



# Introduction of ART in a community based cohort in Uganda and its impact on HIV related mortality

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# Contributors



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# Introduction



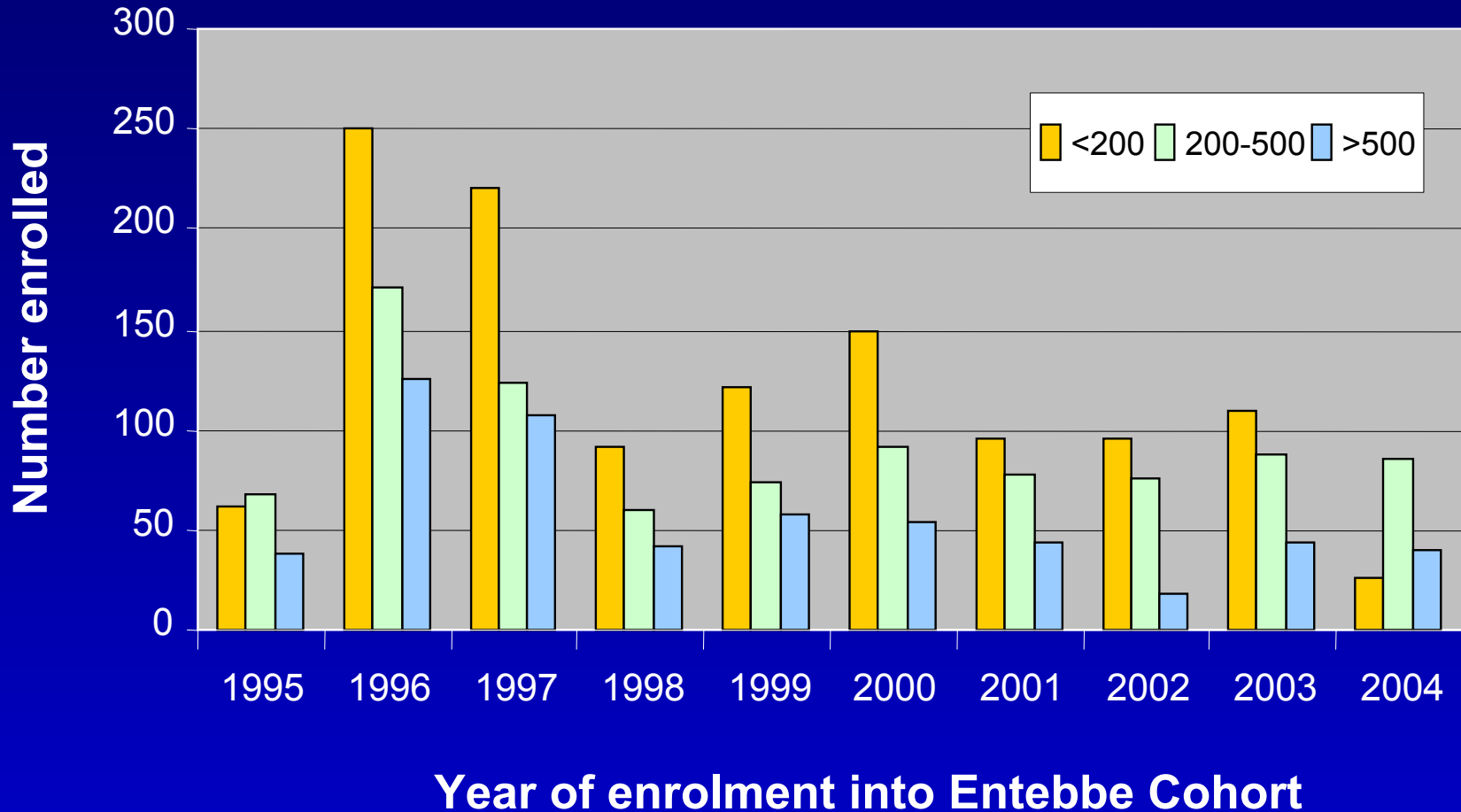
- There are encouraging global efforts to scale up availability of ART in developing countries with high HIV burden
- There is uncertainty about the feasibility of ART in developing country settings
- The benefits of ART in developing country settings have not been widely documented
- We present a historical comparison of HIV related **mortality rates before and after introduction of ART in a Ugandan cohort**

# Background: the Entebbe cohort



- Set up in 1995, initially to evaluate a pneumococcal vaccine in HIV-1 infected adults
- Enrolls adults with HIV infection, age 15 – 59 residing in and around Entebbe who consent to participate. WHO stage IV excluded.
- Aims to evaluate interventions that reduce progression to AIDS or death
- The cohort has so far enrolled 2766 participants with 5942.7 person years of observation

# CD4 at enrolment into the Entebbe Cohort

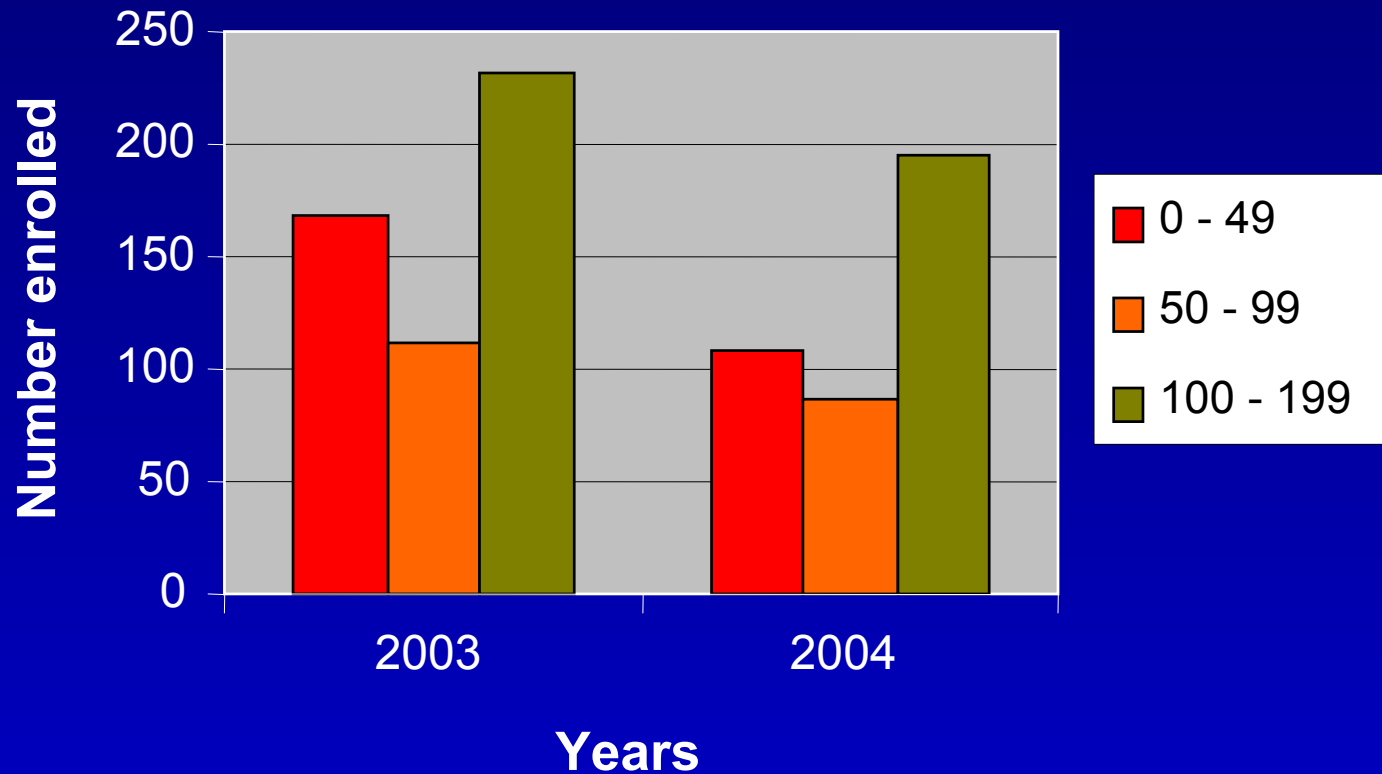


# Background: the DART trial



- A randomised trial of monitoring practice and structured treatment interruptions
- Started in February 2003
- Enrolls symptomatic ARV naïve adults with  $CD4 < 200$  cells/mm<sup>3</sup>, aged 18 years or more, residing in and around Entebbe, who fulfill clinical criteria for ART and consent to participate
- All members of Entebbe cohort eligible for ART were put onto DART

# CD4 at enrolment into the DART Trial



# Methods: Enrolment procedures



## Entebbe Cohort

- Contact information
- Confirmatory HIV test
- WHO clinical staging
- Appropriate management of current illness
- FBC, CD4/CD8

## DART Trial

- Contact information
- Confirmatory HIV test
- WHO clinical staging
- Appropriate management of current illness
- FBC, Biochemistry, CD4/CD8
- **Triple Therapy ART**



# Methods: Follow up procedures



## Entebbe Cohort

- Follow up every 6 mnths
- Document clinical events
- WHO clinical staging
- FBC, CD4/CD8
  
- Plasma and serum storage
- Extra visits for acute clinical events
- Deaths recorded

## DART Trial

- Follow up every 4 wks
- Document clinical events
- FBC, biochemistry
- CD4/CD8 12 wkly
- Check adherence to ART
  
- Plasma storage 12 wkly
- Extra visits for acute clinical events
- Deaths recorded

# Methods: Analysis



## Entebbe Cohort

- observation period  
May 1995 to Jan 98

to match DART population data  
restricted to

- CD4 < 200 at enrolment
- Hb >8mg/dl
- neutrophils >0.5x10<sup>9</sup>/l

## DART Trial

- observation period  
Feb 2003 to May 2004

3 patients contribute time at risk in both Entebbe Cohort and the DART Trial

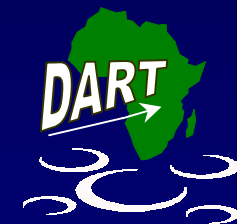
# Results I



- ❖ Compare the death rate during the first 27 months of follow up in the Entebbe Cohort to that during the first 15 months of the DART trial

	Entebbe Cohort	DART Trial
Period of observation	May 95 - Jan 98	Feb 03 - May 04
Total number of subjects	<b>456</b>	<b>745</b>
Total person years of follow up	<b>347</b>	<b>358</b>
Total number of deaths	<b>211</b>	<b>20</b>

# Results II



	Entebbe Cohort			DART Trial		
Baseline CD4 count	Number of subjects	Person years of f/u	Number of deaths	Number of subjects	Person years of f/u	Number of deaths
0-49	171	96	94	234	106	13
50-99	109	85	56	163	84	3
100-199	176	166	61	348	168	4
Total	456	347	211	745	358	20

# Results III



	Entebbe Cohort		DART Trial			
Baseline CD4 count	Death rate per 1000 py	95%CI	Death rate per 1000 py	95%CI	RR	p
0-49	975.3	[796.8-1193.8]	123	[71.3 - 211.7]	7.9	<0.001
50-99	662.5	[509.8-860.9]	35.5	[11.4 - 110.0]	18.5	<0.001
100-199	367.7	[286.1-472.6]	23.8	[8.9 - 63.4]	15.4	<0.001
Total	608.4	[531.6-696.3]	55.8	[36.0-86.5]	10.9	<0.001

# Discussion



- Previous study interventions within the Entebbe cohort may have contributed to the observed reduction in mortality
  - Cotrimoxazole prophylaxis study  
Aug 2000 to Feb 2002 and continued
  - INH prophylaxis study Nov 1998 to Oct 1999
- Adherence to therapy reinforced in a clinical research setting

# Conclusion



- The introduction of ART in this Ugandan cohort is associated with a significant reduction in HIV related mortality
- Initiation of ART even in those most severely immunosuppressed (CD4 <50 cells/mm<sup>3</sup>) is still highly beneficial

# Appreciation



- Study participants
- TASO Entebbe
- Entebbe Study teams
- MRC UK; DFID
- Boehringer Ingelheim; Glaxo Smith Kline  
and Gilead