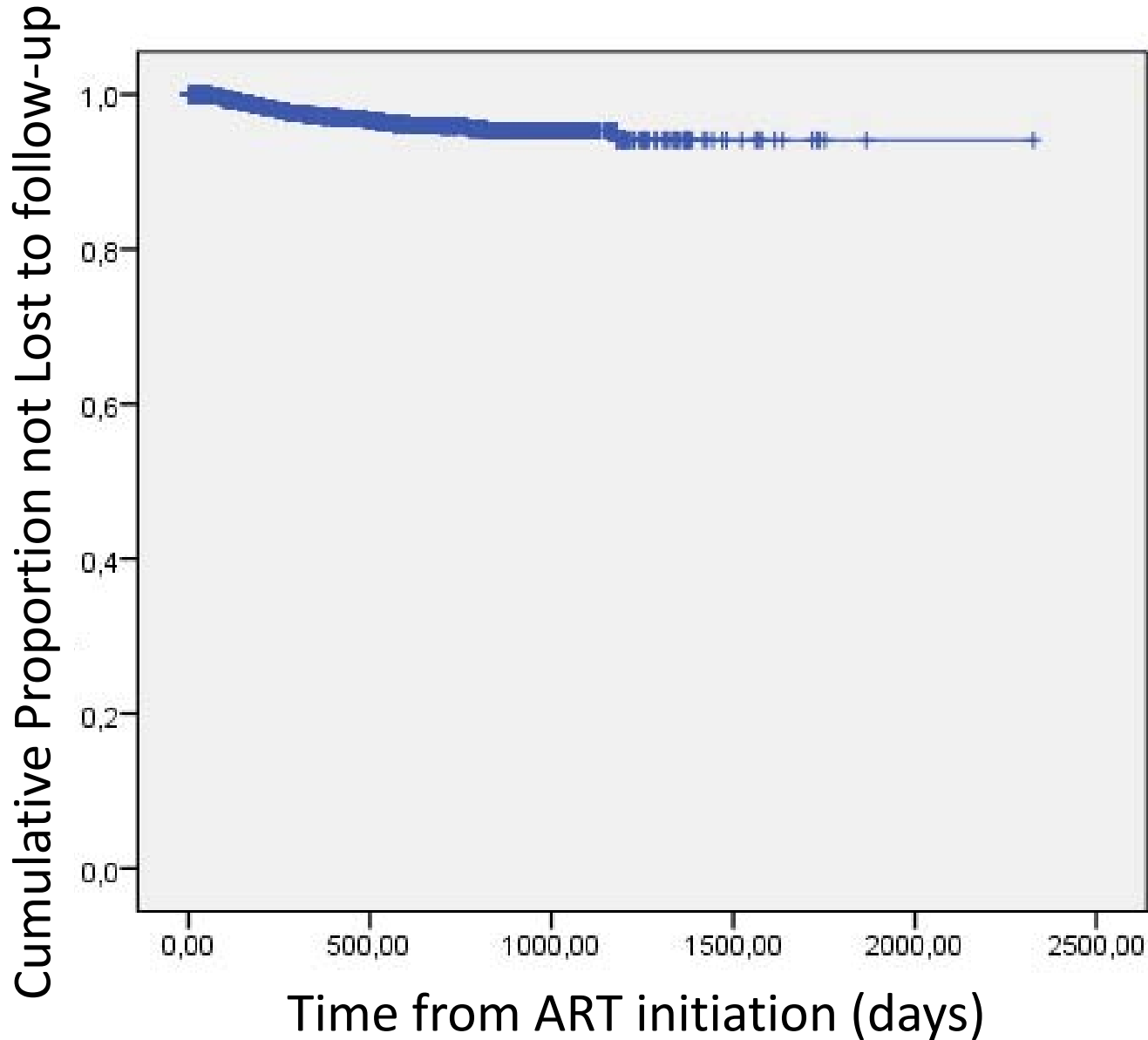


Death
incidence:
6.7/100 PYFU

Predictors of mortality (n=238 deaths in 3,456 PYFU)

Variable	Univariable analysis		Multivariable analysis*	
	Hazard ratio for death (95% CI)	P	Hazard ratio for death (95% CI)	P
Age (per 1 year older)	0.93 (0.89-0.96)	<0.001	Ne	
Baseline CD4% (per 1% higher)	0.98 (0.97-1.00)	0.023	Ne	
Baseline HIV RNA (per 1 log ₁₀ cp/mL higher)	1.40 (1.19-1.64)	<0.001	1.22 (1.04-1.44)	0.016
Baseline age-adjusted weight z-score (per 1 higher)	0.55 (0.50-0.61)	<0.001	0.58 (0.52-0.64)	<0.001
Baseline age-adjusted height z-score (per 1 higher)	0.78 (0.72-0.84)	<0.001	Ne	
Baseline hemoglobin (per 1 g/dL higher)	0.76 (0.72-0.81)	<0.001	Ne	

Kaplan Meier plot of patients retention to care



Incidence of
LTFU:
1.8/100 PYFU

Predictors of time to LTFU (n=63 events)

Variable	Univariable analysis	
	Hazard ratio for death (95% CI)	P
Age (per 1 year older)	0.89 (0.82-0.96)	0.003
Baseline CD4% (per 1% higher)	1.00 (0.98-1.02)	0.895
Baseline HIV RNA (per 1 log ₁₀ cp/mL higher)	1.43 (1.01-2.03)	0.043
Baseline age-adjusted weight z-score (per 1 higher)	0.81 (0.62-1.07)	0.143
Baseline age-adjusted height z-score (per 1 higher)	1.07 (0.86-1.33)	0.553
Baseline hemoglobin (per 1 g/dL higher)	0.84 (0.74-0.96)	0.012

Summary

- In this cohort of HIV-infected children treated with ART in the Sub-Saharan African setting, treatment was followed by a high survival rate and by high retention to care.
- Immunological and weight/growth parameters improved significantly.
- A high incidence of opportunistic or other infections and a significant proportion of suboptimal virological responses were observed.
- High baseline viral load and low baseline children weight were independently predictive of death.

Conclusions

- Despite the significant benefits observed by the use of ART in this setting, future efforts to improve treatment and care of this pediatric population are needed
- These should focus, among others, on
 - earlier diagnosis of HIV-infection
 - improvement of the virological outcomes
 - prevention and treatment of the co-morbid conditions.

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