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A 5-year comparison of viral load and CD4 cell count monitoring for ART patients in rural Uganda

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Background

- The Home-Based AIDS Care (HBAC) project was a clinical trial which found no difference in clinical outcomes between participants who were randomized to viral load (VL) monitoring and CD4 cell count monitoring in comparison to CD4 cell count monitoring alone after 3 years of follow-up.
- We further report on clinical outcomes from this study with an additional 2 years of follow-up.

Methods

- Beginning in May 2004, HIV-infected members of The AIDS Support Organisation (TASO) - Tororo with a CD4 count of <250 cells/mm^3 or WHO Stage 3 or 4 disease were offered ART and randomized to one of three monitoring groups:
  - Arm A) Clinical monitoring and quarterly CD4 cell counts and VL;
  - Arm B) Clinical monitoring and quarterly CD4 cell counts; or
  - Arm C) Clinical monitoring alone.
- Field workers delivered ART to participants' homes and collected data to monitor potential toxicity, morbidity and mortality.
- **In April 2007**, following analysis of the first phase of the study which demonstrated that Arm C participants were at increased risk for death and/or new opportunistic infections (OIs); These individuals were **re-randomized to Arms A or B** and all participants were followed until March 31, 2009.
- We conducted bivariate analyses of clinical and demographic characteristics of study participants in the remaining two arms and used Cox Proportional Hazard models to determine if study arm was independently associated with the development of OIs or death.
- We examined the proportion of individuals in each arm who ever had a VL VL ≥500 copies/ mL after 6 months from enrollment or re-randomization and calculated the relative risk
- All regression models were adjusted for differences in baseline Age, CD4 cell count, viral load, BMI and gender. Clinical events prior to re-randomization in Arm C patients were not included in this analysis.

Results

- A total of 1012 participants (73.7% female) were randomized to one of the 3 original study arms. 316 survivors from Arm C were re-randomized to Arms A and B. The median age was 38 years and the median CD4 cell count at enrollment was 134 cells/ mm3.

Table 1: Bivariate analysis of participant characteristics at enrollment or re-randomization

	ALL		Viral load arm		CD4 arm		
Variable	N	%	n	%	n	%	p-value
Sex							
F	813	72.7	410	73.0	403	72.4	0.821
M	306	27.3	152	27.0	154	27.6	
Baseline CD4							
<50	197	17.7	97	17.3	100	18.0	0.850
50 - 200	649	58.2	324	57.9	325	58.6	
>200	269	24.1	139	24.8	130	23.4	
Baseline viral load							
<1000	36	3.3	17	3.1	19	3.5	0.369
1,000-9,999	48	4.4	29	5.2	19	3.5	
10,000-99,999	311	28.2	148	26.7	163	29.7	
>=100,000	708	64.2	361	65.0	347	63.3	
Baseline BMI							
<18.5	302	27.7	149	27.3	153	28.0	0.347
18.5-24.9	717	65.7	353	64.7	364	66.7	
25-29.9	53	4.9	32	5.9	21	3.8	
>=30	20	1.8	12	2.2	8	1.5	

Table 2 : Cox proportional hazards analysis of time to first OI or death

Arm	# people	# Events	Person years	Rate per 100 pyrs	Hazard Ratio (95% CI) ‡	p_value
Original Viral load and CD4 arms						
Viral load arm	397	55	1872.9	2.9	ref.	
CD4 arm	391	54	1864.7	2.9	1.1 (0.74 to 1.62)	0.640
Re-randomized from Clinical arm						
Viral load arm	165	9	431.8	2.1	ref.	
CD4 arm	166	10	437.0	2.3	1.1 (0.41 to 2.72)	0.906
All combined						
Viral load arm	562	64	2304.7	2.8	ref.	
CD4 arm	557	64	2301.7	2.8	1.1 (0.75 to 1.54)	0.687

Results (continued)

- There were no significant differences in clinical or sociodemographic characteristics between two groups at randomization or re-randomization (Table 1).
- 509 individuals were followed in Arm A/C and the 503 in Arm B/C for a median of 4.4 years of follow-up. Over the entire length of the study, 38 deaths and 20 new OIs occurred in Arm A patients and 36 deaths and 21 new OIs occurred in Arm B patients.
- Randomization to Arm B was not associated with the risk for new OIs or death (adjusted hazard ratio [AHR] = 1.03; 95% CI 0.75 - 1.43). We also found no effect on randomization when we excluded the original Arm C patients (AHR = 0.97; 95% CI 0.68 - 1.39).

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Table 3: Participants with at least one VL ≥500 copies/ mL after 6 months from enrollment or re-randomization

				Relative Risk	
Arm	# people	n	%	(95% CI) ‡	p-value
Original Viral load and CD4 arms					
Viral load arm	385	61	15.8		
CD4 arm	377	81	21.5	1.40 (0.96 to 2.05)	0.080
Re-randomized from Clinical arm					
Viral load arm	165	19	11.5		
CD4 arm	166	21	12.7	1.06 (0.53 to 2.10)	0.876
All combined					
Viral load arm	550	80	14.5		
CD4 arm	543	102	18.8	1.32 (0.95 to 1.83)	0.102

Conclusions

- We found no differences in clinical outcomes associated with the addition of quarterly VL monitoring to quarterly CD4 cell count monitoring.
- These data continue to support expanding access to ART in resource-limited settings, irrespective of the availability of VL testing.

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