

Impact of Facility- and Community-Based Peer Support Models on Maternal Uptake and Retention in Malawi's Option B+ HIV Prevention of Mother-to-Child Transmission Program: A 3-Arm Cluster Randomized Controlled Trial (PURE Malawi)

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Background: Many sub-Saharan African countries have adopted Option B+, a prevention of mother-to-child transmission approach providing HIV-infected pregnant and lactating women with immediate lifelong antiretroviral therapy. High maternal attrition has been observed in Option B+. Peer-based support may improve retention.

Methods: A 3-arm stratified cluster randomized controlled trial was conducted in Malawi to assess whether facility- and community-based peer support would improve Option B+ uptake and retention compared with standard of care (SOC). In SOC, no enhancements were made (control). In facility-based and community-based models, peers provided patient education, support groups, and patient tracing. Uptake was defined as attending a second scheduled follow-up visit. Retention was defined as being alive and in-care at 2 years without defaulting. Attrition was defined as death, default, or stopping antiretroviral therapy. Generalized estimating equations were used to estimate risk differences (RDs) in uptake. Cox proportional hazards regression with shared frailties was used to estimate hazard of attrition.

Results: Twenty-one facilities were randomized and enrolled 1269 women: 447, 428, and 394 in facilities that implemented SOC, facility-based, and community-based peer support models, respectively. Mean age was 27 years. Uptake was higher in facility-based (86%; RD: 6%, confidence interval [CI]: -3% to 15%) and community-based (90%; RD: 9%, CI: 1% to 18%) models compared with SOC (81%). At 24 months, retention was higher in facility-based (80%; RD: 13%, CI: 1% to 26%) and community-based (83%; RD: 16%, CI: 3% to 30%) models compared with SOC (66%).

Conclusions: Facility- and community-based peer support interventions can benefit maternal uptake and retention in Option B+.

Key Words: PMTCT, Option B+, uptake, retention, peer support, Malawi

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INTRODUCTION

In 2011, the Malawi Ministry of Health (MOH) introduced a pragmatic public health approach to improve the effectiveness of its prevention of mother-to-child HIV transmission (PMTCT), referred to as Option B+.^{1,2} Option B+ provides universal lifelong antiretroviral therapy (ART) for all HIV-infected pregnant and breastfeeding women, regardless of CD4 count and/or any clinical stage.

By eliminating complex PMTCT algorithms, delays from CD4⁺ cell testing, and ART re-initiations with each pregnancy, Option B+ simplified the PMTCT process with expected benefits for HIV-infected women, their HIV-exposed infants and HIV-uninfected sex partners.²⁻⁴ Although results reflected dramatic increases in ART initiation for the target population, concerns have been observed about suboptimal uptake and retention.⁵⁻⁷ Threats identified at the national level included potential suboptimal uptake by a relatively asymptomatic population of pregnant women due to low treatment literacy, stigma, and the lack of psychosocial support for long-term retention.¹ Identification of interventions to support PMTCT uptake and retention is a step toward the program improvement.

Peer support strategies seem effective for improving maternal and infant uptake and retention in diverse settings, including Malawi's national program.^{6,8-13} However, most of the published studies have not been conducted in an Option B+ setting, and their effectiveness in this setting is not known. Furthermore, the limited number of randomized studies makes it difficult to determine whether selection of higher functioning facilities or good care-seeking behavior influenced outcomes. Nor is it known whether facility- or community-based models will be effective in initiating and retaining patients on treatment and returning them to care after they drop out.

The PMTCT Uptake and REtention (PURE) study was a 3-arm stratified cluster randomized controlled trial that evaluated whether facility- and community-based peer support by women with similar experience would improve uptake and retention of mothers and infants in Malawi's Option B+ program. The outcomes of interest improved maternal uptake of PMTCT services, retention in care, and viral suppression compared with the national standard of care (SOC) at 2 years postinitiation of treatment.

METHODS

Study Design and Setting

The study was conducted in 3 of the 5 health zones in Malawi: Central West, South East, and South West. Under Malawi's Option B+ program, HIV-infected women start first-line regimen 5A [tenofovir/lamivudine (3 TC)/efavirenz], with alternative regimens available for patients with toxicity [Malawi HIV Clinical Guidelines, 2011]. ART is started as soon as HIV is diagnosed, ideally as early as possible in pregnancy at the first antenatal visit, but including during labor or the postnatal breastfeeding period. Patients initiating standard first-line ART are reviewed every month for the first 6 months and 3 monthly thereafter.

The full protocol of this trial has been described previously.¹⁴ Briefly, a 3-arm stratified cluster randomized controlled trial was conducted comparing facility-based and community-based models of peer support with SOC. Health facilities (clusters) were eligible for inclusion if they could be expected to enroll at least 20 HIV-infected pregnant or breastfeeding women within a 6-month period; provided antenatal care, maternity, or postnatal services; and did not have other ongoing PMTCT interventions or research activities. Twenty-one clusters were included. These clusters were first stratified into 7 strata based on prebaseline volume (numbers of Option B+ women enrolling in the previous quarter) and retention rates (based on the national program). Facilities in each stratum were then randomized into 1 of the 3 arms.

Sample Size Calculations

Sample size methods for cluster randomized controlled trials were used¹⁴ with specific parameters for number of clusters per arm ($N = 7$), mean number of participants per cluster ($N = 50$), variation in cluster size (variance = 37), and intracluster correlation (intracluster correlation coefficient = 0.04). A sample size of 1080 women was required for the study to have 80% power to detect a difference of 65% retention (SOC arm) and 82.5% retention (facility- or community-based arm) at an alpha level of 0.05.

Recruitment and Follow-up

Pregnant and breastfeeding women were recruited from antenatal care, maternity, postnatal and ART clinics. Women were eligible for inclusion if they were 15 years or older, known previous HIV positive or newly tested HIV positive, and ART naive. Pregnant or breastfeeding women were invited to participate in the study by a trained clinical staff member before ART initiation. This standard recruitment procedure was used across the facilities. Women who provided written informed consent for themselves and their infants were enrolled in the study. All women who did or did not consent to enroll in the study were advised to start on lifelong ART according to the national policy. Women who enrolled in the study were followed up to 2 years or until the end of the study. All infants born to women in the study were enrolled at birth or at maternal enrollment, if breastfeeding. Figure 1 describes the enrollment flow for facilities and participants.

Interventions

The 3 study arms differed with respect to the availability and place of one-on-one patient education, support groups, visit reminders, and missed visit follow-up. Activities are described in detail elsewhere.¹⁴

At facilities randomized to SOC, participants received routine HIV care according to Malawi MOH guidelines, including ART education and routine ART adherence counseling. According to national guidelines, women who do not attend the clinic within 60 days of a missed

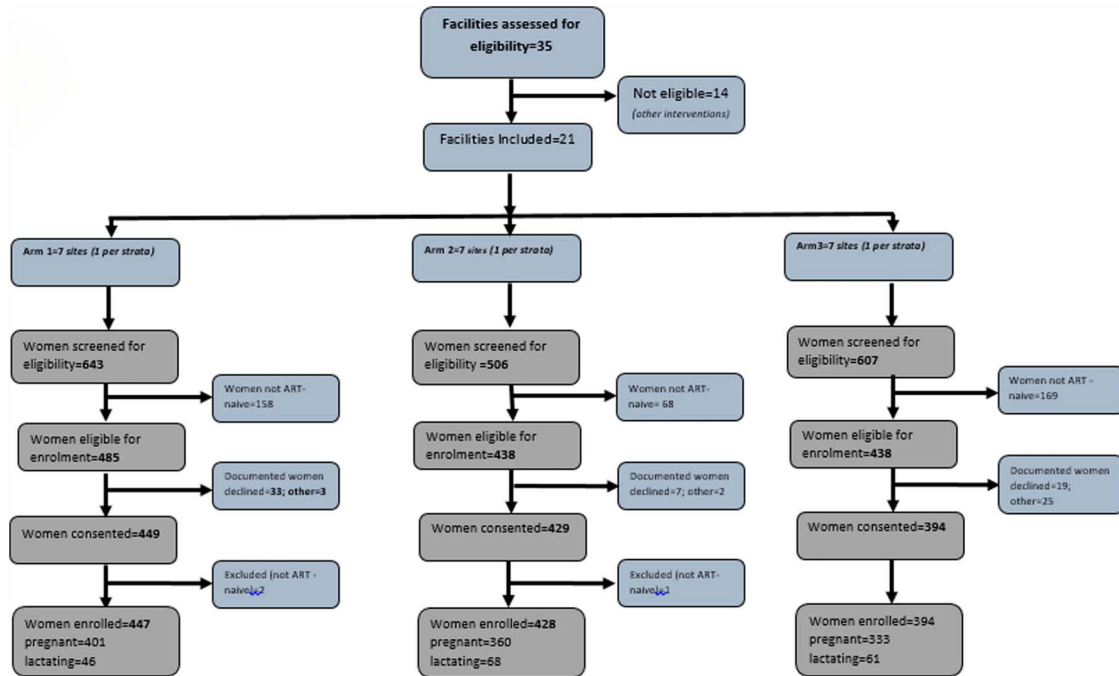


FIGURE 1. Consort diagram.

appointment are supposed to be traced with the aim of bringing them back to care. However, this rarely occurs in the routine program.

At facilities randomized to facility-based peer support, women received SOC and met with “mentor mothers.” Mentor mothers were women living with HIV who recently underwent PMTCT and were on ART. Mentor mothers provided one-on-one support at each clinic visit, led weekly clinic-based support groups, and contacted women within 1 week of a missed appointment. Contact was by phone call, text message, or home visit based on the woman’s preference and was recorded at enrollment. This model was adapted from the mothers2mothers model of clinical service delivery.¹²

At facilities randomized to community-based peer support, women received SOC and met with “expert mothers.” Expert mothers were women living with HIV who recently underwent PMTCT and were on ART. Expert mothers conducted routine home visits to study participants to provide HIV education and clinic visit reminders. In addition, expert mothers led monthly community-based support group meetings. Expert mothers obtained information about missed visits from ART providers and registers at the facility and were responsible for contacting these women in the community within 1 week of a missed scheduled clinic visit. Expert mothers conducted 1 home visit to remind women of a scheduled visit and a maximum of 3 home visits for each missed appointment.

Data Collection and Laboratory Samples

Routine antenatal clinic and ART visit data were recorded in MOH registers and treatment master cards. At

each ART clinic visit, visit and next appointment dates were recorded on patients’ ART master cards. The next appointment date was based on the recommended MOH guidelines, the number of tablets newly dispensed, and tablets remaining at present visit. National program outcomes (alive and on ART, stopped ART, transferred out, or died) are recorded at each clinic visit.

Dried blood spots for HIV RNA testing in women were collected at the 6- and 24-month visits from ART initiation. Dried blood spot samples were collected from HIV-exposed infants at 6 weeks of age and sent to a reference laboratory. At 12 and 24 months of age, infants received rapid HIV tests. Routine visit and HIV test data were recorded on infants’ treatment cards.

Study Outcomes

The primary outcomes for women were ART uptake and retention in care, measured over a 2-year period from ART initiation. The definitions used to indicate the primary outcome were as follows:

- Uptake: Documented receipt of antiretroviral drugs at the initial and second scheduled appointment dates. This definition was selected because some women have 1 initial ART visit and never returned to the clinic.
- Defaulted: Failed to return within 60 days after a scheduled appointment date. In time-to-event analysis, this is an adverse outcome.
- Stopped treatment: Documented stop of ART for more than 60 days. This decision could be initiated by the patient or clinician. In time-to-event analysis, this is an adverse outcome.

- Died: Reported and documented death of any cause. In time-to-event analysis, this is an adverse outcome.
- Attrition: Composite of all patients who defaulted, stopped ART, or died.
- Retained: Alive and on ART without any gap in care >60 days after a scheduled visit. In time-to-event analysis, this was a censored event.
- Transfer out: Documented transfer to another facility. In time-to-event analysis, this was a censored event.

These definitions are consistent with Malawi's national program, with one important deviation. In this analysis, once a woman achieved interrupted treatment for more than 60 days (stopped or defaulted), she no longer contributed person-time, even if she resumed taking ART. To explore consistency with the national program, 2-year retention was also explored and included all women in care at 2 years, regardless of earlier outcomes.

Several additional outcomes were reported. Punctuality was calculated based on the proportion of times each woman presented on time (<7 days late). Return to ART was calculated as the proportion of persons who defaulted within the first 18 months and then returned to care within 6 months. Virologic suppression was calculated as the proportion of women who had a viral load <1000 copies per milliliter at 6 or 24 months. Viral load testing coverage at 6 months included women who were tested from 4 to 11 months and coverage at 24 months included women who were tested from 22 to 33 months. These measures were restricted to those women retained at 6 and 24 months respectively.

For infants who were born before their mothers enrolled in the study, the proportion who were already HIV positive at enrollment was explored. For infants who were born during the study period, the proportion of live births and the proportion of these infants who were HIV-positive were explored at 6 weeks, 12, and 24 months of age.

Statistical Analysis

The primary analytic approach was "intention-to-treat." Participants in each intervention arm were compared with participants in the SOC arm, but the 2 intervention arms were not compared with each other.

The data set included variables for participant ID, study arm, study facility, study strata, pregnancy or breastfeeding status at enrollment, age at baseline, ART initiation, date, visit date, next appointment date, and primary outcome. Current visit date, next visit date, and appointment date were used to determine whether a woman was retained in care or not at each visit. Participants entered into the analysis when they were initiated on ART. Their observation time ended with an event at the time of attrition or with censoring (at 24 months after initiation, July 31st 2016, or date of transfer) whichever came first.

Time-to-event methods were used to estimate our primary outcome of interest: time to attrition. Kaplan-Meier curves were fit to the data to visualize retention curves. These curves did not account for clustering by facility or adjust for strata. Cox proportional hazards

models with shared frailties were fitted to the data to calculate hazard ratios (HRs) and 95% confidence intervals (CIs). The shared frailties accounted for correlation by study facility. A term for strata was included to control for the design effect. A model that adjusted for baseline pregnancy or breastfeeding status was run to control for potential confounding.

To compare the arms for the proportions with uptake, 1-year retention, 2-year retention, return to care after default, and suppression generalized estimating equations with an identity link and binomial distributions were implemented. From these models, risk differences (RDs) and 95% CIs were calculated. These models had an exchangeable correlation matrix and robust variance estimator to account for correlation by facility.

Ethics Consideration

The protocol was approved by Malawi's National Health Sciences Research Committee, the University of North Carolina Institutional Review Board, the University of Toronto, and WHO Ethics Review Committees. All female participants provided informed consent for themselves and their infants.

RESULTS

Between November 2013 and November 2014, 1756 women were screened for eligibility from the 21 facilities (clusters) and 484 declined or were ineligible for participation (Fig. 1). A total of 1272 women gave consent and were enrolled in the study. Three women were later excluded because they were not ART naïve, and 1269 HIV-infected women (pregnant = 1094, breastfeeding = 175) were included in analysis. There were 447 in SOC, 428 in facility-based, and 394 in community-based arms. The median age was 27 (interquartile range [IQR] 22–31) years, and most women were married. There were fewer breastfeeding women in SOC (10%) than in facility-based (16%) and in community-based (16%) (Table 1).

In facility-based peer support model, participants had an average of 5.8 clinical encounters with mentor mothers in year 1 and 4.0 clinical encounters in year 2. In year 1, mentor mothers documented 246 missed visits of which the women were successfully reached 142 times (57%) either at home or by phone. In year 2, mentor mothers documented 237 missed visits, of which 189 (80%) were actually reached. All facilities with facility-based peer support offered support groups. There were 262 support group meetings that were held with records of 893 attendances. On average, each woman attended 2.1 support groups during the study period. In facilities that offered community-based peer support, expert mothers visited each woman a mean of 2.4 times in the first year and 2.1 times in the second year. They documented 152 missed visits, of which 142 (93%) were reached. In year 2, expert mothers documented 128 missed visits, of which 103 (80%) were reached. In both facility- and community-based models, support groups were poorly attended.

TABLE 1. Baseline Characteristics of Facilities (Clusters) and HIV-Infected Women by Trial Arm

Characteristics	Study Arms		
	SOC	Facility-based peer support	Community-based peer support
	n (%)	n (%)	n (%)
Total women enrolled	447	428	394
Strata (based on facility size and historic retention*)			
Large	127 (28.4)	125 (29.2)	125 (31.7)
Medium	75 (16.8)	78 (18.2)	77 (19.5)
Small, high retention	74 (16.6)	52 (11.6)	52 (13.2)
Small, very high retention	52 (11.6)	51 (11.9)	52 (13.2)
Very small, high retention	49 (11.0)	40 (9.3)	26 (6.6)
Very small, medium retention	20 (4.5)	40 (9.3)	31 (7.9)
Very small, low retention	50 (11.2)	42 (9.8)	31 (7.9)
Pregnant/lactating			
Pregnant	401 (89.7)	360 (84.1)	333 (84.5)
Lactating	46 (10.3)	68 (15.9)	61 (15.5)
Age			
15–21	79 (17.7)	100 (23.4)	87 (22.2)
22–28	174 (38.9)	175 (40.9)	139 (35.3)
29–35	157 (35.1)	120 (28.0)	129 (32.7)
≥36	35 (7.8)	31 (7.2)	37 (9.4)
Missing	2 (0.4)	2 (0.5)	2 (0.5)
Marital status			
Never married	7 (1.5)	5 (1.2)	9 (2.3)
Married	419 (93.7)	393 (91.8)	363 (92.1)
Divorced	12 (2.7)	18 (4.2)	19 (4.8)
Widowed	5 (1.1)	9 (2.1)	3 (0.8)
Missing	4 (0.9)	3 (0.7)	0 (0.0)
Currently having a sexual partner			
Yes	426 (95.3)	400 (93.4)	364 (92.4)
No	13 (2.9)	20 (4.7)	27 (6.9)
Partner in catchment area			
Yes	355 (83.3)	328 (82.0)	308 (84.6)
No	49 (11.5)	50 (12.5)	33 (9.1)
Missing	22 (5.2)	22 (5.5)	23 (6)

Strata were grouped based on facility size and/retention. Facility size: large ≥ 125 women, Medium ≥ 75 women, Small ≥ 20 ; 1-year retention: low $< 50\%$; medium 50%–74%; high 75%–84%; and very high $\geq 85\%$.

*Retention was defined as being alive and in care at 12 months after ART retention regardless of earlier transfer out, stopping ART, or default status; Cluster interclass correlation: 0.072.

Among the enrolled women, overall ART uptake was 85% (1082) and 97% received their first ART dose within 1 week from study enrollment. ART uptake was higher in facility-based models, (86%; RD: 6%, CI: -3% to 15%) and community-based (90%; RD: 9%, CI: 1% to 18%) compared with SOC (81%), although not statistically significant. Among those who started ART, 12-month retention was similar across the study arms (Table 2). At 24 months, retention was lower in SOC (66%) compared with facility-based (80%) or community-based (83%) models (Table 2). Facility-based (HR: 0.71, 95% CI: 0.50 to 0.99) and community-based (AHR 0.62, 95% CI: 0.44 to 0.87) models had lower 24-month attrition compared with SOC using the study definition of retention. As reflected in Figure 2, the effect of the interventions increased considerably from 12 months after ART initiation, resulting in 44% and 52%

reduction in attrition in facility-based (aHR 0.56, 95% CI: 0.35 to 0.90) and community-based models (AHR 0.48, 95% CI: 0.30 to 0.78), respectively. Results were comparable when using the national definition of retention: (facility-based support versus SOC HR: 0.76, 95% CI: 0.50 to 1.17) (community-based support versus SOC HR: 0.58, 95% CI: 0.37 to 0.90).

The proportion of women who defaulted and returned to ART was higher in community-based models (68%; RD 30%, CI: 14%–46%), but similar in facility-based models (40%; RD 0%, CI -26% to 16%) when compared with SOC (39%). Among women who returned after a scheduled clinic appointment, the proportion of women who presented to the clinic on time was higher in facility-based (74%; IQR: 65%–81%) and community-based (64% IQR: 60%–75%) models than in SOC (57%; IQR: 56%–78%). Viral load testing

TABLE 2. Maternal Outcome HIV-Infected Women Enrolled in the Trial

	SOC (1)	Facility-Based Support (2)	Community-Based Support (3)	RD 95% CI	
	N (%)	n (%)	n (%)	Arm 2 versus 1	Arm 3 versus 1
Total women enrolled	447	428	394		
Maternal outcomes					
ART uptake*	447	428	394		
No	86 (19)	62 (14)	39 (10)	0.06 (−0.03 to 0.15)	0.09 (0.01 to 0.18)
Yes	361 (81)	366 (86)	355 (90)		
Retained at 1 year (N)	361	366	355		
No	91 (26)	79 (22)	88 (26)	0.06 (−0.06 to 0.18)	0.08 (0.04 to 0.20)
Yes	261 (74)	277 (78)	258 (74)		
Transferred out	9	10	9		
Retained at 2 years (N)	261	277	258		
No	87 (34)	53 (20)	42 (17)	0.13 (−0.01 to 0.26)	0.16 (0.03 to 0.30)
Yes	169 (66)	223 (80)	211 (83)		
Transferred out	5	1	5		
Two-year outcomes (trial)†	447	428	394		
Retained	169 (38)	223 (52)	211 (54)		
Transfer out	14 (3)	11 (3)	14 (4)		
Default	260 (58)	185 (43)	154 (39)		
Stopped treatment	3 (<1)	6 (1)	9 (2)		
Dead	1 (<1)	3 (1)	6 (1)		
Two-year outcomes (national program)‡	447	428	394		
Retained	255 (57)	298 (70)	292 (74)		
Transfer out	14 (3)	10 (2)	15 (3)		
Default	172 (38)	109 (25)	73 (19)		
Stopped treatment	4 (1)	5 (1)	8 (2)		
Dead	2 (1)	6 (1)	6 (1)		
Defaulted and returned	228	152	139		
No	140 (61)	91 (60)	45 (32)	0 (−0.16 to 0.16)	0.30 (0.14 to 0.46)
Yes	88 (39)	61 (40)	94 (68)		
Punctuality (median, (IQR))*	57 (56–78)	74 (65–81)	64 (60–75)		
6-month viral suppression					
In care at 6 mo	315 (70)	323 (75)	312 (79)	0.02 (−0.05 to 0.08)	0.05 (−0.01 to 0.11)
Viral load tests done	207 (66)	251 (78)	213 (68)		
<1000	174 (84)	215 (86)	189 (89)		
≥1000	33 (16)	36 (14)	24 (11)		
Twenty-four months viral suppression					
In care at 24 mo	169 (38)	223 (52)	211 (54)	−0.02 (−0.07 to 0.03)	−0.12 (−0.07 to 0.04)
Viral load tests done	138 (81)	209 (94)	193 (91)		
<1000	132 (96)	196 (94)	181 (94)		
≥1000	6 (4)	13 (6)	12 (6)		

*Punctuality was calculated based on the proportion of times each woman presented on time (<7 days late).

†We applied to separate definitions for retained; retained in trial outcomes was defined as alive and on ART without any gap in care >60 days after a scheduled visit while, in national program, it was defined as being alive and in care at 2 years regardless of earlier outcomes.
IQR, interquartile range; SOC, standard of care.

uptake was 71% and 90% among women who were alive at 6 and 24 months, respectively. Testing uptake at 24 months was lower in SOC (81%) compared with facility-based (94%) or community-based (91%) models; however, there was no difference in uptake at 6 months across the arms (Table 2). Viral suppression (defined as <1000 copies/mL) at 6 and 24 months was 86% and 94%, respectively but similar across all arms at each time points (Table 2).

Infants

Of the total of 1094 pregnancies, 893 (82%), 7 (1%), 2 (0.2%) were live births, still births, and early fetal loss, and 192 with unknown delivery outcomes. Among infants who were alive at 6 weeks, 12 months, and 24 months, HIV testing uptake was 66%, 71%, and 63%, respectively. Testing uptake at 12 months was lower in SOC (64%) compared with facility-based (80%) or community-based

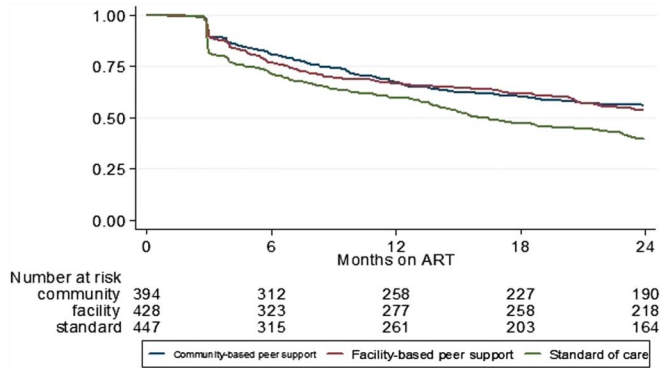


FIGURE 2. Kaplan–Meier uptake and retention estimates for Option B+ by trial arm.

(68%) models. At 24 months, testing uptake was similar among all arms. The cumulative proportion of infants testing HIV positive was similar across SOC (2%), facility-based (1%), and community-based (1%) models (Table 3).

A total of 121 (10%) women ever presented with a partner in the health facility. There were fewer partners present in SOC (7%) than in facility-based (11%) and in community-based (12%) models.

DISCUSSION

In this stratified cluster randomized controlled trial, community-based models of peer support contributed to improved maternal uptake and retention in Malawi's Option B+ program. Both interventions were more effective in the second year on ART follow-up. Women in the community-based peer support intervention who defaulted in the first 18 months were more likely to return on ART within 6 months. In addition, women in both peer support intervention groups had higher uptake of viral load testing at 24 months post-ART initiation and more infants were tested for HIV at 1 year of age. This study shows that peer support interventions in diverse settings within the context of Option B+ improve uptake of ART and retention among mothers.

This study's findings support the observational work that preceded this trial that suggested peer support strategies for improving maternal and infant uptake, and retention may be effective.^{6,8–13} The Tingathe program, a case manager support program in Malawi, used a pre–post model to demonstrate an improvement in 6-month retention from 51.1% to 65% after implementation of Option B+. Although this study's primary definitions of uptake and retention differ slightly with previous studies, comparison with the national definition suggests that this study demonstrated higher rates of retention than earlier descriptions.

The 2 intervention arms had many similarities, but the community-based arm was more labor intensive. Both interventions involved peer mothers who were HIV infected and had been through the PMTCT program. Peers in both arms had similar credentials, training, and supervision. Both interventions included support groups, with differences in the location of these groups although these were poorly attended. Both groups included comparable back-to-care elements, and

TABLE 3. Outcomes of Infants Born to HIV-Infected Women Enrolled in the Trial

Outcomes	SOC (1)	Facility-Based Support (2)	Community-Based Support (3)
	N (%)	n (%)	n (%)
Infants of lactating women	46	68	61
Registered infant	38 (83)	66 (97)	56 (92)
Tested	23 (61)	61 (92)	51 (91)
Positive at enrollment	7 (20)	5 (11)	13 (27)
Positive after enrollment*	0	2	1
Infants of pregnant women	401	360	333
Birth status			
Live birth	285 (71)	316 (88)	292 (88)
Still birth	2 (0)	3 (1)	2 (1)
Early fetal loss	1 (0)	0 (0)	1 (0)
Unknown	113 (28)	41 (11)	38 (11)
Infant HIV test @ 6 weeks			
In care	273 (96)	289 (91)	286 (67)
Not tested	104 (38)	89 (31)	91 (32)
Tested	169 (62)	200 (69)	195 (68)
HIV status			
Negative	167 (99)	199 (99)	193 (99)
Positive	2 (1)	1 (1)	2 (2)
HIV status at 1 year			
In care	213 (78)	253 (88)	252 (88)
Not tested	76 (36)	51 (20)	81 (32)
Tested	137 (64)	202 (80)	171 (68)
HIV status			
Negative	136 (99)	200 (99)	171 (100)
Positive	1 (1)	2 (1)	0 (0)
HIV status at 2 years			
In care	85 (40)	124 (49)	112 (44)
Not tested	32 (38)	42 (34)	40 (40)
Tested	53 (62)	82 (66)	67 (60)
HIV status			
Negative	51 (96)	81 (99)	67 (100)
Positive	2 (4)	1 (1)	0 (0)

SOC, standard of care.

this was usually done through community tracing. However, the community-based also provided reminders to women before each visit. In addition, the peer-to-participant ratio was lower in the community-based arm. The finding that the facility-based peer support arm was as effective as the community-based support arm but less-intensive is noteworthy, suggesting that a less-intensive intervention is probably sufficient.

From these analyses, it is difficult to determine which aspects of each intervention were most influential in improving uptake and retention. In the facility-based arm, we observed frequent encounters between mentor mothers and clients, but somewhat lower uptake of support groups. In community-based, we observed somewhat lower than expected reminder visits and few support groups. In fact, some clinics did not have any support groups at all. In both interventions, more than half

of the missed visits resulted in a successful contact with a participant, and this success rate was somewhat higher in community-based than facility-based, especially during the first year. We speculate that contacting participants and encouraging them to come back to care was most effective for improved uptake and retention, as similar HIV back-to-care interventions have been observed in other sub-Saharan African settings. However, from these descriptive analyses, we are not able to make causal statements. Understanding causal mechanisms is the focus of a future secondary analysis. Our findings are consistent with an emerging body of work that task shifting,^{15,16} community tracing,¹⁷ and visit reminders¹⁸ can enhance retention in HIV programming.

This study's overall estimates of retention are considerably lower than those reported by the national HIV program. This difference is due to the study's more stringent definition of retention. In this study, women who defaulted and returned subsequently on ART were not reintroduced into the analysis, whereas in the national program they are registered as retained in care. This analytic decision was made based on the detrimental effect that periods without ART can have for both the mother and her infant. These observations suggest that a substantial portion of those retained in the national program may experience long periods without ART, a finding observed at a national level.¹⁹ Alternatively, these "missed visits" could actually be missed documentation.

Regardless of definition, retention was below the UNAIDS "90%" target. This suboptimal retention suggests that additional interventions are needed. In PURE qualitative work, it was observed that lack of male disclosure was a challenge,²⁰ and in the trial few men presented with their enrolled female partners. Addressing partner disclosure and male involvement is an area that may further enhance maternal retention, a finding observed in similar settings.^{16,21,22}

The conduct of the trial in a range of Malawian settings and populations is a strength of this study. PURE study was implemented in different types of clinics with both pregnant and breastfeeding women. Varied inclusiveness at the clinic and patient level allows for broad generalizability to the larger Option B+ program in Malawi. However, the study may not generalize to other settings with different health systems and patient barriers. Randomizing to clusters, rather than participants, is an additional strength of our trial. Previous similar studies evaluated peer-based programs in a nonrandomized fashion and suffer from self-selected intervention participants, many of whom are probably already good careseekers. Cluster randomized trials are sometimes prone to contamination of interventions especially when facilities that are close to each other. Our study addressed this problem by including facilities that are geographically far from each other, a phenomenon commonly observed when multiple interventions are coimplemented at the same facilities, and allows for full implementation of the intervention at the facilities.

Differential outcome ascertainment is one potential source of bias in this analysis. If mentor mothers or expert mothers supported documentation of treatment outcomes on clinical forms, the intervention arms could have had more positive outcomes ascertained. To mitigate against this,

outcomes documented by mentor or expert mothers were not used to determine retention in this analysis and mentor and expert mothers were not trained to document outcomes on clinical forms.

The results of the PURE trial have relevance for Malawi, and similar settings in sub-Saharan Africa. This study indicates that facility- and community-based peer support improve maternal uptake of ART and increase long-term retention in the national Option B+ program in Malawi compared with the national SOC. In our setting and similar settings with limited resources where health workers have high workload and less time for patient care and follow-up, alternative approaches such as peer support interventions could significantly improve maternal uptake of ART as well as long-term retention (on ART).

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