Six-Month Antiretroviral Therapy Dispensing and Viral Suppression Rates in Zambia

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Background

- Facility-based multi-month dispensing of antiretroviral therapy (ART) for HIV may reduce burdens on patients and providers and improve outcomes but has not yet been evaluated in rigorous randomized studies.

- INTERVAL was a cluster-randomized, non-blinded, non-inferiority trial of standard of care (1-3 months) versus three- versus six-month dispensing of ART in Malawi and Zambia performed between May 2017-April 2018.

- Participants had to be stable on ART at entry, defined by viral suppression <20 copies/mL within six months of study entry, on first-line ART, and not pregnant or breastfeeding.

- Each participant was followed for 12 months to establish the primary outcome of retention.

- Routine viral load monitoring was not performed by the study but was recommended annually by the Zambian national guidelines and recorded in study records if obtained.

- We sought to understand rates of viral suppression in Zambian HIV participants in the INTERVAL study among participants who received viral load follow up.

Methods

- We performed a post hoc analysis of Zambian INTERVAL participants to explore viral suppression outcomes using participants at the 15 sites in Malawi (5 in each arm). Figure 1 describes the flow of INTERVAL for both countries.

- Chi-square and Wilcoxon rank-sum test were used to evaluate differences in socio-demographic and clinical characteristics of those with and without viral load data and to compare those with and without viral suppression using a threshold of 20 copies/mL.
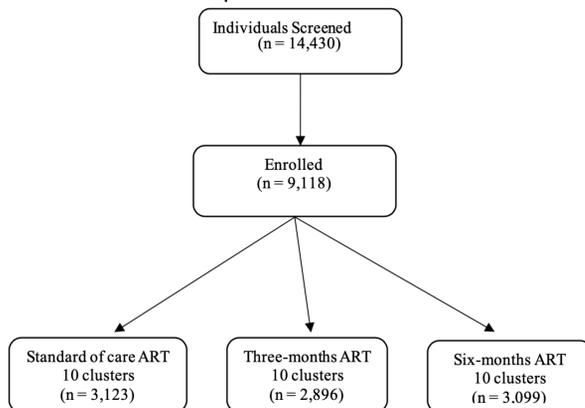
Figure 1: Screening and Enrollment for the INTERVAL study for both Malawi and Zambia (cluster = facility)

Individuals Screened (n = 14,430)
→ Enrolled (n = 9,118)
→ Standard of care ART 10 clusters (n = 3,123) | Three-months ART 10 clusters (n = 2,896) | Six-months ART 10 clusters (n = 3,099)

Results

- Of the 4,169 Zambian participants in INTERVAL, 1587 (38.1%) did not have a viral load and 2,582 (61.9%) had at least one viral load during follow-up a median of 309 days on study (IQR 219, 362).

- Table 1 summarizes the characteristics of those with versus without viral load data:

  - There were no differences in those with versus without viral load by age (median 43 years) or sex (men 61.6% and women 62.1%, p=0.78).

  - Participants from wealthier households were more likely to have a viral load performed compared to those from the poorest households (65.3% versus 56.1%, respectively, p=<0.01).

- Figure 2 showcases the significant differences in viral load completion rates by facility (p<0.01) likely related to differences in infrastructure to perform viral load during study implementation.

- Table 2 describes characteristics of those with versus without viral suppression using a threshold of 20 copies/mL

  - Participants in the 6-month arm had the highest rates of viral suppression (82.3%) compared to those in the three-month (79.2%) and standard of care arms (75.8%) (p<0.01).

  - Women were more likely to be virologically suppressed than men (18.9% versus 25.3%, p<0.01).

  - Viral suppression was not significantly associated with age, marital status, time on ART at entry, educational attainment, work status, or household wealth.

Table 1: Comparisons of Zambian Participants With Versus Without Viral Load Data (n=4,169)

Characteristic	No Follow-Up Viral Load 1,587 (38.1%)	1 or More Follow Up Viral Load 2,582 (61.9%)	P-value:
Sex			P= 0.78
Male	491 (38.4%)	788 (61.6%)	
Female	1096 (37.9%)	1794 (62.1%)	
Age			P=0.0358
Median	43	43	
IQR	36, 49	37, 50	
Missing	4 (33.3%)	8 (66.7%)	
Marital Status			P=0.67
Single/Widowed/Divorced/Separated	521 (37.7%)	862(62.3%)	
Married/Long-term Partner	725 (38.8%)	1,144 (61.2%)	
Missing	341 (37.2%)	576 (62.8%)	
Wealth index			P= 0.006
Poorest	286 (43.9%)	365 (56.1%)	
Poor	268 (40.1%)	401 (59.9%)	
Middle	240 (37.6%)	398 (62.4%)	
Richer	247 (35.1%)	456 (64.9%)	
Richest	205 (34.7%)	386 (65.3%)	
Missing	341 (37.2%)	576 (62.8%)	

[1] χ² test for categorical variables and Wilcoxon rank-sum test for continuous variables
[2] Principal Component Analysis (PCA) was used to construct the wealth index, using household asset indicators (e.g. electricity, refrigerator, radio, floor material other than mud).
A total of 17 household asset indicators were collected in the survey and used for constructing the index.

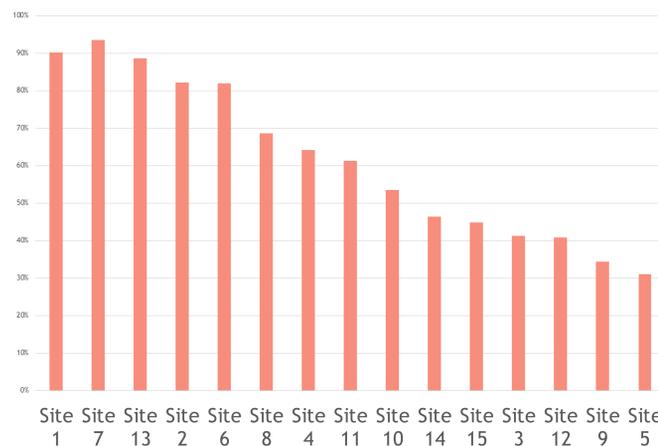**Figure 2: Viral Load Completion by Facility (n=2,582)**

Site 1, Site 7, Site 13, Site 2, Site 6, Site 8, Site 4, Site 11, Site 10, Site 14, Site 15, Site 3, Site 12, Site 9, Site 5

Table 2: Characteristics of those with versus without viral suppression (<20 copies/mL)

Characteristic	Viral Load Not Detectable (<20 copies/mL) N= 2,044 (79.2%)	Viral Load Detectable (≥20 copies/mL) N= 538 (20.8%)	P-value:
Sex			P=0.000
Male	589 (74.8%)	199 (25.3%)	
Female	1455 (81.1%)	339 (18.9%)	
Age			P= 0.4384
Median	43	43	
IQR	37, 50	36, 51	
Missing	7	1	
Study Arm			P= 0.005
Standard of care	634 (75.8%)	202 (24.2%)	
3 Month	686 (79.2%)	180 (20.8%)	
6 Month	724 (82.3%)	156 (17.7%)	
Years on ART prior to enrollment			P=0.896
Median	5.7	5.8	
IQR	3.2, 8.7	3.1, 8.6	
Marital Status			P= 0.99
Single/Widowed/Divorced/Separated	682 (79.1%)	180 (20.9%)	
Married/Long-term Partner	907 (79.3%)	237 (20.7%)	
Missing	455	121	
Education			P=0.443
Primary (1-8)	644 (77.8%)	184 (22.2%)	
Secondary (9-12)	708 (79.6%)	182 (20.4%)	
College (>13)	162 (83.9%)	31 (16.1%)	
Missing	530	141	
Work Status			P=0.996
Formally Employed	304 (78.8%)	82 (21.2%)	
Informally Employed	640 (79.3%)	167 (20.7%)	
Unemployed	643 (79.3%)	168 (20.7%)	
Missing	457	121	
Wealth index			P= 0.479
Poorest	278 (76.2%)	87 (23.8%)	
Poor	314 (78.3%)	87 (21.7%)	
Middle	320 (80.4%)	78 (19.6%)	
Richer	373 (81.8%)	83 (18.2%)	
Richest	304 (78.8%)	82 (21.2%)	
Missing	455	121	
Difficulty Making Clinic Visits Due to Transportation and Task Switching Cost			P=0.154
Not difficult at all	1,029 (80.0%)	257 (20.0%)	
Somewhat difficult	406 (79.9%)	102 (20.1%)	
Very difficult	153 (72.5%)	58 (27.5%)	
Missing	456	121	

[1] ND/TND was defined as viral load with less than 20 viral copies
[2] TD was defined as a viral load with greater than 20 viral copies
[3] χ² test for categorical variables and Wilcoxon rank-sum test for continuous variables
[4] Missing category includes unknown and refuse to answer observations
[5] Principal Component Analysis (PCA) was used to construct the wealth index, using household asset indicators.
A total of 17 household asset indicators were collected in the survey and used for constructing the index.

"I am very happy with this program of giving medicines for 6 months. I am very happy, as it will help me be more productive and strong as I work. I feel this has prolonged my life."

–Zambian INTERVAL Participant

Conclusions

- Among stable patients in the INTERVAL study, those in the six-month dispensing arm had the highest rates of viral suppression, suggesting that a six-month supply of ART may improve HIV-related outcomes. Further work is needed to confirm our findings.

- Our analysis is limited by the high amount of missing viral load data and differences between those with and without viral loads - which may introduce bias and limit generalizability of our results.

- Future directions include conducting a multivariate regression analysis on our data and utilizing a viral load threshold of <200 copies/mL to see how results vary by different suppression thresholds.

References

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Acknowledgements