



The Development of AntiRetroviral Therapy in Africa (DART) trial

What have we learnt?

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What have we learnt? (I)

A trial provides an excellent way to build partnerships and teams



DART partners

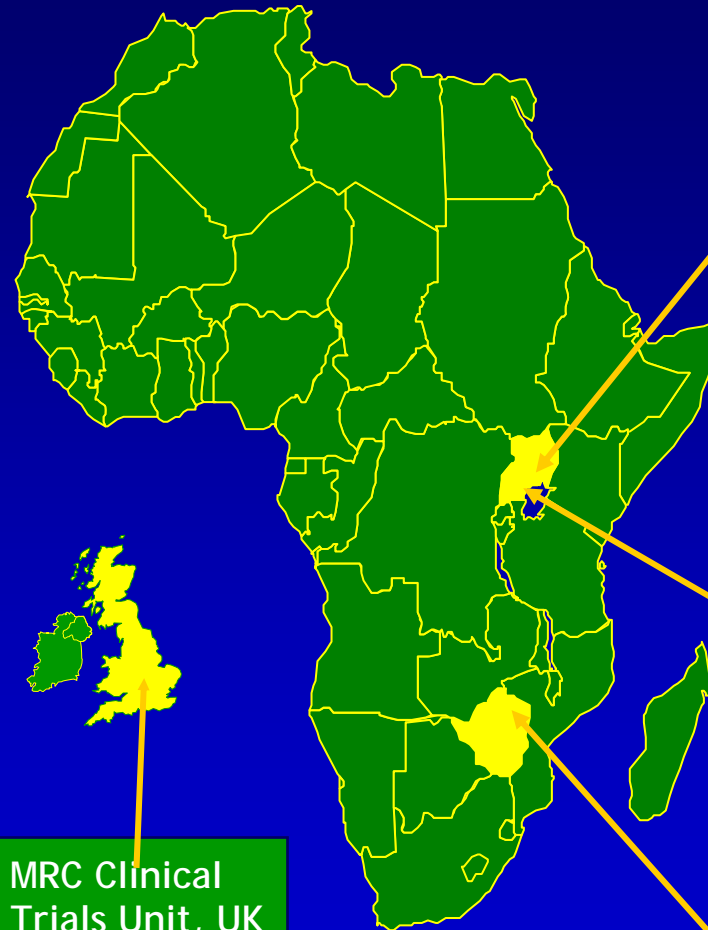
Support:

MRC, UK

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Joint Clinical Research
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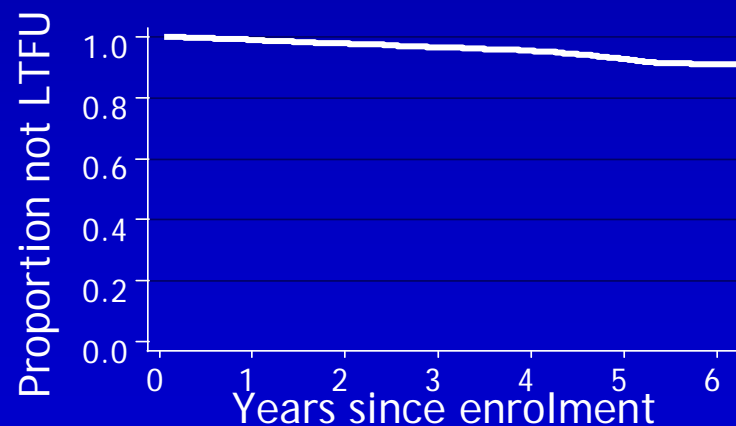
MRC Clinical
Trials Unit, UK

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



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 2nd 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...**

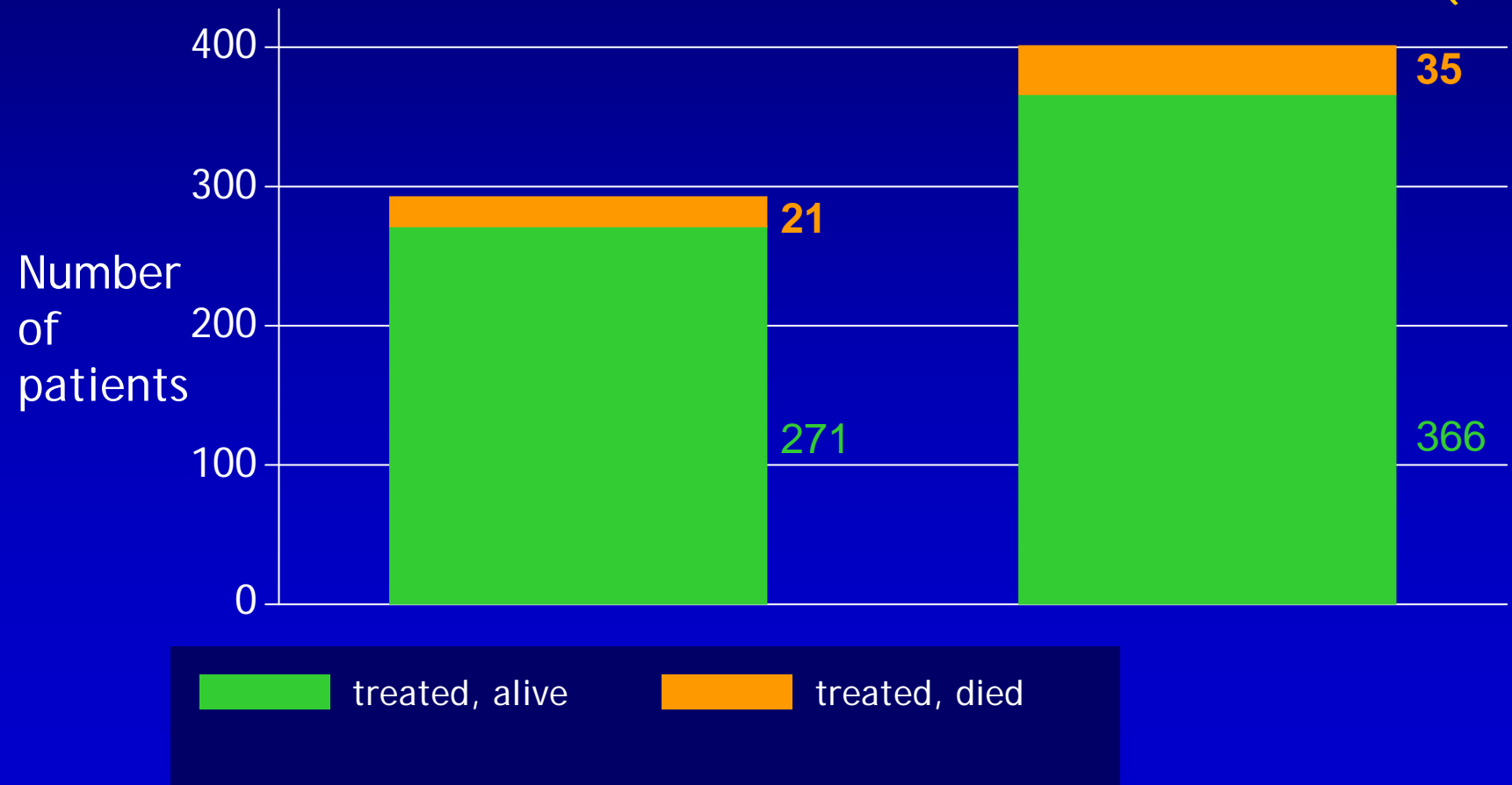


For \$1,000,000 over 5 years

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

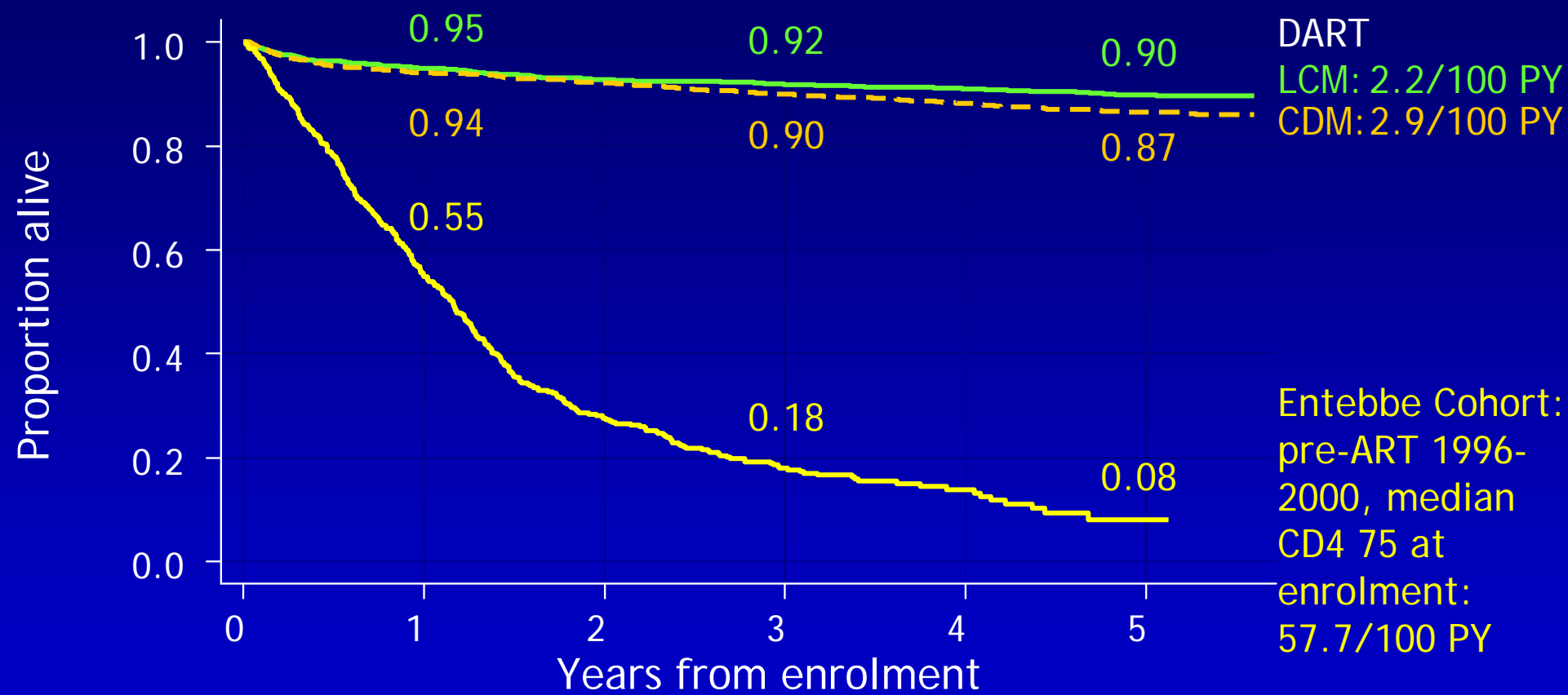
LCM: TREAT 292

CDM: TREAT 401 (extra 109)





Survival



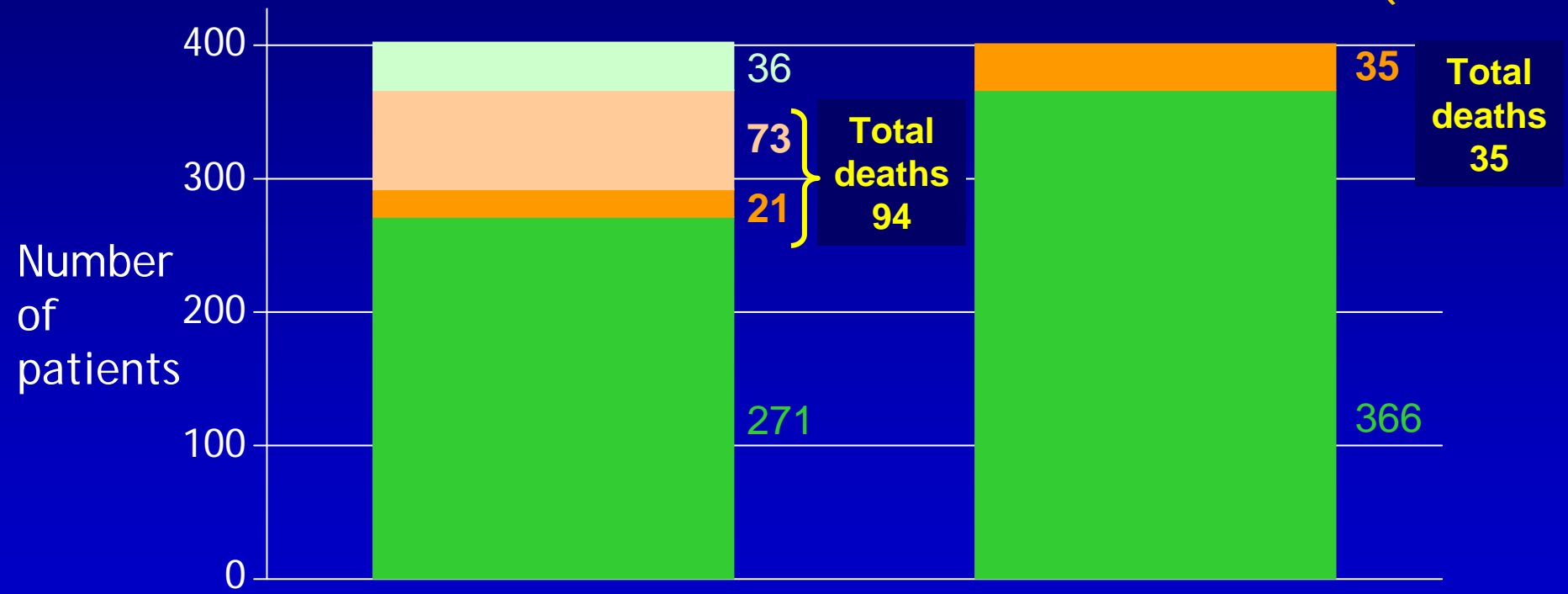


For \$1,000,000 over 5 years

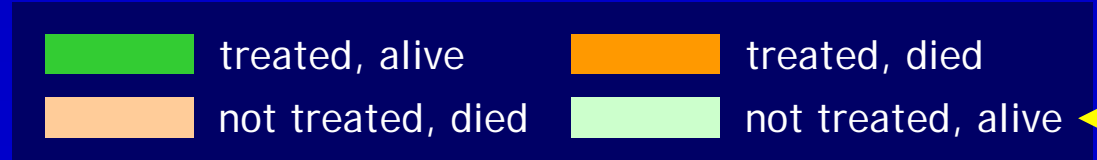
Mean cost/patient: LCM \$3,425, CDM \$2,493

LCM: TREAT 292

CDM: TREAT 401 (extra 109)



Number of patients



← from Entebbe Cohort data



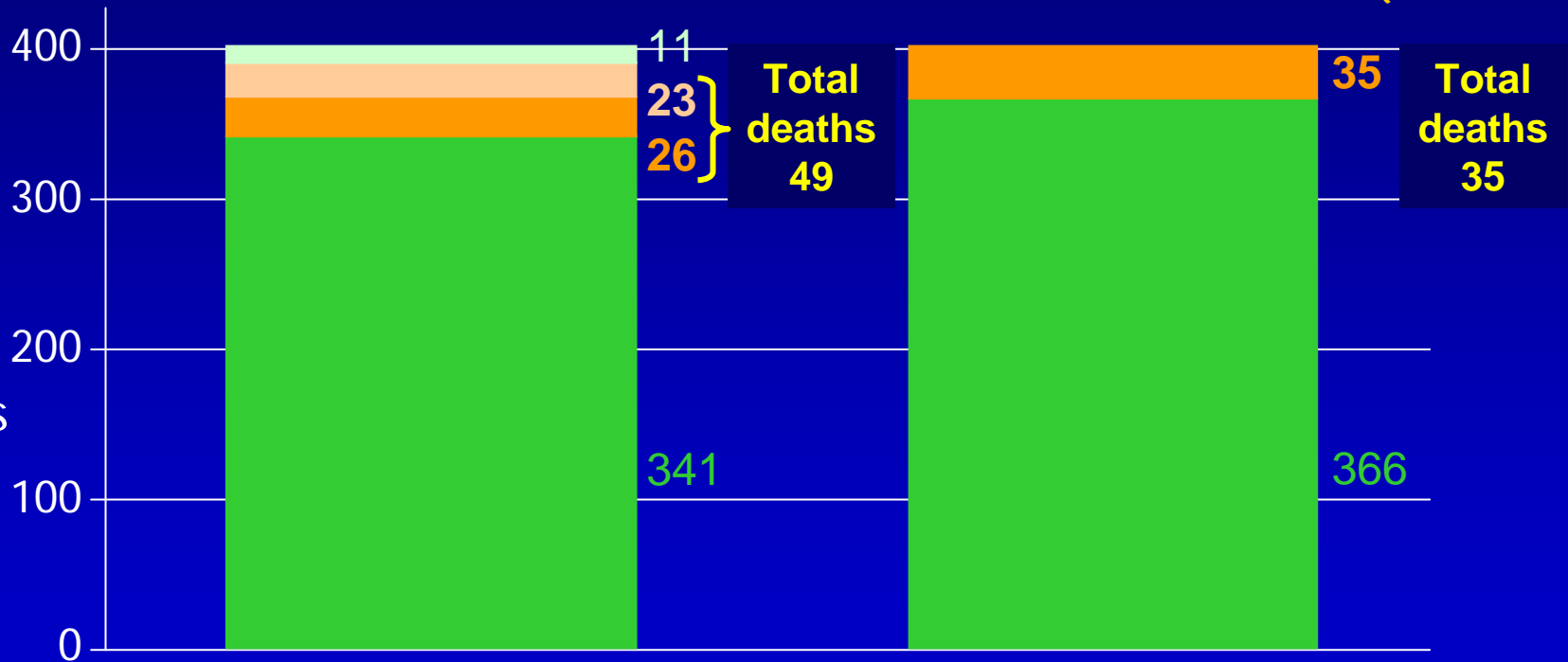
Excluding routine toxicity tests in LCM



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

LCM: TREAT 367

CDM: TREAT 401 (extra 34)



■ 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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