The Antiretroviral Treatment in Lower Income Countries (ART-LINC) Collaboration

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Primary Aims

- To define prognosis of HIV-infected patients treated with HAART in resource-poor settings
- To compare experiences between different settings, delivery modes, and types of monitoring
- To compare prognosis in resource-limited settings with that observed in industrialized nations

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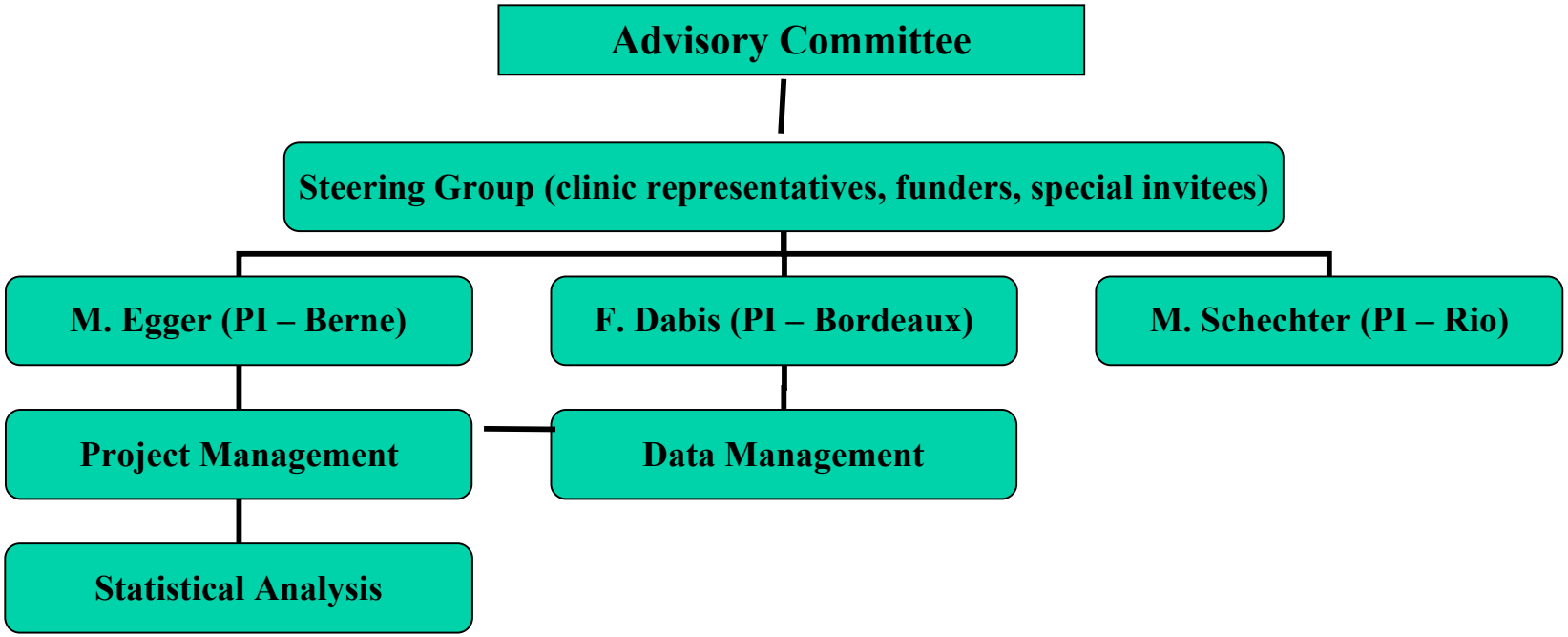
ART-LINC Organizational Structure



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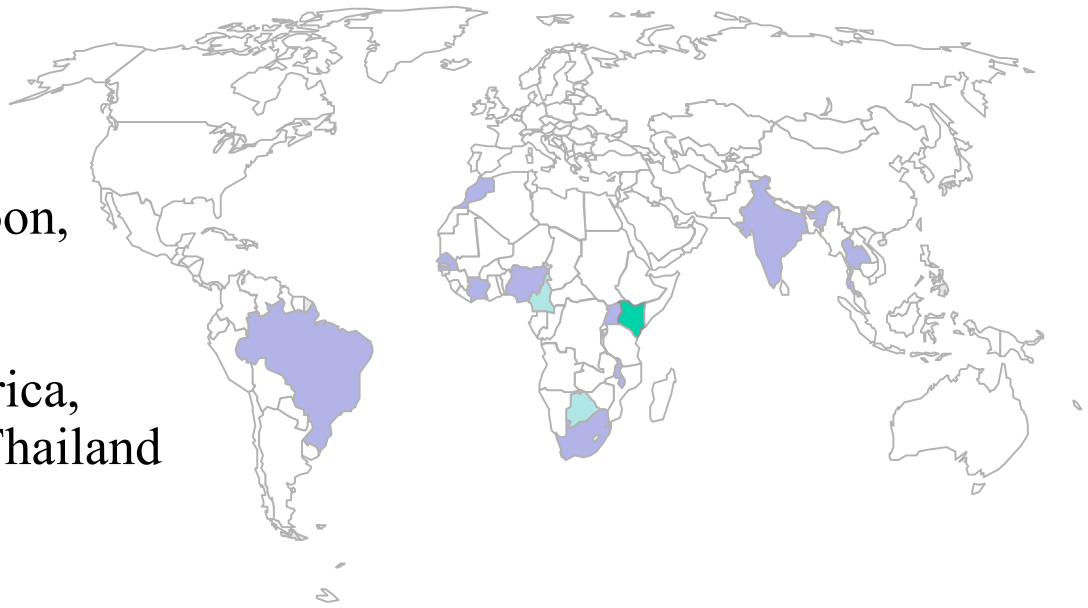
Results from 1st data merger (1996-2003)

- 8734 patients
- 23 centres
- 16 countries
  - Botswana, Burundi, Cameroon, DRC, Côte d'Ivoire, Kenya, Malawi, Morocco, Nigeria, Rwanda, Senegal, South Africa, Uganda, Brazil, India, and Thailand



- Characteristics of centres
  - 9 public, 4 private for-profit, 10 private not-for-profit (NGO)
  - 18 provided VCT
  - 15 provided PMTCT
  - 13 had specialised TB clinic

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ART-LINC Collaboration *Int J Epidemiol* 34:979-986; 2005

Patients

- 7075 (81%) patients had complete socio-demographic data, known date of starting HAART and at least one follow-up visit
- 6498 (92%) were treatment-naïve
- 5193 (73%) had a CD4 count at baseline
  - Those with a documented baseline CD4 count were less likely to be male and more likely to be treated in publicly funded centres or programmes offering free care.
  - The proportion of patients with a documented baseline CD4 count was lower in the more recent calendar period (2002-2003) compared to the earlier periods.

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Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries

The Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration and ART Cohort Collaboration (ART-CC) groups

Summary

Background Highly active antiretroviral therapy (HAART) is being scaled up in developing countries. We compared baseline characteristics and outcomes during the first year of HAART between HIV-1-infected patients in low-income and high-income settings.

Methods 18 HAART programmes in Africa, Asia, and South America (low-income settings) and 12 HIV cohort studies from Europe and North America (high-income settings) provided data for 4810 and 22 217, respectively, treatment-naïve adult patients starting HAART. All patients from high-income settings and 2725 (57%) patients from low-income settings were actively followed-up and included in survival analyses.

Findings Compared with high-income countries, patients starting HAART in low-income settings had lower CD4 cell counts (median 108 cells per μL *vs* 234 cells per μL), were more likely to be female (51% *vs* 25%), and more likely to start treatment with a non-nucleoside reverse transcriptase inhibitor (NNRTI) (70% *vs* 23%). At 6 months, the median number of CD4 cells gained (106 cells per μL *vs* 103 cells per μL) and the percentage of patients reaching HIV-1 RNA levels lower than 500 copies/mL (76% *vs* 77%) were similar. Mortality was higher in low-income settings (124 deaths during 2236 person-years of follow-up) than in high-income settings (414 deaths during 20 532 person-years). The adjusted hazard ratio (HR) of mortality comparing low-income with high-income settings fell from 4·3 (95% CI 1·6–11·8) during the first month to 1·5 (0·7–3·0) during months 7–12. The provision of treatment free of charge in low-income settings was associated with lower mortality (adjusted HR 0·23; 95% CI 0·08–0·61).

Interpretation Patients starting HAART in resource-poor settings have increased mortality rates in the first months on therapy, compared with those in developed countries. Timely diagnosis and assessment of treatment eligibility, coupled with free provision of HAART, might reduce this excess mortality.

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Introduction

The increasingly widespread use of highly active antiretroviral therapy (HAART) since 1996 has substantially improved the prognosis of HIV-infected patients who have access to these drugs.[1–4] In resource-poor settings in Africa, Asia, and South America, where 90% of people with HIV/AIDS live, access to HAART is limited. With falling prices of proprietary drugs, the increasing availability of generic formulations and the

tuberculosis and other bacterial diseases might also affect prognosis.[6–8] Here we report on the Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration, a network of treatment programmes in Africa, Asia, and South America.[9] Our objective was to compare early mortality and immunological and virological response in patients starting HAART in these settings with outcomes in patients participating in a similar collaboration of cohort studies in high-income

Baseline Characteristics

	ART-LINC N=4,810	ART-CC N=22,217
Age (median, IQR)	36 (30 - 42)	36 (31 - 43)
Women	2461 (51%)	5486 (25%)
Baseline CD4 (median, IQR)	108 (37 – 210)	234 (98 - 380)
Baseline HIV RNA (median $\log_{10}$, IQR)	5.1 (4.6 – 5.6)	4.87 (4.2 – 5.4)
Initiated ART with 2 NRTI + PI	923 (22%)	10,434 (83%)
Initiated ART with 2 NRTI + 1 NNRTI	3391 (70%)	5125 (23%)

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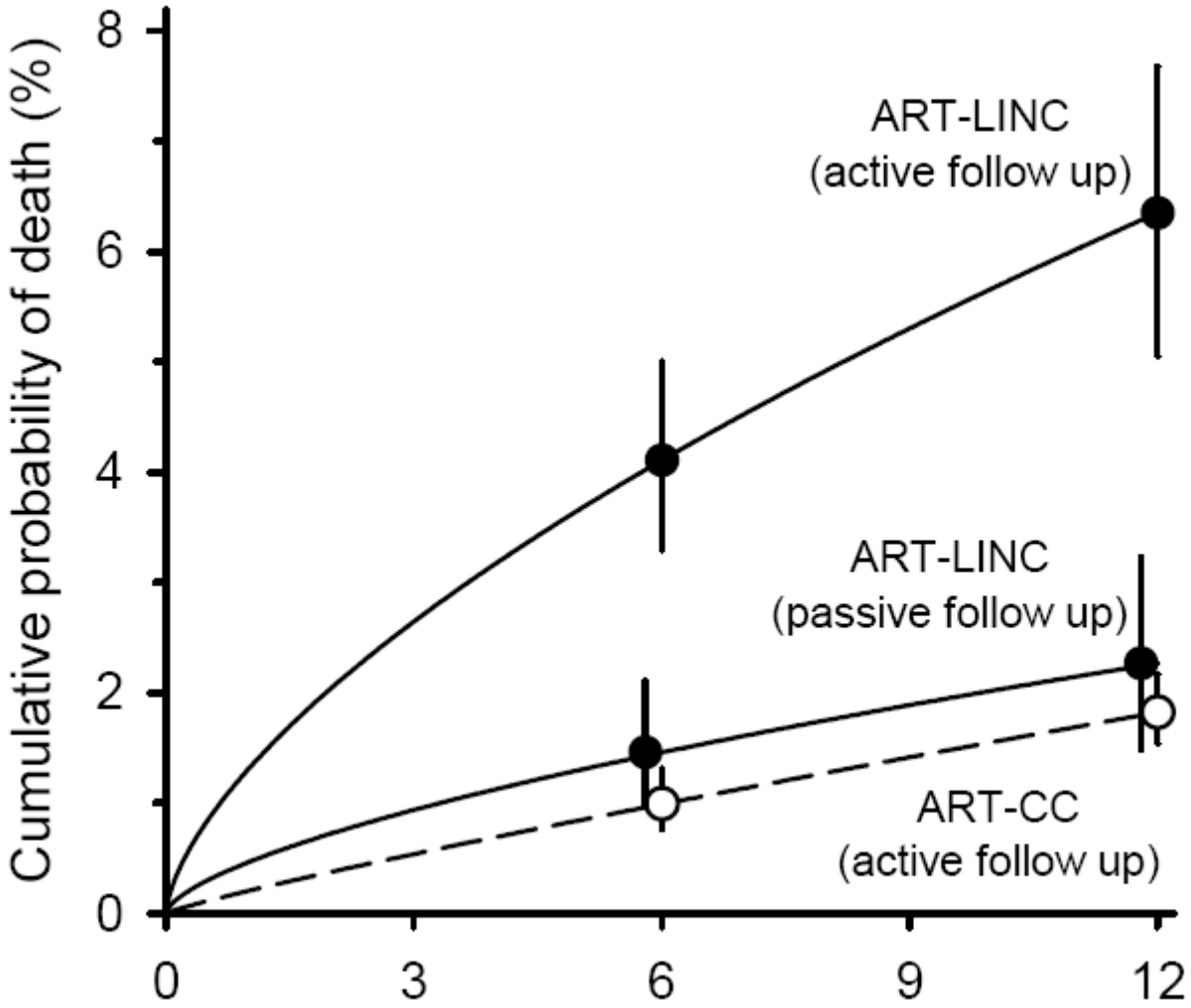
Cumulative mortality in first year



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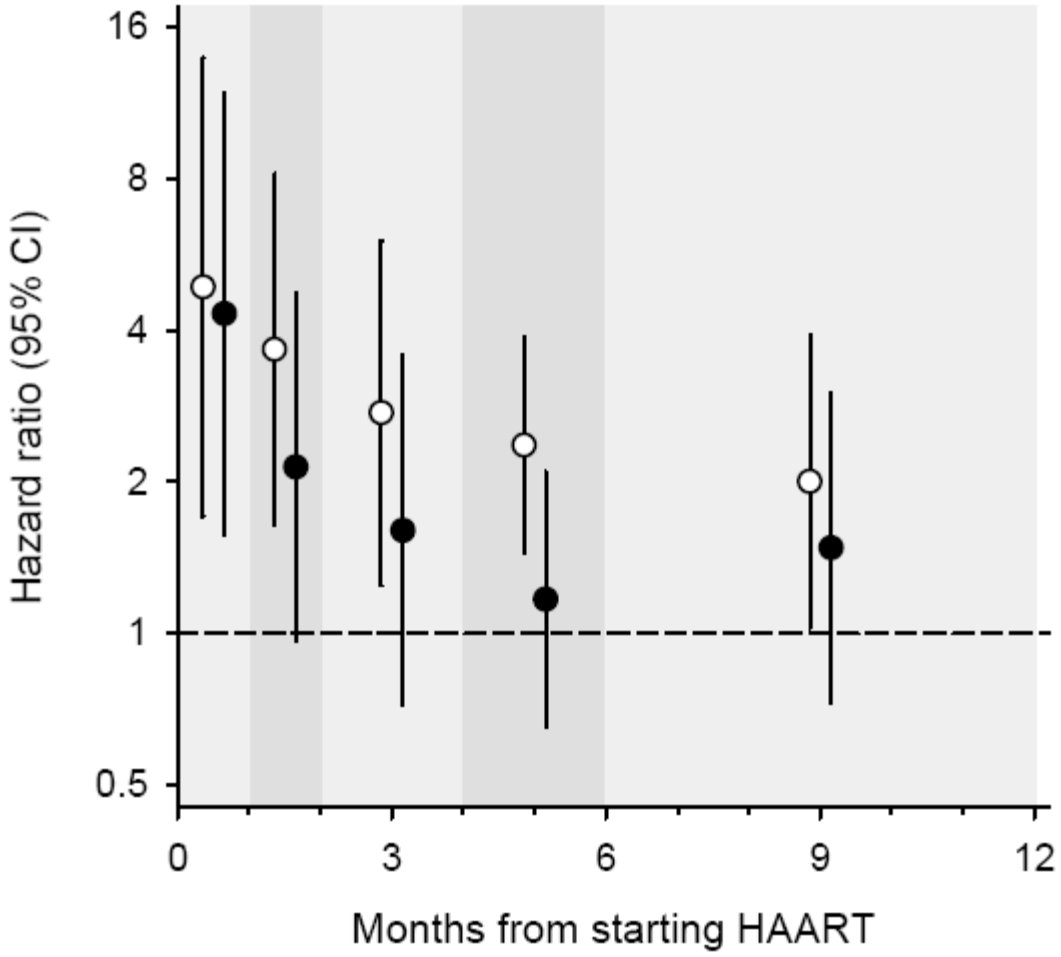
Relative hazard of mortality: ART-LINC (active follow up) vs. ART-CC



○ unadjusted HR
● adjusted HR

(adjusted for cohort, age, sex, baseline CD4, ART-regimen, disease stage)

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Losses to Follow-up (LTFU)

- 727 (15%) patients LTFU in ART-LINC (range 0-44%)
- ART-LINC centres with active follow-up:
  - LTFU: 12%
  - Median baseline of LTFU: 115 cells/μL vs. 123 cells/μL in those followed
- ART-LINC centres with passive follow-up:
  - LTFU: 19%
  - Median baseline of LTFU: 64 cells/μL vs. 123 cells/μL in those followed

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Active follow up	
Total	**2725**
Died in year 1	124
Lost to follow up	331
Less than 1 year of additional follow up after last visit in first year	1001
At least 1 year of additional follow after last visit in first year	**1269**
Subsequent follow up visit	
Months 1 -3	414 (33%)
Months 4 -6	487 (38%)
Months 7 -9	169 (13%)
Months 10 -12	52 (4%)
Month >12	**147 (12%)**
Passive follow up	
Total	**22085**
Died in year 1	41
Lost to follow up	396
Less than 1 year of additional follow up after last visit in first year	575
At least 1 year of additional follow after last visit in first year	**1073**
Subsequent follow up visit	
Months 1 -3	69 (6%)
Months 4 -6	417 (39%)
Months 7 -9	64 (6%)
Months 10 -12	71 (7%)
Month >12	**452 (42%)**

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2nd Merger (underway)

- Expecting data on 25 clinics and networks (including MTCT+ Network)
- 18 countries
- 40,000+ people on HAART
- Data quality?

2nd Merger Preliminary Evaluation

Table 1: Number of patients, follow-up duration and vital status for received dataset

# Cohort	Total Number of patients	Number of patients with baseline data (%)*	Median (IQR) Follow-up in months	Total Follow-up time in person months	Number of deaths (%)
1	97	96 (99)	20.8 (14.9-27.4)	614	18 (18.6)
2	253	214 (84.6)	19.6 (5.6-32.5)	5152	14 (5.5)
3	160	155 (97)	20.4 (10.7-24.8)	2809	7 (4.4)
4	429	427 (99)	48.9 (27.2-67.0)	20641	20 (4.7)
5	1079	1046 (97)	43.7 (18.3-73.2)	49722	46 (4.3)
6	2631	2406 (91)	8.9 (1.4-23.6)	37845	163 (6.2)

* Baseline CD4 cell count (at HAART initiation), known age and gender

2nd Merger contents: Laboratory f les

Table 4: Number of virological, immunological and biological measurements (mean) per patient

Cohort	CD4	HIV-RNA	TLC	ALAT	Albumin	Haemoglobin	Lactate
1	5.3	4.8	0	0	0	3.7	0
2	5.9	3.1	0	0	0	0	0
3	3.5	0	0	1.5	0	3.9	0
4	5.4	3.8	5.3	0	0	5.4	0
5	10.7	10.2	0.2	0	0	0.2	0
6	3.1	0.4	3.1	3.2	0	0	0

A joint initiative of

African Network for the Care of Children Affected by AIDS (ANECCA), Kampala, Uganda

&

Institut de Santé Publique, Epidémiologie et Développement (ISPED), Bordeaux, France

Up-date (February 2006)

- 28 sites have agreed to collaborate, including the MTCT-Plus network
- Funds from NIH and USAID for the first year
- 19 sites have been visited
- First Steering Committee meeting in Nairobi on January 23-24
- First data merger contemplated no later than June 2006
- Desperately seeking funds for year 2 and beyond!
- Links with the adult ART-LINC network are clear
- Links with IEDEA to be defined

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Advisory Committee: Zackie Achmat, Chris Bailey, Kevin de Cock, Wafaa El-Sadr, Ken Freedberg, Helene Gayle, Charlie Gilks, Catherine Hankins, Tony Harries, Elly Katabira, Joia Mukeherjee, Jonathan Sterne, Mark Wainberg

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