



# Acceptability of a Structured Treatment Interruption (STI) strategy of 12 week cycles on and off ART in patients in the DART trial

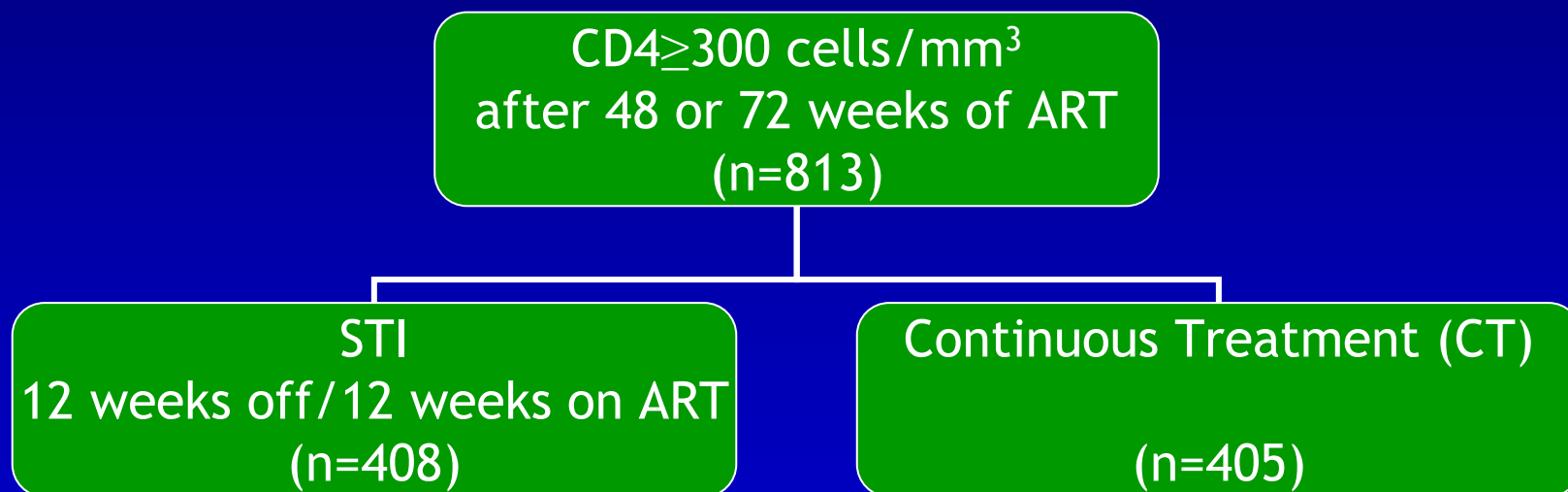
D Tumukunde, G Lillian, S Mutsai, R Nalumenya, J  
Komunyena, D Nsibambi, J Machingura, A Burke  
on behalf of the **DART** Trial Team



# Background: STI trial design within DART

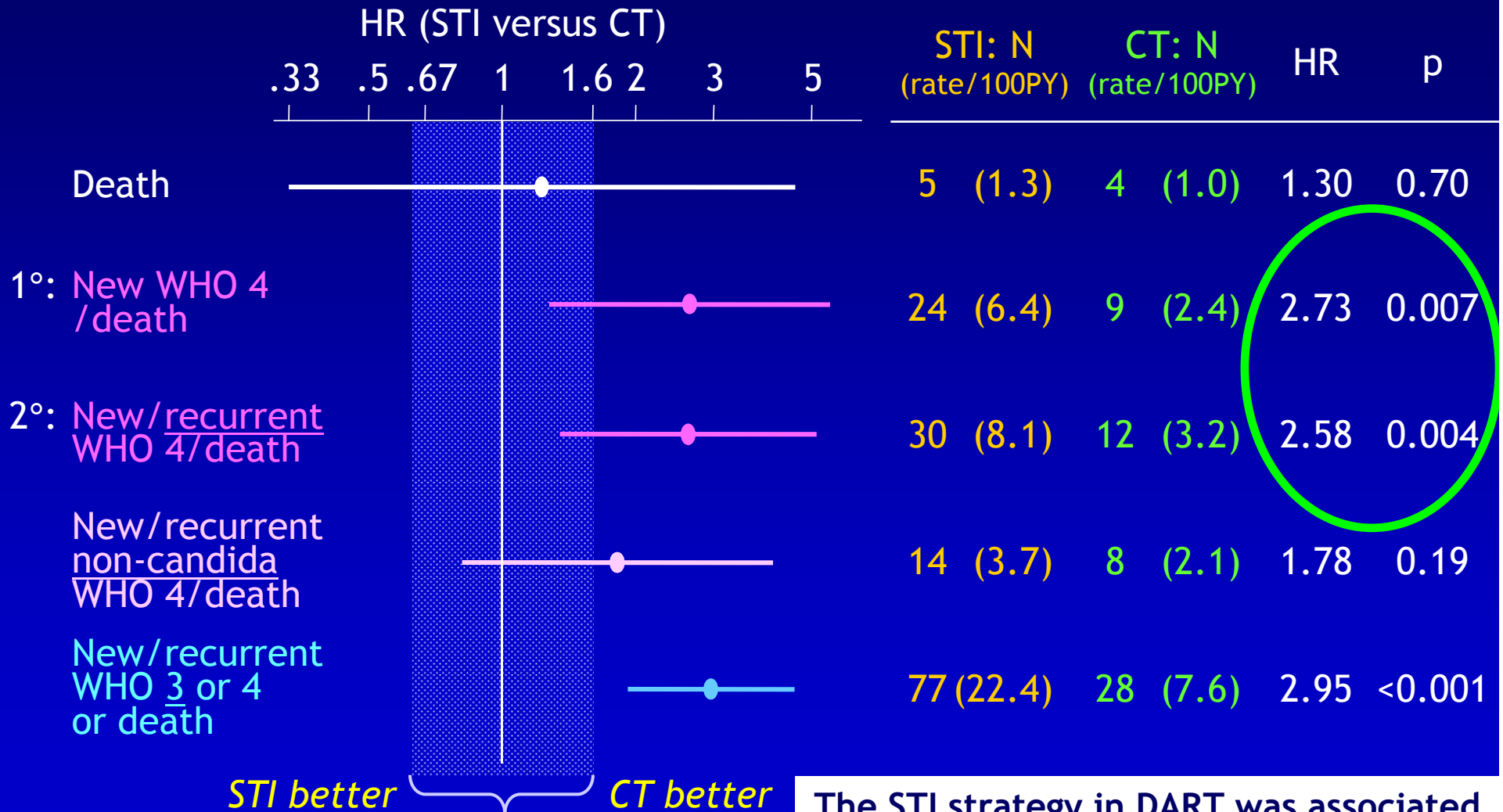


- A second randomisation in a subset of the total 3316 patients in the Development of AntiRetroviral Therapy in Africa (DART) trial, initiated in July 2004



Following 2nd DSMC review in March 2006 (data to Jan 2006) the STI/CT randomisation was terminated on 15 March 2006 (median follow-up 51 weeks). All patients were moved to continuous therapy.

# Background: Summary of clinical outcomes



The STI strategy in DART was associated with a more than 2 fold increased rate of clinical WHO stage 4 events



# Objective and design



- To explore participants perceptions of the fixed cycle STI strategy evaluated in DART
  - using a structured cross-sectional questionnaire completed with a counsellor soon after closure of STI study
- To relate perceptions to key factors using multivariable ordinal/logistic regression
  - sex, centre
  - factors related to the strategy
    - weeks of continuous ART before 1st interruption
    - number of STIs completed
    - weeks since last interruption
    - ever restarted ART early for symptoms
    - experienced WHO 3 or 4 events

# Data completeness

Randomised to STI  
n=408

median age 37 (range 21-67) years  
median CD4 357 (range 300-1054) cells/mm<sup>3</sup>

Questionnaires not requested  
n=17

5 died before 15 March 2006  
7 lost to follow-up before 15 March 2006  
2 never interrupted (wrong allocation given to clinic)  
3 received <3 weeks STI

Questionnaires requested  
n=391

Questionnaires completed  
n=361 (92%)

- response rate 82% to 98% across centres  
- missing individual items in <2%

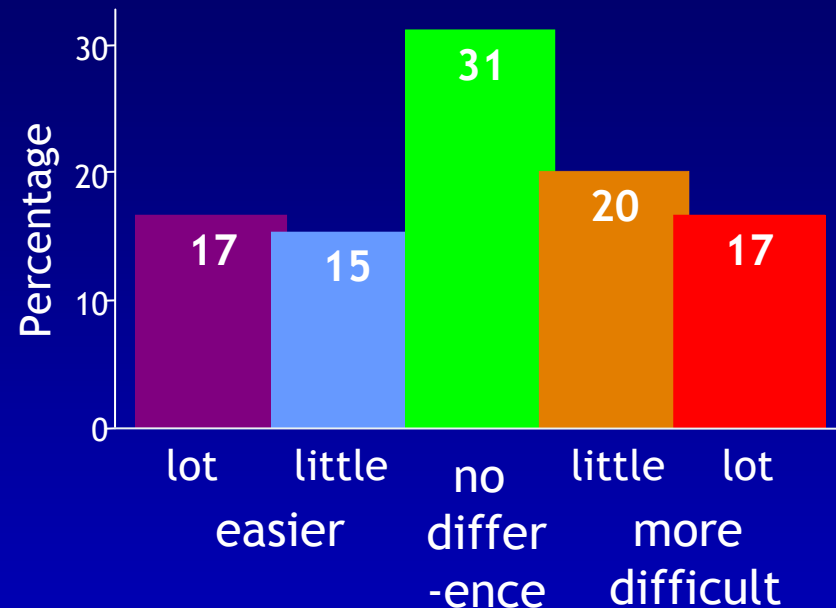


# Characteristics of those who completed questionnaires



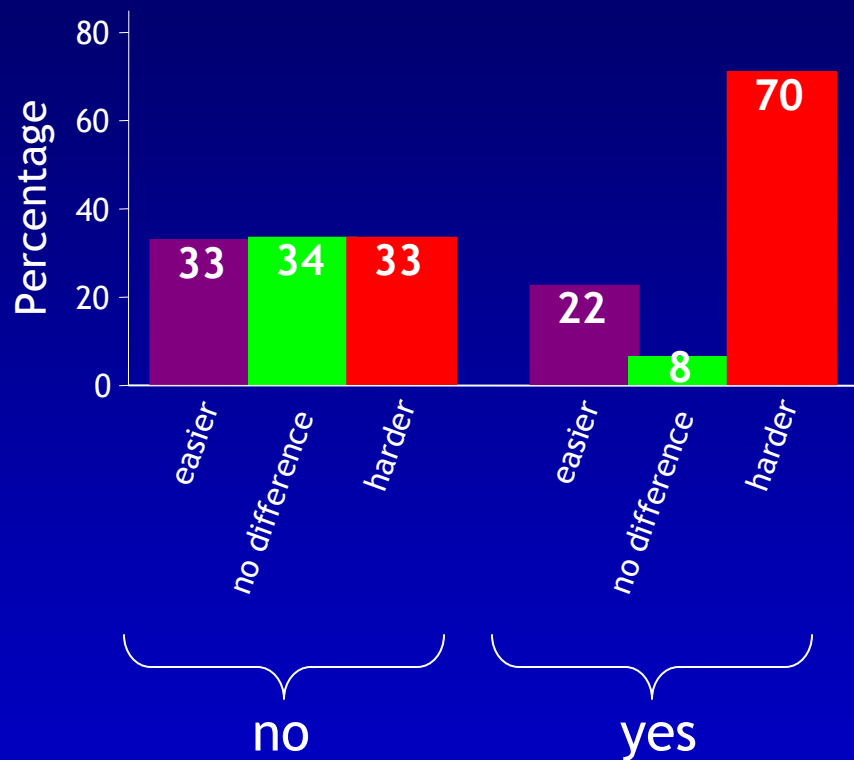
		(n=361)	
Women		265	(73%)
Centre	Entebbe (Uganda)	141	(39%)
	JCRC (Uganda)	77	(21%)
	AA (Uganda)	18	(5%)
	Harare (Zimbabwe)	125	(35%)
Weeks of continuous ART before 1st STI	52	222	(62%)
	76	139	(38%)
Weeks since last interruption when questionnaire completed	<12	136	(38%)
	12 to <24	145	(40%)
	24 or more	80	(22%)
# STI cycles	1	73	(20%)
	2	132	(37%)
	3 or 4	156	(43%)
Ever restarted ART early for symptoms/low CD4		31	(9%)
New/recurrent WHO 4 event		23	(6%)

"Compared to when you were taking medicines all the time, did stopping medicines make things for you?"

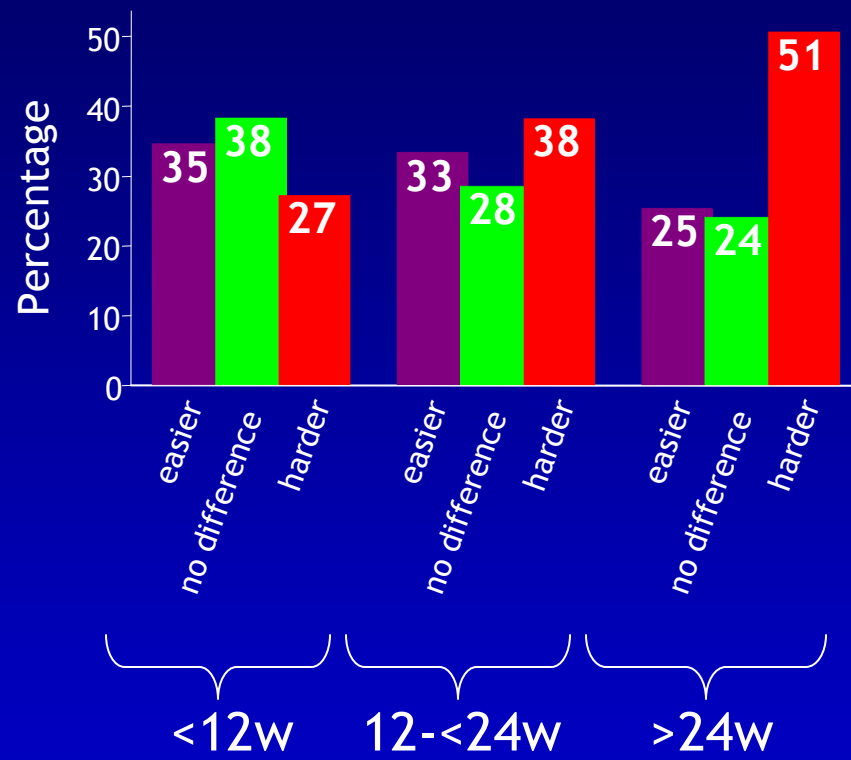


- 32% a little/lot easier, 37% a little/lot harder, 31% no difference
- participants reported STIs made things harder
  - if they had had to restart ART early or had WHO 4 events ( $p=0.02$ )
  - the longer since they last interrupted ( $p=0.02$ )
  - if they had 76 weeks continuous ART before STIs ( $p=0.04$ )

# Effect of STIs on participant's lives



Had to restart ART early during STI or had WHO 4 events



Weeks since last interrupted ART

Note: independent effects on multivariable regression





# Problems restarting ART



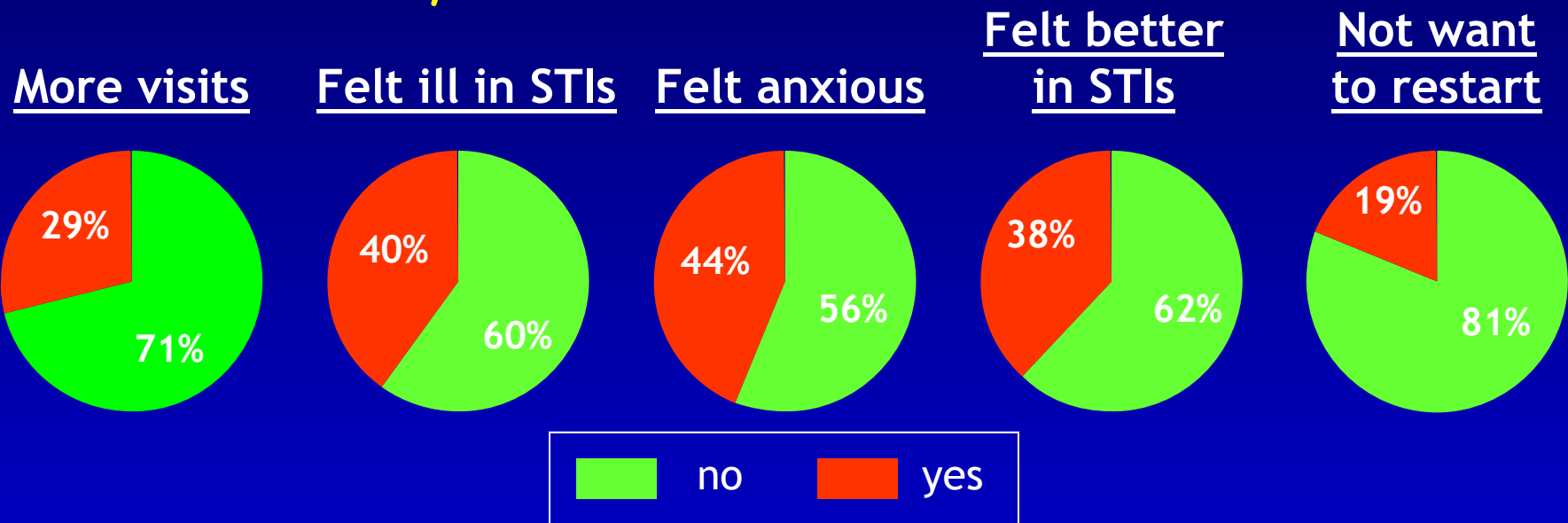
“Were any of the following a problem with antiretroviral drugs after re-starting them?”

	Never/ Rarely	Sometimes/ Frequently
Remembering	8%	92%
Timing	12%	88%
Taste	12%	88%
Side-effects	26%	74%

- participants who had interrupted most recently reported
  - fewer problems remembering to take ART (p=0.05)
  - more problems with side effects (p=0.05) after restarting

# What happened during the study?

"Did any of the following occur while you were participating in the STI study?"



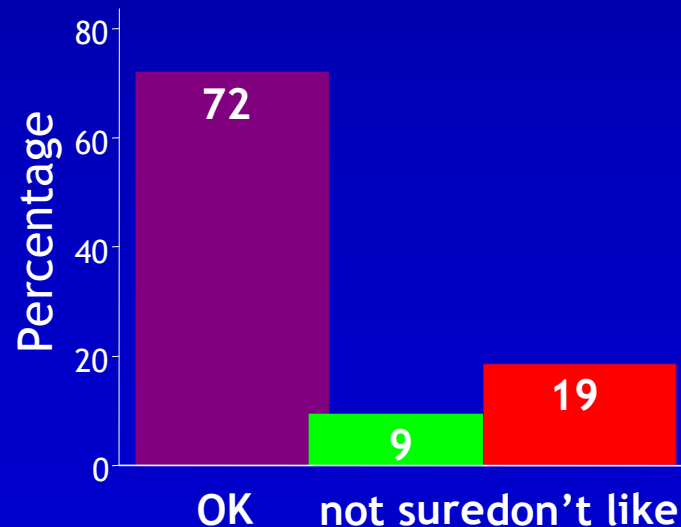
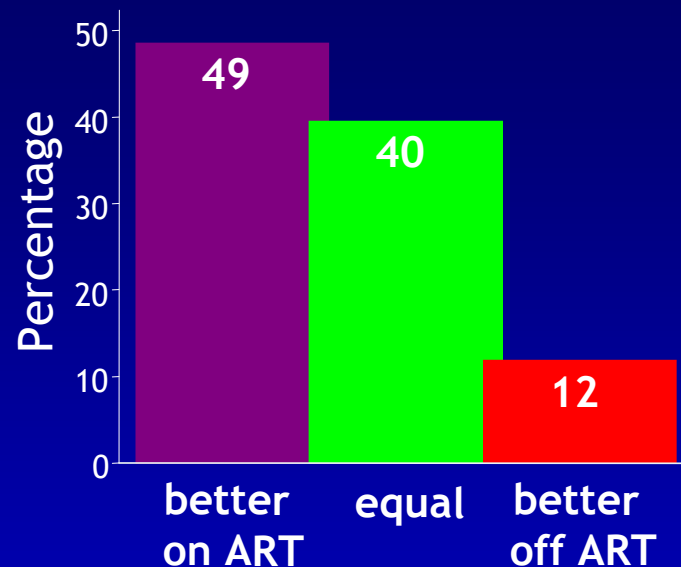
- as expected, patients with WHO 3 or 4 events or who had to restart ART early for symptoms had more negative experience of STI across all questions
- participants who had interrupted >24 weeks ago ( $p=0.04$ ) or who had 76 weeks continuous ART ( $p=0.03$ ) were more likely to report feeling ill
- participants with 3 or more STIs were less likely to report more visits ( $p=0.02$ )

"Overall, how did you feel whilst you were on and off medicines?"

*participants who had interrupted less recently were more likely to report feeling better on ( $p=0.02$ )*

"How do you feel about taking medicines without stopping for the rest of your life?"

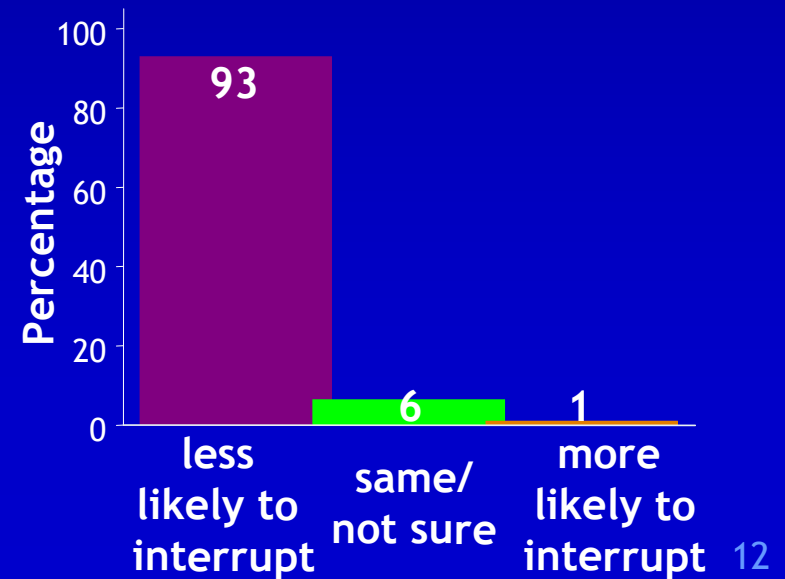
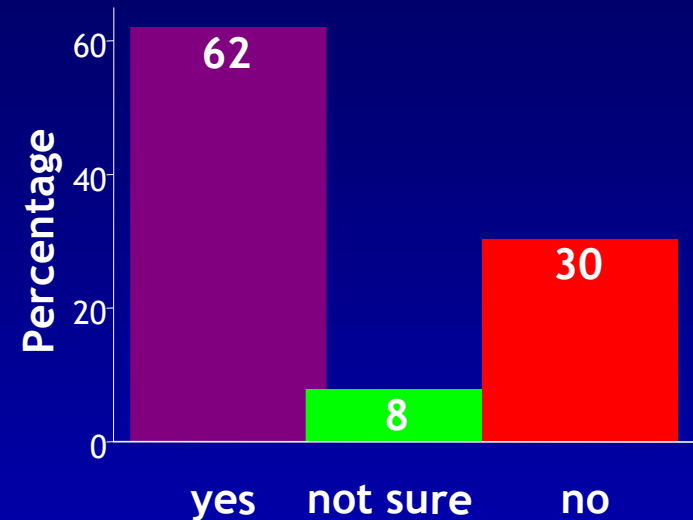
*participants who had interrupted less recently were more likely to report feeling OK with ART for life ( $p=0.01$ )*



“Would you agree to planned interruptions of ART under medical supervision in the future?”

*participants who had done 2 or 3 cycles were more likely to say yes ( $p=0.01$ )*  
*participants with WHO 4/restarted early more likely to say no ( $p=0.02$ )*

“People sometimes make a choice to stop medicines themselves for a while (a drug holiday) but against their doctor’s advice. Compared with before the STI study, are you now”





# Predictors (see poster)



- as expected, those with WHO 3/4 events or restarted ART early for symptoms had negative experiences of STI
- generally more negative experiences of STI in
  - those who were last off ART >24 weeks ago (but fewer reported problems with side-effects?)
    - ? recall bias, changing perceptions over time, feeling better about ART after being back on it for longer
  - those starting STIs after 76 weeks of continuous therapy
    - ? more used to being on ART before stopping
- generally more positive experiences of STI in
  - those who had 3 or 4 STI cycles
    - ? familiarity with strategy, survivorship effect



# Qualitative comments



- volunteered symptoms off ART (mostly stage 2)
  - fever, skin rashes, sores, mouth ulcers, appetite loss, weakness/fatigue
- volunteered symptoms restarting ART
  - nausea, appetite loss, weakness, headache, rash
- problems with STI reported at different stages
  - first STI only, first 4 weeks off ART, last 4 weeks off ART, restarting ART
- anxiety expressed about stopping and restarting ART
- fears
  - toxicity, body getting used to drugs
  - drug supplies running out
  - resistance, CD4 dropping, VL increasing
- comments about personal freedom with STI
  - inconvenience of taking drugs, no need to remember, less bother, easier to travel, time to think about other things
- happy not to stop any more as healthier/safer/used to CT
- trust in study doctors



# Conclusions



- Around 40% patients reported problems with STIs
  - more likely those with WHO 3 or 4 events during the study, needing to restart ART early during STI, 76 weeks continuous therapy before STI, and last STI >24 weeks ago
- Around 30% did not have a preference
- A sizeable minority (~30%) perceived some advantages of fixed cycle STIs
  - more likely those who had been through more cycles of STIs
  - supported by qualitative comments
  - few said they would interrupt STI against medical advice
- **Although the STI strategy in DART cannot be recommended, identification of predictors of poor response to STI and strategies with lower risks remains important**

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- **Trial Steering Committee:** I Weller (Chair), A Babiker (Trial Statistician), S Bahendeka, M Bassett, A Chogo Wapakhabulo, J Darbyshire, B Gazzard, C Gilks, H Grosskurth, J Hakim, A Latif, C Maposhere, O Mugurungi, P Mugenyi; Observers J Leith, E Loeliger, P Naidoo, M Palmer, J Rooney, J-M Steens.
- **Data and Safety Monitoring Committee:** A McLaren (Chair), C Hill, J Matenga, A Pozniak, D Serwadda
- **Endpoint Review Committee:** T Peto (Chair), A Palfreeman, M Borok, E Katabira.
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