



# The Development of AntiRetroviral Therapy in Africa (DART) trial

What have we learnt?

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*on behalf of the **DART** Trial Team*



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London





## What have we learnt? (I)

A trial provides an excellent way to build partnerships and teams



# DART partners



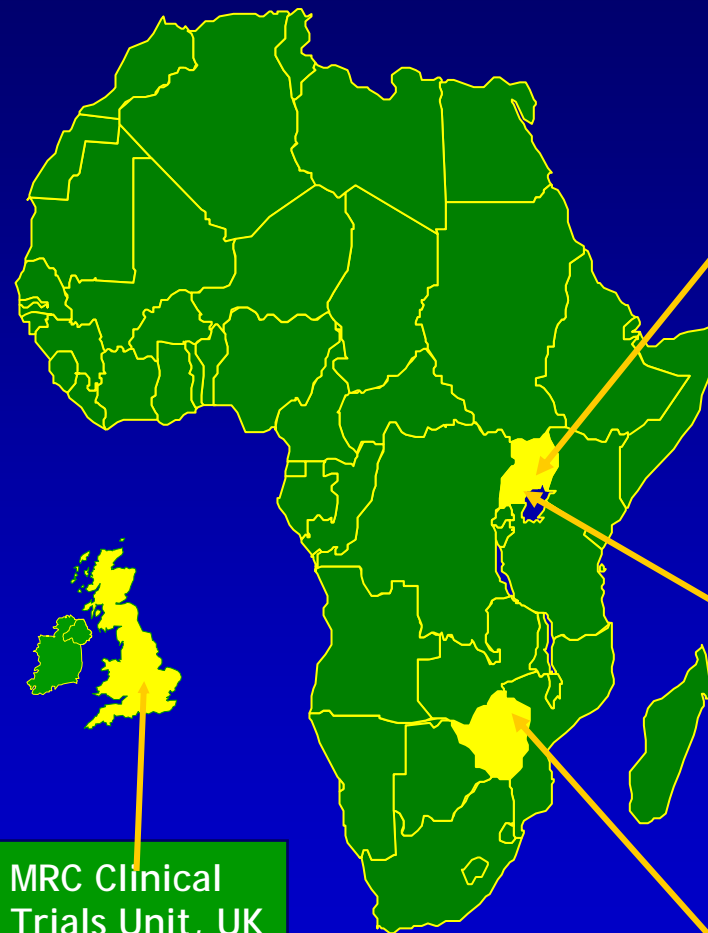
## Support:

MRC, UK

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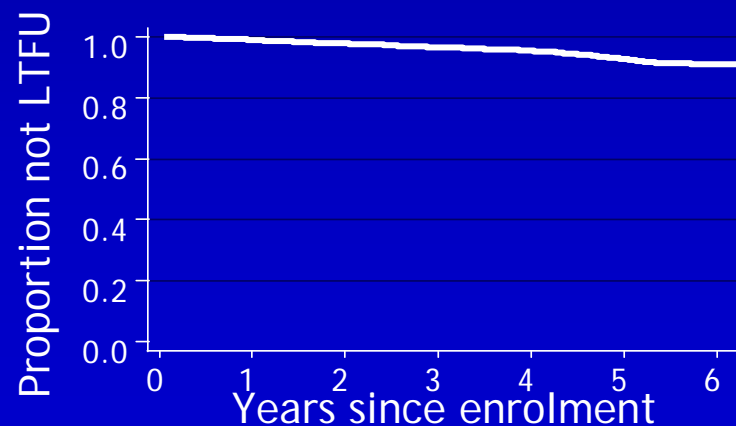
Imperial  
College, UK



# Research infrastructure



- Local trial centres and databases
- Local independent trial monitors
- Superb participant retention
  - 7% lost to follow-up at 5 yrs



# Capacity development



- IT, pharmacy, laboratory development
- Training & mentoring
  - clinicians, nurses, counsellors
  - pharmacists
  - trial & data managers
  - statisticians
  - health economists
- Masters in Biostatistics (3), Epidemiology (1); PhDs in Biostatistics (1), Epidemiology (1)

[www.ctu.mrc.ac.uk/dart](http://www.ctu.mrc.ac.uk/dart)



# Community involvement



- Partnership with the DART participant community
  - annual participant days
- Grassroots community activism from clinic “days”
  - encouragement for adherence
  - micro-economic projects
  - family support groups
- Advocacy for prevention and against stigma led by DART participants





## What have we learnt? (II)

DART results provide evidence to  
inform ART policy & delivery





# Overall results



*Overall survival at 5 years in 3316 participants with advanced HIV disease pre-ART was excellent (CDM 87%, LCM 90%)*

- Retention was very high
- Survival was better than predicted, given advanced disease stage at enrolment
  - emphasises the importance of excellent clinical care including access to concomitant medications & diagnostics
- ART can be given wherever people live: next steps
  - widening distribution of drugs
  - focussing resources on strengthening healthcare systems and training HCWs to deliver life-saving treatment
    - benefits health infrastructure for everyone



# Toxicity monitoring



*Routine laboratory monitoring for toxicity did not impact adverse events or substitutions in first-line*

- Differences between arms are driven by HIV events
- More tests done in LCM
  - routine monitoring does not prevent extra tests being requested
- Routine laboratory tests for toxicity were the most costly part of ART provision in DART
- Laboratories are still needed
  - eg screening; diagnosis and management of acute illnesses



# CD4 monitoring

*12-weekly CD4 monitoring had no impact on disease progression during the first 2 years on ART: after this, a small impact on clinical disease progression appeared to be driven by later switch to second-line in CDM*

- **Targeted CD4 monitoring from the 2<sup>nd</sup> year on ART may be clinically useful for decisions about switching ART**
  - further research is needed to explore
    - the minimum frequency of CD4 monitoring required
    - the impact of different switching criteria
  - those initiating ART with higher CD4 counts may be able to defer CD4 monitoring for longer than 12-18 months
  - economic considerations are important for implementation
    - e.g. availability of cheaper and simpler CD4 monitoring tests



# Cost-effectiveness



- Cost per life-year gained of **\$9,016** in **LCM arm**
  - 7-fold higher than WHO/CMH threshold for cost-effectiveness
- Finances are limited and priorities need to be set
  - e.g. balancing resource use to monitor patients on ART versus initiating more patients on therapy
- For CD4 monitoring to be cost effective, the cost needs to fall below **\$3.80**



# What have we learnt? (III)

The wider context



# Survival





# Resource allocation



- 6.7 million adults and children in Sub-Saharan Africa were estimated to need ART in December 2007
  - only 2.2 million were receiving ART
- Global economic crisis is threatening programme funding
- Using DART to help resource allocation
  - **what could be achieved in an ART programme with \$1,000,000 over 5 years...**

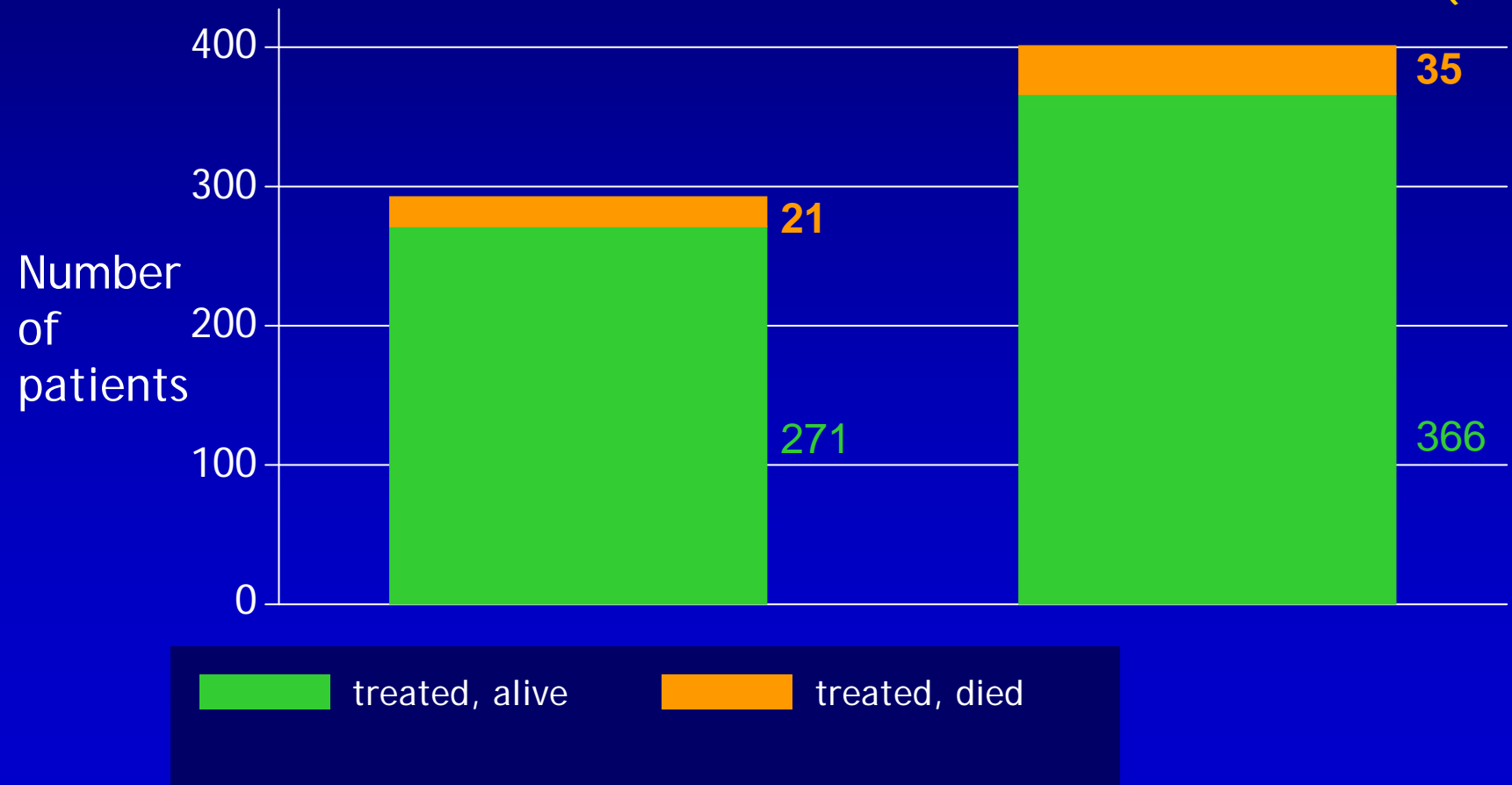


# For \$1,000,000 over 5 years

Mean cost/patient: LCM \$3,425, CDM \$2,493

LCM: TREAT 292

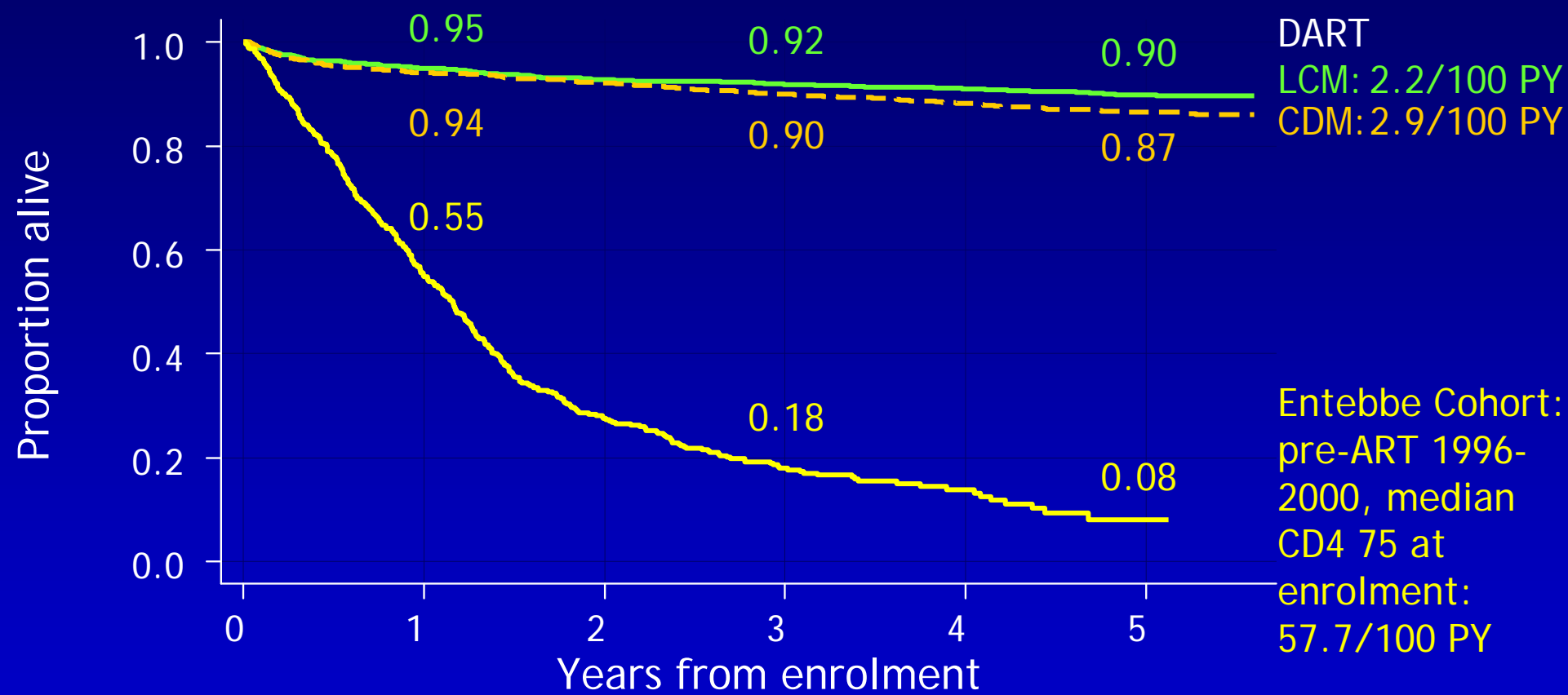
CDM: TREAT 401 (extra 109)







# Survival



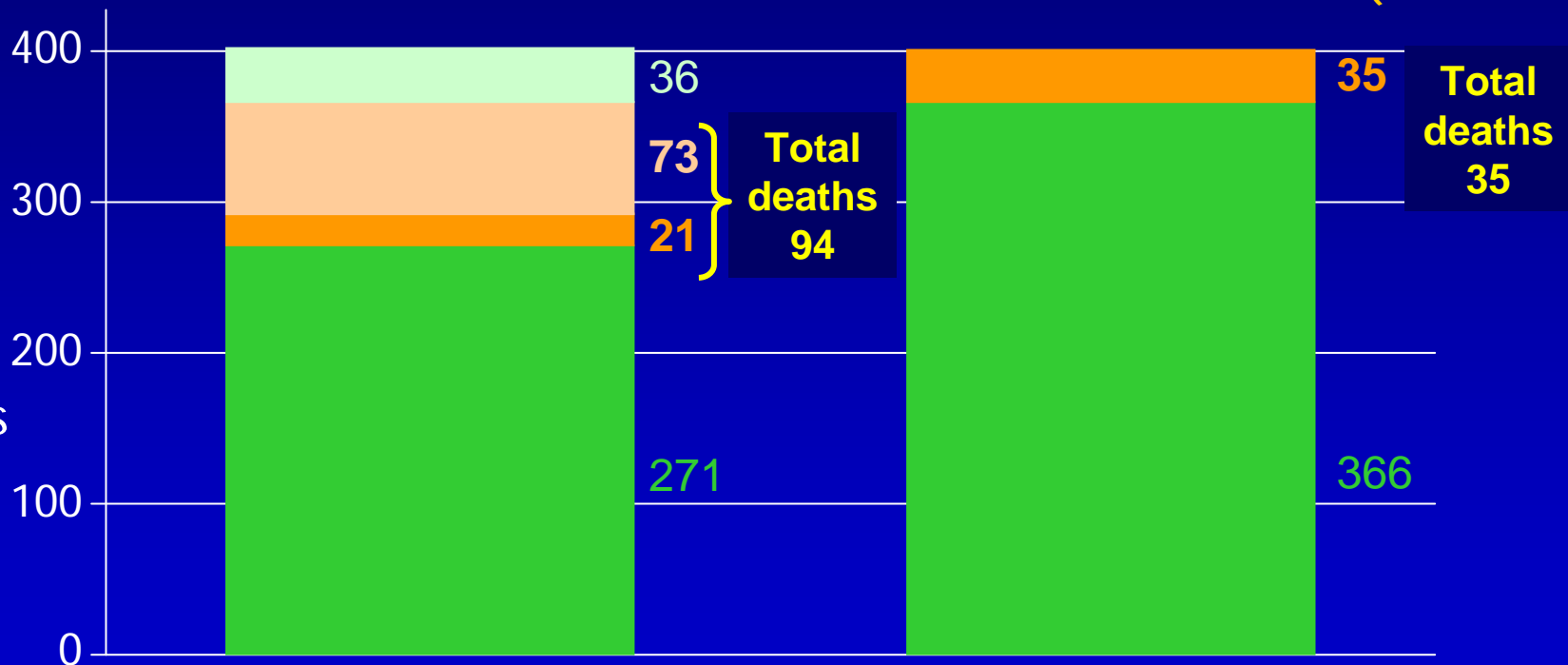


# For \$1,000,000 over 5 years

Mean cost/patient: LCM \$3,425, CDM \$2,493

LCM: TREAT 292

CDM: TREAT 401 (extra 109)



■ treated, alive      ■ treated, died  
■ not treated, died      ■ not treated, alive

← from Entebbe Cohort data



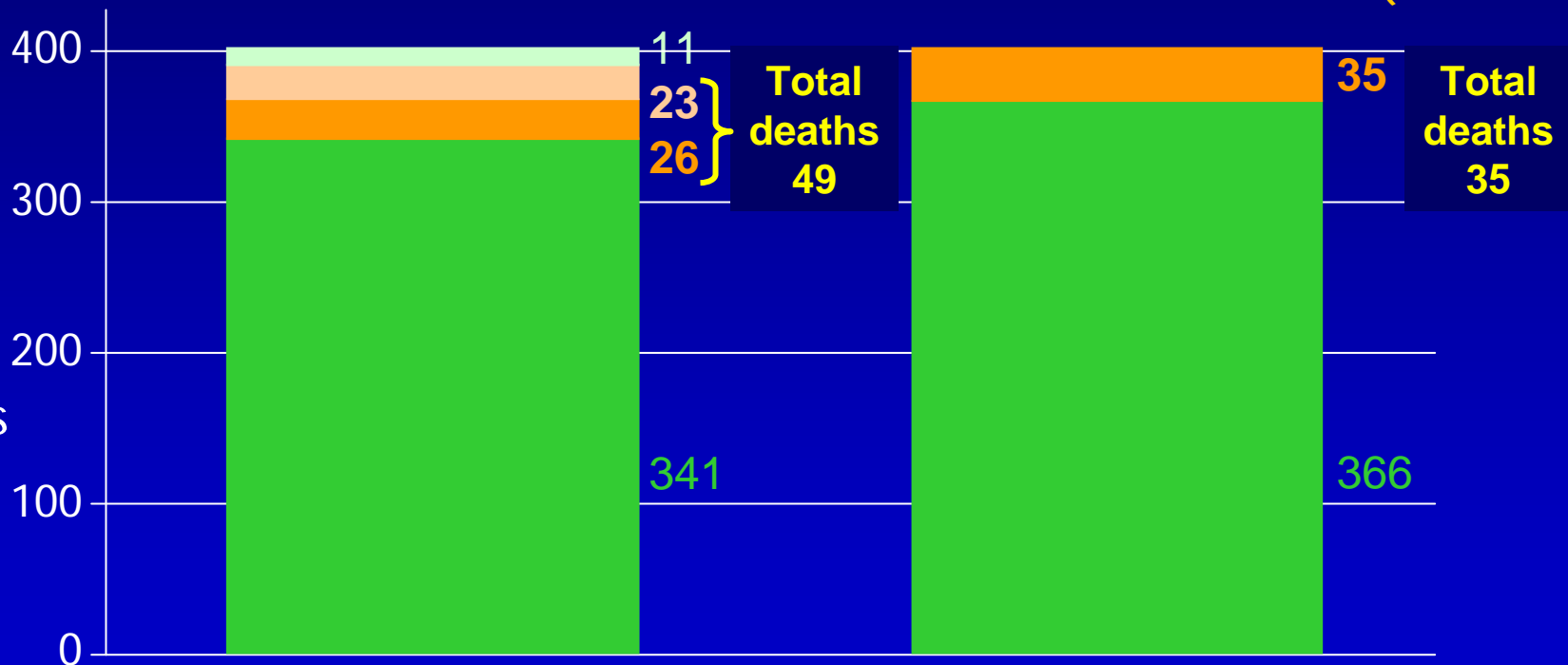
# Excluding routine toxicity tests in LCM



Mean cost/patient: LCM \$2,726, CDM \$2,493

LCM: TREAT 367

CDM: TREAT 401 (extra 34)



Legend:  
■ treated, alive  
■ treated, died  
■ not treated, died  
■ not treated, alive

← from Entebbe Cohort data



# Other aspects of healthcare delivery



- DART focused on the contribution of **routine laboratory testing** to benefits and costs of ART provision
- However, other aspects of service delivery are also key to sustainability, benefits and costs
  - local health centre vs hospital based service provision  
**the JINJA trial [MOAD101]**
  - nurse vs doctor led service provision  
**the CIPRA-SA-1 trial [http://www.cipra-sa.com/project1.asp]**



# Conclusion



- DART provides clear evidence to help governments and policymakers determine priorities for ART programmes
- DART adds to the evidence base for ART in Africa in ways beyond those originally anticipated
- DART created highly skilled teams of ART clinical trialists and centres of ART and research excellence in Uganda and Zimbabwe
- Partnerships have been developed, additional resources leveraged and a broader scientific agenda realised



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