3 vs 6-monthly dispensing of Antiretroviral Treatment in Community ART Refill Groups: a Cluster-Randomized Trial in Zimbabwe

1088

AUTHORS: Geoffrey Fatti,[1] Nicoletta Ngorima-Mabhena,[2] Eula Mothibi,[1] Trish Muzenda,[1,3] Regis Choto,[4] Tonderai Kasu,[4] Taurayi A. Tafuma,[5] Nyika Mahachi,[5] Kudakwashe C. Takarinda,[4] Tsitsi Apollo,[4] Owen Mugurungi,[4] Charles Chasela,[6,7] Risa M. Hoffman,[8] Ashraf Grimwood[1]

1. Kheth'Impilo AIDS Free Living, Cape Town, South Africa; 2. Kheth'Impilo, Harare, Zimbabwe; 3. Division of Public Health Medicine, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa; 4. Ministry of Health and Child Care, Zimbabwe; 5. FHI360, Zimbabwe; 6. EQUIP Health, Centurion, South Africa; 7. Department of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; 8. Division of Infectious Diseases, Department of Medicine, David Geffen School of Medicine at the University of California, Los Angeles, USA

INTRODUCTION

- Multimonth dispensing (MMD) of antiretroviral treatment (ART) is a differentiated service delivery model that aims to reduce patient-related barriers to care and improve health system efficiency in low-income settings through the dispensing of 3 to 6 months of treatment.
- Thus there is increased health policy interest in MMD models, however, randomized evidence of its effectiveness is lacking.
- We performed a cluster-randomized trial comparing three and six-monthly MMD of ART in community-based ART refill groups (CARGs) versus standard-of-care facility-based ART delivery in Zimbabwe.

METHODS

- A three-arm, unblinded, pragmatic cluster-randomized, non-inferiority trial was performed. Participants were enrolled between Aug 2017 and Feb 2018.
- Thirty healthcare facilities (clusters) and linked CARGs were allocated to either: ART collected three-monthly at facility (3MF, control); ART provided three-monthly in CARGs (3MC); or ART provided six-monthly in CARGs (6MC).
- Cluster allocation occurred in three strata, ie urban facilities (6); rural clinics (12) and rural hospitals (12).
- Stable nonpregnant adults receiving first-line ART ≥ six months, with baseline viral load (VL) <1000 copies/ml, and without recent opportunistic infections or ART tolerability issues were eligible to be enrolled.
- CARGs consisted of 6-12 people, and met in a community venue of their choice to receive ART refills. A single alternating CARG member collected ART at the facility on a 3-monthly (3MC) or six-monthly (6MC) basis and distributed the medication to other CARG members at the CARG meeting on the same or following day.
- CARG participants were scheduled to receive a clinical consultation and viral load testing at the facility twelve months after enrolment.
- Control group (3MF) participants received ART directly from the clinic at three-monthly intervals, and were scheduled to receive viral load testing after 12 months.
- The primary outcomes was retention in ART care 12 months after enrolment, with a pre-specified non-inferiority limit of -3.25% (risk difference [RD]).
- Viral suppression (VS) 12 months after enrolment was a secondary outcome.
- Outcomes were analysed using generalized estimating equations specified for clustering.
- Trial registration: ClinicalTrials.gov, NCT03238846.

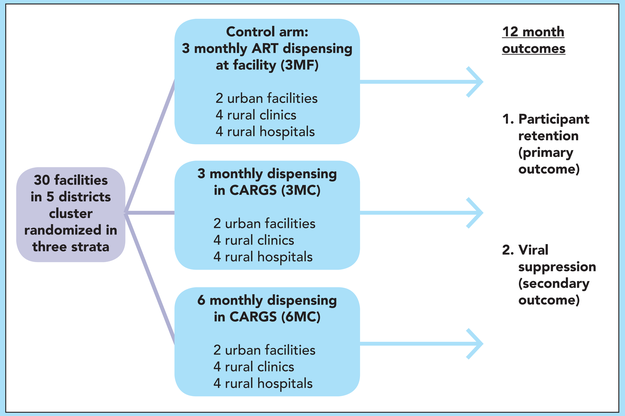

Figure 1: Study design diagram

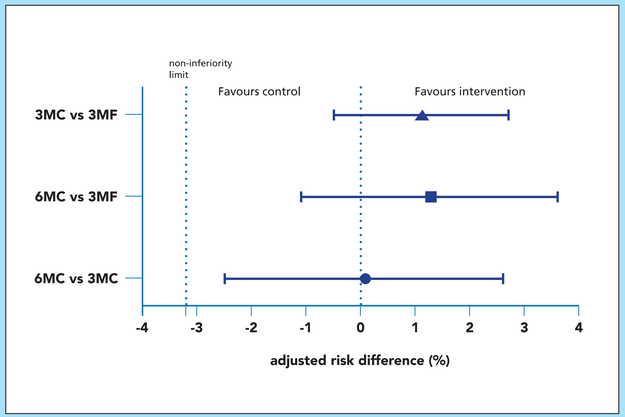

Figure 2: Comparison of arms for participant retention in antiretroviral treatment care (primary outcome) after 12 months

Table 1: Characteristics at enrolment

Baseline characteristic	Arm 3MF (N=1919)	Arm 3MC (N=1335)	Arm 6MC (N=1546)
Age, years, median (IQR)	44.8 (38.2–53.8)	46.5 (40.6–55.8)	44.8 (38.2–53.8)
Age categories, n (%)			
18–24 years	52 (2.7)	15 (1.1)	35 (2.3)
25–49 years	1252 (65.2)	807 (60.5)	994 (64.3)
≥ 50 years	615 (32.1)	513 (38.4)	517 (33.4)
Female gender, n (%)	1378 (71.8)	984 (73.7)	1101 (71.2)
CD4 cell count, cells/µL, median (IQR)	514 (356.0–709.0)	509 (377.0–700.0)	525 (357.0–720.0)
CD4 cell count categories, n (%)			
< 200 cells/µL	46 (2.4)	26 (2.0)	29 (1.9)
< 200–499 cells/µL	334 (17.4)	273 (20.5)	237 (15.3)
500–749 cells/µL	245 (12.8)	218 (16.3)	201 (13.0)
≥ 750 cells/µL	168 (8.8)	121 (9.1)	130 (8.4)
Not available	1126 (58.7)	697 (52.2)	949 (61.4)
Weight, kg, median (IQR)	60 (54.0–68.0)	60 (54.0–68.0)	60 (53.6–67.0)
WHO stage, n (%)			
I or II	837 (43.6)	606 (45.4)	535 (34.6)
III	1061 (55.3)	703 (52.7)	977 (63.2)
Not available	21 (1.1)	26 (2.0)	34 (2.2)
Current employment, n (%) (n=4782)			
Employed	765 (40.0)	319 (24.0)	800 (51.9)
Not employed	1148 (60.0)	1009 (76.0)	741 (48.1)
Distance from home to facility, n (%)			
< 4 km	791 (41.3)	596 (44.9)	567 (36.9)
4–9 km	594 (31.0)	495 (37.3)	697 (45.3)
> 9 km	520 (27.1)	236 (17.8)	273 (17.8)
Unknown	11 (0.6)	1 (0.0)	1 (0.0)
Time from ART initiation to study enrolment, months, median (IQR) (n=4707)	54.3 (30.9–83.4)	59.9 (33.5–87.8)	48.3 (29.9–76.7)
Year of starting ART, median (IQR) (n=4709)	2013 (2010–2015)	2012 (2010–2015)	2013 (2011–2015)
Randomization stratum, n (%) (n=4800)			
Urban facility	387 (20.2)	387 (29.0)	337 (21.8)
Rural clinic	777 (40.5)	439 (32.9)	670 (43.3)
Rural hospital	755 (39.3)	509 (38.1)	539 (34.9)
District, n (%) (n=4800)			
Gutu	376 (19.6)	84 (6.3)	75 (4.8)
Zaka	585 (30.5)	243 (18.2)	189 (12.2)
Mberengwa	380 (19.8)	425 (31.8)	856 (55.4)
Beitbridge	191 (9.9)	196 (14.7)	426 (27.6)
Chitungwiza	387 (20.2)	387 (29.0)	0 (0)

Table 2: Participant retention in ART care and viral suppression after 12 months

	Retention (primary outcome)[1]						Viral suppression (secondary outcome)					
	En-rolled	Retained[2]		Adjusted Risk Difference (RD)[3]			Viral load done	Viral load com-pletion	Suppressed		Relative Risk (RR)[4]		
Arm	**N**	**n**	**%**	**RD**	**95% CI**	**P**	**N**	**%**	**n**	**%**	**RR**	**95% CI**	**P**
3MF (control)	1919	1784	93.0	Reference	–	–	865	49.0	857	99.1	Reference	–	–
3MC	1335	1265	94.8	1.1%	-0.5 to 2.8	0.174	566	44.8	564	99.7	1.0	1.0–1.0	0.49
6MC	1546	1477	95.5	1.2%	-1.0 to 3.6	0.277	113	7.7	105	92.9	0.9	0.9–1.0	0.070
6MC vs 3MC	–	–	–	0.1%	-2.4 to 2.6	0.932	–	–	–	–	0.9	0.9–1.0	0.083

1. Outcome analyses were by intention-to-treat using population-averaged generalized estimating equations specified for clustering by facility, estimating risk differences between exposure groups. All models were adjusted for randomization stratum.
2. The intracluster correlation coefficient for retention was 0.025.
3. Estimates adjusted for age category, district and randomization stratum.
4. Estimates from log-binomial regression with generalized estimating equations specifying for clustering by facility and adjusted for randomization stratum, including only participants with available viral load results.

RESULTS

- 4800 participants were enrolled; 1919, 1335 and 1546 in 3MF, 3MC and 6MC, respectively.
- Arms were reasonably balanced with regards to participant's baseline demographic characteristics, excepting that 3MF had a slightly higher proportion of youth (aged 18-24 years) and employment status varied between arms (Table 1). 3MC had a higher proportion from urban facilities. 3MF had a larger proportion living > 9km from the facility. There were differences in the numbers enrolled by district, with no 6MC sites allocated to Chitungwiza (allocation was not stratified by district).
- Retention was high and similar in all arms, 93.0%, 94.8% and 95.5% in 3MF, 3MC and 6MC, respectively (Table 2).
- The pre-specified non-inferiority limit (-3.25%, risk difference [RD]) was met for comparisons between all arms; 3MC vs. 3MF, adjusted RD=1.1% (95% CI: -0.5% to 2.8%); 6MC vs. 3MF: aRD=1.2% (CI: -1.0% to 3.6%); and 6MC vs. 3MC: aRD=0.1% (CI: -2.4% to 2.6%) (Table 2; Figure 2).
- Viral load completion at 12 months was 49%, 45% and 8% in 3MF, 3MC and 6MC, respectively.
- VS in 3MC (99.7%) was high and not different to 3MF (99.1%), relative risk=1.0 (CI: 1.0-1.0) (Table 2).
- The relative risk of VS in 6MC (92.9%) vs. 3MF was 0.9 (CI: 0.9-1.0).

CONCLUSIONS

- Retention in CARGs receiving three and six-monthly MMD of ART was high and noninferior to standard-of-care facility-based ART delivery in Zimbabwe for stable patients, and is a strategy that can be scaled-up.
- Viral suppression in 3-monthly CARGs was high. Viral load result availability was lower in 6MC. Viral load availability was high in Chitungwiza municipality; however no 6MC sites were allocated to Chitungwiza. Targeted viral load testing amongst higher-risk 6MC participants was likely to have occurred, due to lower viral load testing availability.
- Viral load uptake and viral suppression in CARGs receiving six-monthly MMD requires further evaluation.

Source of funding
The United States Agency for International Development/President's Emergency Plan for AIDS Relief, through Equip health (agreement number AID-OAA-A-15-00070).

Disclaimer
This presentation and the data made herein was made possible through the support of our funders; the content of this presentation is the sole responsibility of the authors and does not necessarily reflect the views or opinions of our funders.

Acknowledgements
The authors wish to acknowledge the Zimbabwe MOHCC; Equip Health; the Organization for Public Health Interventions and Development, Zimbabwe; FHI360 Zimbabwe; Population Services International Zimbabwe; and the Data Safety and Monitoring board: Mazvita Sengayi, Richard Chawana, and Tov Manene.

PEPFAR

USAID FROM THE AMERICAN PEOPLE

EQUIP Innovation for Health

Kheth'Impilo Innovation in Public Health

Presented at the 2020 CROI Conference

Presentation Number: 1088