

Outcomes of 3 vs 6-monthly Dispensing of Antiretroviral Treatment (ART) for Stable People Living with HIV in Community ART Refill Groups: a Cluster-Randomized Trial in Zimbabwe

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Introduction

- Multi-month 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 ART.
- In the context of COVID-19, community-based MMD of ART is particularly important as it decongests clinics, promotes social distancing and reduces clinic visits for people vulnerable to SARS-CoV-2.
- We performed a cluster-randomized trial comparing 3 and 6-monthly MMD of ART in community ART refill groups (CARGs) versus standard-of-care 3-monthly facility-based ART delivery in Zimbabwe for stable people living with HIV.
- We also report subgroup analyses of the primary outcome (retention in ART care) stratified by gender, distance from home to facility, and facility location.

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) (fig 1).
- Cluster allocation occurred in three strata, ie. urban facilities (6); rural clinics (12) and rural hospitals (12).
- Stable nonpregnant adults receiving first-line ART \geq 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 outcome was retention in ART care 12 months after enrolment, with a pre-specified non-inferiority margin of -3.25% (risk difference [RD]).
- Participants who either died or who were lost to follow were considered lost to care.
- Risk differences in retention in ART care were estimated using generalized estimating equations specified for clustering.

Results

- 4800 participants were enrolled; 1919, 1335 and 1546 in 3MF, 3MC and 6MC, respectively.
- Retention was high and similar in all arms, 93.0%, 94.8% and 95.5% in 3MF, 3MC and 6MC, respectively.
- The pre-specified non-inferiority margin 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 1).
- Amongst men, retention was particularly improved in 3MC, adjusted RD=3.4% (95% CI: 0.0-6.7%), figure 2.
- Participants who lived >9 km away from the facility benefitted the most from receiving ART both 3 monthly and 6 monthly in CARGs, adjusted RD=4.2% (95% CI: 0.5% to 7.9%) and adjusted RD=5.5% (95% CI: 3.5% to 7.5%), (figure 3).
- Amongst participants at rural hospitals (who likely need to travel long distances to access facility care), retention was particularly improved in 6MC vs control, adjusted RD=3.3% (95% CI: -1.0% to 7.6%), although this was not statistically significantly improved at the 5% level. (figure 4).

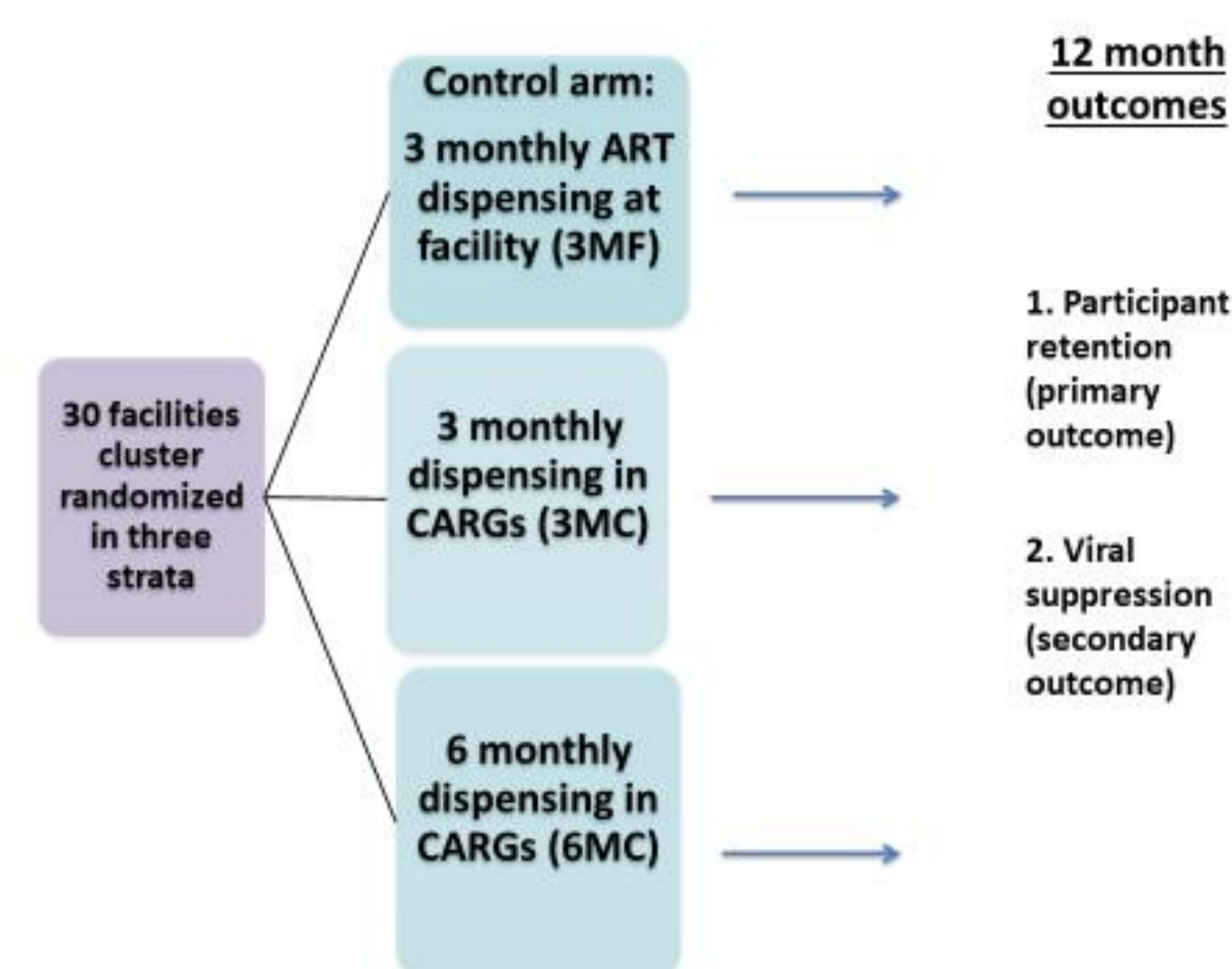


Figure 1: Study design diagram

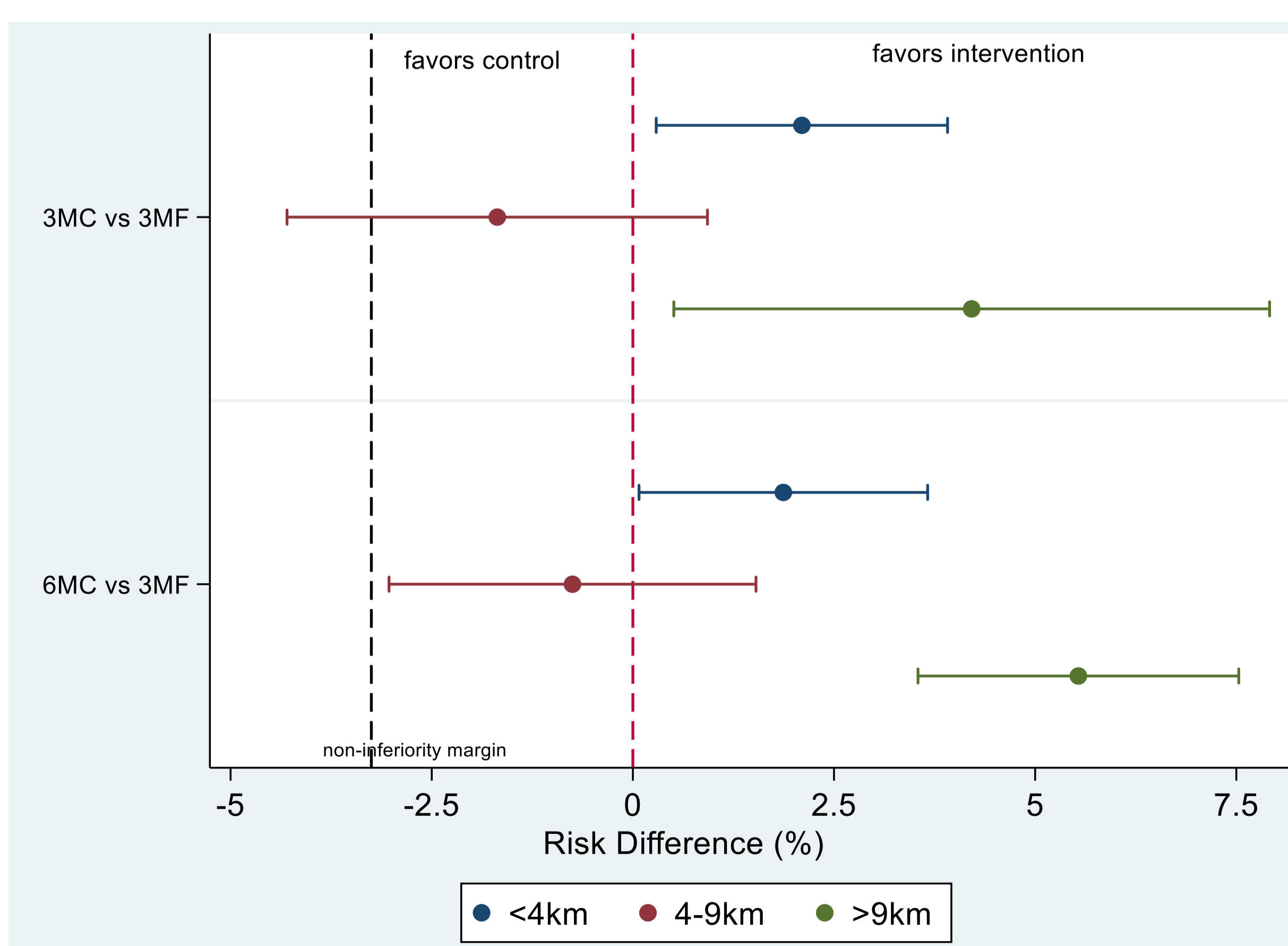


Figure 3: Comparison of arms for retention in ART care stratified by distance from home to facility

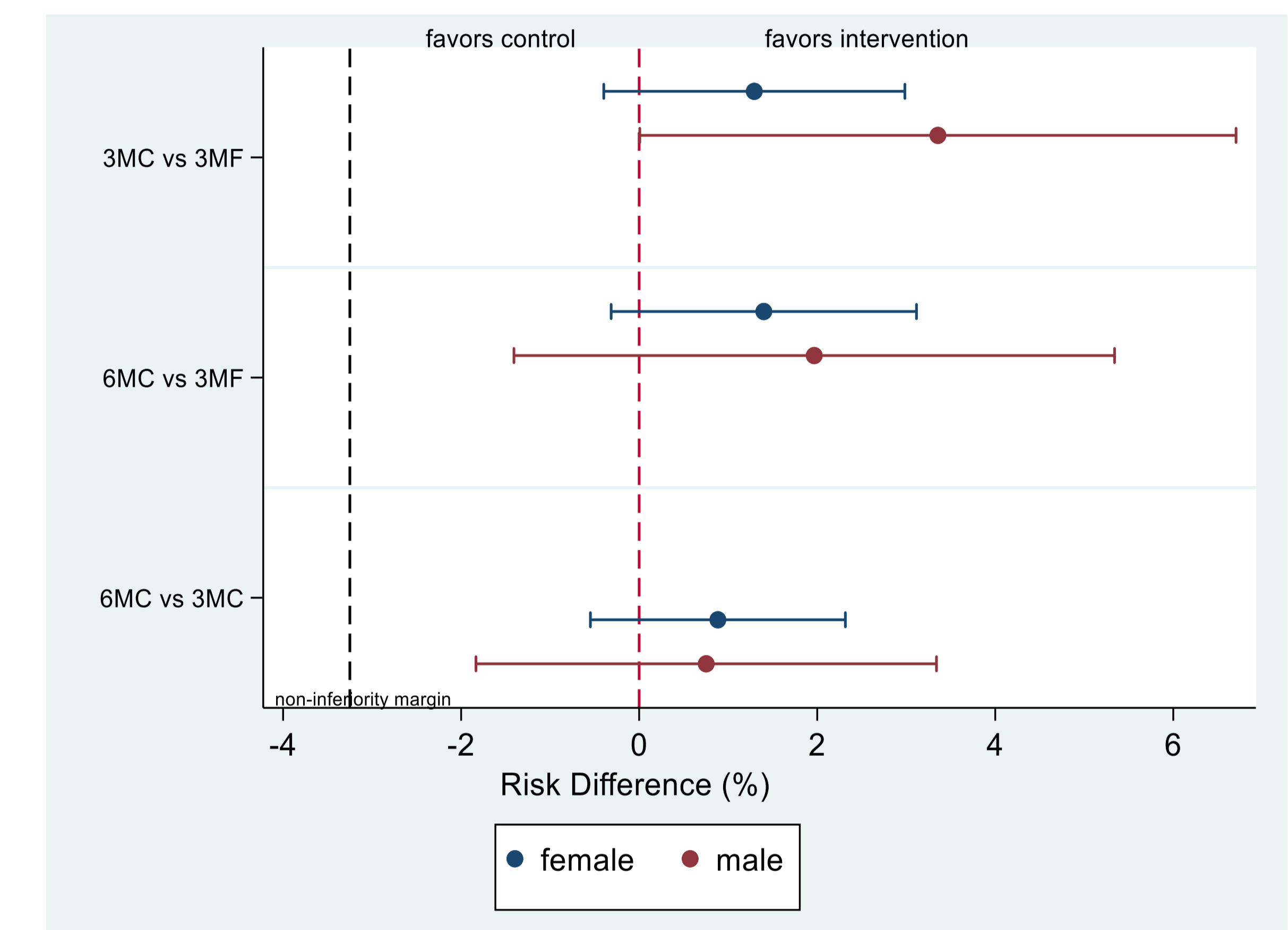


Figure 2: Comparison of arms for participant retention in ART care stratified by gender

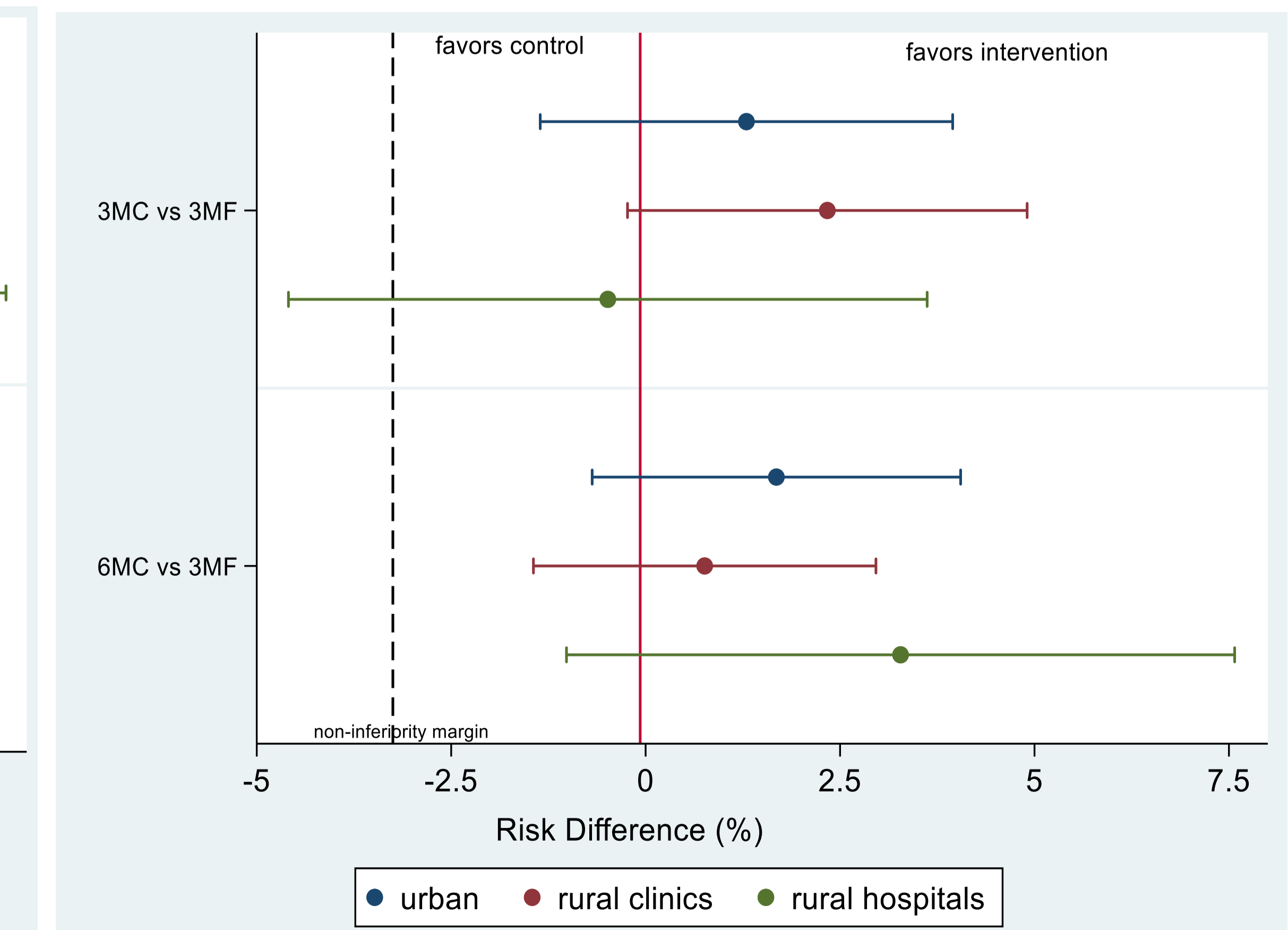


Figure 4: Comparison of arms for participant retention in ART care stratified by facility location

Conclusions

- Retention in CARGs receiving 3 and 6-monthly MMD of ART was high and noninferior vs. standard-of-care 3-monthly facility-based ART delivery in Zimbabwe for stable patients, and is a strategy that can be scaled-up.
- Retention amongst men was particularly improved in those receiving ART at three-monthly intervals in CARGs.
- Participants who lived >9 kms away from facilities benefitted the most from receiving ART in CARGs both three and six-monthly.
- Six-monthly ART receipt in CARGs appears particularly favorable for participants associated with rural hospitals as this reduces the long travel times associated with frequently needing to access facility-based care.

Retention in CARGs receiving 3 and 6-monthly MMD was high and noninferior vs. standard-of-care 3-monthly facility-based ART delivery in Zimbabwe for stable patients, and is a strategy that can be scaled-up.

Table 1: Participant retention in ART care (primary outcome) after 12 months (all participants)

Arm	Retention (primary outcome)			Adjusted Risk Difference (RD)		
	Enrolled N	Retained n	%	RD	95% CI	P
3MF (control)	1919	1784	93.0%	Ref	-	-
3MC	1335	1265	94.8%	1.1%	-0.5 to 2.8	0.17
6MC	1546	1477	95.5%	1.2%	-1.0 to 3.6	0.27
6MC vs. 3MC				0.1%	-2.4 to 2.6	0.93

Analyses were by intention-to-treat using population-averaged generalized estimating equations specified for clustering by facility. Estimates adjusted for age category and district

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