A Streamlined ART Initiation Algorithm of Care Reduces Time to ART Initiation

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Background

Over the last two decades combination antiretroviral therapy (ART) has markedly reduced HIV associated morbidity and mortality (1) and the benefits of early ART initiation that include delayed HIV associated events has been shown (2). However, multi-step ART initiation algorithms that include pre-treatment counseling, clinical and laboratory assessment may result in loss of patients between eligibility and treatment, thus eroding gains towards achieving the 90-90-90 targets. Although individual randomized trials show improved outcomes with accelerated ART initiation, the success of accelerated ART practices in real world settings is less understood. We evaluated a revised ART initiation approach based on same-day readiness assessment and point of care CD4 assessment, among public facilities in Zambia as compared to standard of care (SOC) procedures including three pre-treatment counseling sessions.

Methods

- **Setting:** Public health clinics supported by Centre for Infectious Disease Research in Zambia (CIDRZ), a Zambian non-governmental organisation that supports HIV care and treatment services at a network of 64 clinics across 4 of 10 provinces in Zambia.
- **Population:** The rapid treatment approach was implemented between March and July 2016 in two rural and two urban health facilities and assessed against 5 comparator facilities practicing standard of care (SOC) among ART naïve, treatment eligible patients and followed up for 12 months.
- **Measurements:** Demographic information was obtained from medical record abstraction. Key timeline elements including ART eligibility and ART initiation dates were established by record review. ART eligibility date was determined by laboratory record review (CD4 cell count < 500), pregnancy, WHO staging, and tuberculosis diagnosis record. ART Initiation date was established at first ARV pick-up in the pharmacy record.
- **Analysis:**
  - The primary outcome was time to ART initiation by end of follow up. We summarized background characteristics using proportions for categorical variables and median for continuous variables.
  - We used Pearson's chi-squared test to assess imbalance of background characteristics between control and intervention groups; two-sample Wilcoxon rank-sum test was used to compare median between the two groups.
  - Kaplan-Meier method was used to estimate the fraction of patients who initiated ART in both groups. Logrank test was used to compare the Kaplan-Meier estimates between the two groups. Patients who did not initiate ART were censored at 1 year of follow up.
  - We estimated the average treatment effect on time-to-ART initiation using survival-time inverse-probability-weighted regression adjustment models -the mean survival time was modeled as Weibull, controlling for sex, age at enrolment and level of education; the treatment assignment was modeled as logit with covariates sex, age at enrolment, education, and WHO stage. All analyses were performed using Stata 15 MP (StataCorp, College Station, TX, USA).

Results

Table 1: Background characteristics of patients who became eligible in study window by groups

Characteristics	Control Number of patients (% of total) n=1454	Intervention Number of patients (% of total) n=358	Pearson chi2 p-value
Sex			
Female	894 (61)	195 (54)	0.001
Male	420 (29)	139 (39)	
Age group (Years)			
Median (IQR)	33 (27, 41)	36 (29, 43)	0.003*
14-19	48 (3)	5 (1)	
20-24	156 (11)	36 (10)	0.055
25-34	499 (34)	115 (32)	
35+	611 (42)	178 (50)	
Marital status			
Married	632 (43)	179 (50)	0.861
Single/Divorced/Widowed	393 (27)	114 (32)	
Level of education			
None	140 (10)	22 (6)	0.023
Primary	326 (22)	97 (27)	
Secondary+	617 (42)	186 (52)	
Household income (Kwacha) per month			
<2000	255 (18)	167 (47)	0.171
2000+	47 (3)	21 (6)	
WHO stage			
Stage 1	830 (57)	234 (65)	0.012
Stage 2	135 (9)	23 (6)	
Stage 3	148 (10)	22 (6)	
Stage 4	22 (2)	5 (1)	
CD4 count			
Median (IQR)	297 (136, 491)	283 (136, 574)	0.094*
<500	97 (7)	19 (5)	0.311
500+	29 (2)	9 (3)	
Patients who start ART by:			
Day 0	249 (17)	176 (49)	<0.0001
Day 14	462 (32)	291 (81)	<0.0001
Day 28	717 (49)	308 (86)	<0.0001
Day 365	1144 (79)	341 (95)	<0.0001
Pregnant			
No	40 (3)	4 (1)	0.476
Yes	126 (9)	19 (5)	
Patients who were eligible prior to enrolment:	11/1465 (0.7)	7/364 (2)	0.067

- 894 (61%) females received SOC compared to 195 (54%) who received the intervention (p=0.001). 617 (42%) of patients who received SOC had at least secondary education compared to 186 (52%) who received the intervention (p=0.023) (Table 1).
- About half (49%) of patients who received the intervention had initiated ART within same day of eligibility compared to about one-sixth (17%) who received SOC (p<0.0001) (Table 1).
- The median age of patients who received SOC was 33 years (IQR=27, 41) compared to 36 years (IQR=29, 43) who received the intervention (p=0.003) (Table 1).
- A total of 1,812 patients were included in the analysis, of which 358 were exposed to the intervention and 1,454 to SOC (Tables 1 and 2).

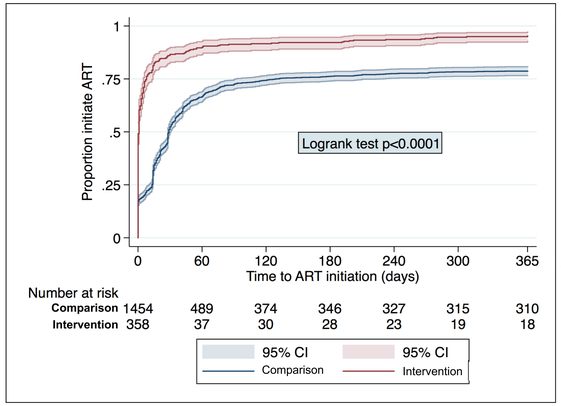
Table 2: Median time (days) to ART initiation by baseline patients characteristics and intervention group

Characteristics	Number of HIV patients (% of total)	Median time to ART initiation (days)	IQR	Log-rank test
Intervention group				
Control	1454 (80)	29	(13, 129)	<0.0001
Intervention	358 (20)	1	(0, 8)	
Sex				
Female	1089 (60)	15	(0, 48)	0.002
Male	559 (31)	24	(7, 61)	
Age group (Years)				
14-19	53 (3)	26	(0, 36)	
20-24	192 (11)	15	(0, 46)	0.058
25-34	614 (34)	21	(1, 56)	
35+	789 (44)	18	(1, 48)	
Marital status				
Married	811 (45)	15	(0, 50)	0.152
Single/Divorced/Widowed	507 (28)	22	(4, 56)	
Level of education				
None	162 (9)	28	(4, 73)	
Primary	423 (23)	15	(0, 46)	0.067
Secondary+	803 (44)	19	(1, 54)	
Household income (Kwacha) per month [1]				
<2000	422 (23)	14	(0, 42)	0.867
2000+	68 (4)	14	(3, 43)	
WHO stage				
Stage 1	1064 (59)	19	(0, 52)	
Stage 2	158 (9)	28	(14, 57)	0.39
Stage 3	170 (9)	18	(10, 43)	
Stage 4	27 (1)	21	(13, 77)	
CD4 count				
<350	116 (6)	28	(1, 177)	0.297
350+	38 (2)	28	(0, 187)	
Functional status				
Healthy, able to work	1062 (59)	21	(0, 52)	
Sick, able to work	82 (5)	14	(2, 55)	0.947
Sick, unable to work/Bedridden	31 (2)	15	(2, 52)	
Total	1812 (100)	22	(1, 77)	

[1] 1 USD=10 Kwacha

- 1,089 (60%) were female, 803 (44%) had at least secondary education, and only 53 (3%) were adolescents aged 14-19 years (Table 2).
- The median time to ART initiation among patients who received the intervention was 1 day (IQR=0, 8) compared to 29 days (IQR=13, 129) among those who received SOC (p<0.0001) (Table 2).

Figure 1: Kaplan-Meier estimate: proportion of patients who initiate ART



- There were more frequent ART initiations within the first 30 days amongst those who received the intervention compared to those who received SOC (Figure 1).
- After day 60, the frequency with which patients initiate ART was similar in both groups (figure 1).

Table 3: Average treatment effect (ATE) on time-to-ART initiation among HIV patients, Zambia

Effects	Coefficient[1]	95%CI	P-value
ATE			
Control	ref		
Intervention	-91	[-131, -51]	<0.0001
Potential Outcome Mean			
Control	137	[108, 165]	<0.0001
Relative ratio	0.67	[0.45, 0.89]	<0.0001

[1] Survival treatment-effects estimation model (Estimator: inverse-probability weight regression adjustment; Outcome model: Weibull with covariates sex, age, education; Treatment model: logit with covariates sex, age, education, WHO stage; Censoring model: none

- Assuming everyone in the population of HIV patients aged 14+ years was exposed to the intervention, the average time-to-ART initiation was estimated to be about 91 days less than when patients are exposed to SOC (ATE=-91 (95%CI: [-131, -51]; p<0.0001) (Table 3).
- The estimated average time to ART initiation when no patient wass exposed to the intervention was 137 days (95%CI: 108, 165) (Table 3).
- When all patients were exposed to the intervention, the time to ART initiation fell by an estimated 67% (95%CI: 45%, 89%) relative to the case in which patients were exposed to SOC (Table 3).

Conclusion

- **Rapid ART initiation as part of routine care in public sector facilities can increase both the rate of ART initiation as well as overall completeness of uptake among treatment eligible patients.**
- **Ongoing expansion of treatment guidelines to include all persons living with HIV may be able to achieve greatest gains when coupled with rapid ART initiation practices, which should include CD4 determination to identify patients with advanced disease and at risk of increased morbidity and mortality.**

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REFERENCES:
1. Collaboration H-C, Ray M, Logan R, Sterne JA, Hernandez-Diaz S, Robins JM, et al. The effect of combined antiretroviral therapy on the overall mortality of HIV-infected individuals. AIDS. 2010;24(1):123-37.
2. Grinsztejn B, Hosseinipour MC, Ribaudo HJ, Swindells S, Eron J, Chen YQ, et al. Effects of early versus delayed initiation of antiretroviral treatment on clinical outcomes of HIV-1 infection: results from the phase 3 HPTN 052 randomised controlled trial. The Lancet Infectious Diseases. 2014;14(4):281-90.

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