

# Retention in care of HIV-infected pregnant and lactating women starting ART under Option B+ in rural Mozambique

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## Abstract

**OBJECTIVE** In 2013, Mozambique adopted Option B+, universal lifelong antiretroviral therapy (ART) for all pregnant and lactating women, as national strategy for prevention of mother-to-child transmission of HIV. We analysed retention in care of pregnant and lactating women starting Option B+ in rural northern Mozambique.

**METHODS** We compared ART outcomes in pregnant ('B+ pregnant'), lactating ('B+ lactating') and non-pregnant non-lactating women of childbearing age starting ART according to clinical and/or immunological criteria ('own health') between July 2013 and June 2014. Lost to follow-up was defined as no contact >180 days after the last visit. Multivariable competing risk models were adjusted for type of facility (type 1 *vs.* peripheral type 2 health centre), age, WHO stage and time from HIV diagnosis to ART.

**RESULTS** Over 333 person-years of follow-up (243 'B+ pregnant', 65 'B+ lactating' and 317 'own health' women), 3.7% of women died and 48.5% were lost to follow-up. 'B+ pregnant' and 'B+ lactating' women were more likely to be lost in the first year (57% *vs.* 56.9% *vs.* 31.6%;  $P < 0.001$ ) and to have no follow-up after the first visit (42.4% *vs.* 29.2% *vs.* 16.4%;  $P < 0.001$ ) than 'own health' women. In adjusted analyses, risk of being lost to follow-up was higher in 'B+ pregnant' (adjusted subhazard ratio [asHR]: 2.77; 95% CI: 2.18–3.50;  $P < 0.001$ ) and 'B+ lactating' (asHR: 1.94; 95% CI: 1.37–2.74;  $P < 0.001$ ). Type 2 health centre was the only additional significant risk factor for loss to follow-up.

**CONCLUSIONS** Retention among PLW starting option B+ ART was poor and mainly driven by early losses. The success of Option B+ for prevention of mother-to-child transmission of HIV in rural settings with weak health systems will depend on specific improvements in counselling and retention measures, especially at the beginning of treatment.

**keywords** Option B+, prevention of mother-to-child transmission, HIV, retention in care, rural Southern Africa, women's health

## Introduction

Mozambique has one of the highest HIV prevalence in the world, reaching 10.8% among adults aged 15–49 years. Of the 190 000 infected children [1], more than 90% acquired HIV through vertical transmission. The risk of mother-to-child transmission (MTCT) of HIV can be reduced to <5% through a combination of preventive measures, including antiretroviral therapy (ART) for the expectant mother and her newborn child and hygienic delivery conditions [2, 3].

In 2013, WHO recommended Option B+ as the preferred strategy for the prevention of mother-to-child transmission (PMTCT) of HIV. Option B+ consists of lifelong ART for all HIV-infected pregnant and lactating women (PLW), irrespective of their clinical status or CD4 cell count. This strategy is expected to improve the clinical prognosis of HIV-infected women, to reduce the incidence of AIDS-related conditions and to significantly reduce MTCT [4, 5]. Most importantly, Option B+ simplifies PMTCT strategies and avoids the reliance on CD4 count measurements, which is an important barrier to the

timely initiation of ART in many rural African settings [6, 7]. Several studies have also shown its cost-effectiveness [8–12]. Despite initial optimistic data on retention in Malawi [13], other reports showed that high losses to follow-up (LTFU) and poor adherence to ART could be major drawbacks of this strategy [14, 15]. In a recent analysis of SolidarMed ART programs in Southern Africa, including health centres in rural Mozambique, LTFU in general HIV care, especially after the first visit, was extremely high [16]. Early LTFU is of particular importance as it also seems to be a bottleneck for retention in Option B+ [15].

Option B+ was adopted as the National PMTCT strategy by the Mozambican National HIV program in 2013. However, only few studies have assessed the challenges of implementing such a strategy in rural sub-Saharan African settings with poor and undersupplied healthcare systems [17]. We evaluated retention in care of PLW starting ART under Option B+ in rural Mozambique and compared their outcomes with those of women of childbearing age starting ART for their own health. We analysed retention in care from the start of the implementation of Option B+ in decentralised clinical settings in Mozambique, allowing early feedback to national health authorities. We also included a comparison with a historical cohort of pregnant women who started lifelong ART under Option A for their own health at Chronic Diseases Units/HIV clinics.

## Patients and methods

### Setting

Ancuabe District is situated in the northern Mozambican province of Cabo Delgado, where HIV infection accounts for at least 20% of the deaths in the province [18]. In Ancuabe District, about 125 000 people live in 64 villages and in Ancuabe town [19], of whom 5600 persons are estimated to be infected with HIV [20]. Ancuabe has no hospital but two big type 1 health centres (HC) and four peripheral type 2 HC, where two doctors and 48 healthcare providers work, including 12 midwives, eight of whom are trained to provide HIV care and treatment. Type 1 HC have inpatient services and are led by a physician, whereas peripheral type 2 HC only have outpatient services and are led by a non-physician clinician. Option B+ has been implemented in the three HC offering ART in Ancuabe since mid-June 2013, the two type 1 HC and the biggest type 2 HC. The catchment populations of the two type 1 HC are 30 394 (Ancuabe Town HC) and 40 600 (Metoro HC), and the type 2 HC (Meza HC) serves 14 568. Metoro HC has good road access,

whereas Ancuabe town and Meza HC have to be reached using unpaved roads. In 2013, PLW starting ART under Option B+ were prescribed zidovudine (AZT) + lamivudine (3TC) + efavirenz (EFV), whereas adults starting ART for their own health received AZT+3TC+nevirapine (NVP). From January 2014 onwards, tenofovir (TDF)+3TC+EFV was given to all ART-eligible individuals if not contraindicated. Infants born to mothers under Option B+ receive 4 weeks of AZT syrup. Since the start of Option B+, a one-stop strategy is implemented: PLW are seen by one of the midwives at an integrated antenatal clinic that includes HIV care. Four midwives were trained to give ART at Ancuabe, 3 in Metoro and 1 in Meza HC. All received comprehensive HIV care and treatment training as by the National HIV Program. Non-pregnant non-lactating HIV-infected women are attended at the Chronic Diseases Units/HIV clinics by a non-physician clinician. Before Option B+ implementation, pregnant women starting ART for their own health were also attended at Chronic Diseases Units/HIV clinics. Despite the different staffing, antenatal clinics and Chronic Diseases Units/HIV clinics were comparable as they were located in the same facility and provided daily service with similar availability of laboratory and treatment services. All HC offered point-of-care HIV testing at different testing points following national guidelines. CD4 testing was centralised at Ancuabe HC since mid-2012 where a PIMA<sup>®</sup> machine was located; CD4 samples from other HC were collected and transported to Ancuabe HC weekly. Adherence counselling was carried out by the ART prescriber and by HIV activists located at every antenatal and HIV clinic in the two type 1 HC and by a single HIV activist shared by the two clinics at the type 2 HC. The national HIV program recommends follow-up visits at 1 week after ART initiation and monthly thereafter for pregnant women and at 2 weeks, 1, 2 and 6 months and every 6 months thereafter for non-pregnant women [21]. Active tracing was started 2 weeks after a patient did not show up for a scheduled pick up of HIV drugs, according to national recommendations. It consisted of a home visit by an HIV activist. The same tracing procedure was followed for women seeking HIV care for their own health and for Option B+ women.

### Study population and data collection

We included all ART-naïve, HIV-infected women of childbearing age (15–50 years) who started ART between 1 July 2013 and 30 June 2014 in any of the three health centres providing Option B+ PMTCT in Ancuabe District. In a secondary analysis, we included

an additional group of pregnant women who received lifelong ART under Option A (those with CD4  $\leq$  350 and/or III or IV WHO stage) between January 2011 and June 2013 at the same HC. ART start and follow-up of pregnant women under option A were performed at the Chronic Diseases Units/HIV clinics. We did not include pregnant women starting prophylaxis with AZT from week 14 plus single dose NVP at onset of labour under option A (those with CD4 > 350 and I or II WHO stage) because data were not available. Most pregnant women received HIV testing and counselling at the antenatal care visit; lactating women were identified mainly when presenting at the clinic for infant follow-up or *post-partum* visit.

Routine programmatic data from patients starting ART were collected prospectively since 2009, in the framework of a collaboration between SolidarMed, a Swiss-based NGO, IeDEA (International Epidemiological Databases for Evaluation of AIDS) [22] and the Pemba Operational Research Nucleus. Data were collected from the medical charts by two trained data clerks using a Microsoft Access<sup>®</sup> database; patient data were anonymised to ensure privacy. The study received approval from the Mozambican National Bioethics Committee, and all patients provided written informed consent before the data were entered into the database. The study was also approved by the Operational Research Committee of SolidarMed.

To ensure quality of data, one of the investigators (JLG) checked the antenatal care clinic registries to ensure the pregnant/breastfeeding status of each woman was correctly recorded and performed a review of a sub-sample of patient charts. Data analyses were performed using SPSS 15.0 (SPSS inc, Chicago, IL, USA) and the R<sup>®</sup> 'cmprsk' package [23, 24].

### Outcomes and definitions

Patients who did not return to care for more than 180 days after their last visit were considered LTFU [25]. For the comparison with the historical cohort of Option A pregnant women, we used a prospective LTFU definition [26]. Patients who missed their first follow-up visit after ART start and did not return to care for more than 180 days were considered to have 'no follow-up after ART initiation' (NFU). Patients were followed from initiation of ART to the date of the outcome of interest (death, LTFU), or database closure (31 December 2014), whichever happened first. A sensitivity analysis was carried out using a 90-day definition for LTFU or NFU. Patients transferred out were considered as active and were censored at the time of the transfer. All

self-reported ART interruptions were recorded in the database. However, ART adherence was not assessed directly.

Participants were classified as follows:

- 'B+ pregnant': pregnant women starting ART under Option B+
- 'B+ lactating': breastfeeding women starting ART under Option B+
- 'Own health': non-pregnant non-lactating women starting ART following clinical (WHO stage III/IV) and/or immunological criteria (CD4 < 350 cells/mm<sup>3</sup>)
- 'A pregnant': pregnant women starting lifelong ART (triple ART) under Option A between January 2011 and June 2013.

### Statistical analyses

Baseline characteristics were compared between the different patient groups. Categorical variables were expressed as absolute frequencies and percentages. Continuous variables were expressed as means and standard deviation (SD) or medians and interquartile ranges (IQR). One sample Kolmogorov–Smirnov tests were performed to assess whether variables were distributed normally. Normally distributed numeric parameters were compared between groups using the *t*-test or ANOVA. Mann–Whitney *U*-test or Kruskal–Wallis tests were used for non-normal variables. Categorical variables were compared between groups using the Pearson chi-squared test or Fisher's exact test if the group was small.

Adjusted odds ratio (aOR) of NFU between women from the 'B+ pregnant', 'B+ lactating' and 'own health' groups were calculated using multivariable logistic regression. Probability of LTFU and death in each group were analysed using cumulative incidence functions (CIF) and significance evaluated with Gray's test [27]. Multivariable competing risk regression was used to model the adjusted subdistribution hazard ratio (asHR) of CIF as proposed by Fine and Gray [28, 29]. A second set of analyses using the same regression models was performed to compare outcomes between 'A pregnant' and 'B+ pregnant' women. All multivariable models were adjusted for type of facility (HC type 1 *vs.* type 2), age, WHO stage and time from HIV diagnosis to ART initiation. *P* values < 0.05 were considered statistically significant.

## Results

### Baseline characteristics

A total of 625 women of childbearing age started ART in Ancuabe District between July 2013 and June 2014. Of

these, 308 initiated ART under Option B+ (243 'B+ pregnant', 65 'B+ lactating') and 317 for their own health. Baseline characteristics were similar between B+ pregnant and B+ lactating women, except for time between HIV diagnosis and ART start, which was longer in lactating women (18 *vs.* 8 days) (Table 1). B+ pregnant were younger ( $P < 0.001$ ), had higher baseline CD4 cell counts ( $P < 0.001$ ) and were less likely to be in WHO stage III or IV ( $P < 0.001$ ) than women in the 'own health' group. Time between HIV diagnosis and ART start was longest in the 'own health' group (44 days). CD4 availability was higher in the 'own health' group (82.0%) than in the 'B+ pregnant' (39.1%) and the 'B+ lactating' (56.9%) groups (Table 1).

### Retention in the different study groups

Over 333 women-years of follow-up, 3.7% of women died and 48.5% were LTFU. Among the latter, 25.6% were lost after the first visit (NFU). Median follow-up was 47 (IQR: 1–245) days in 'B+ pregnant', 185 (1–399) in 'B+ lactating' and 239 (59–399) days in the 'own health' group. Overall 1-year retention was 61.9% in women treated for their own health, 40.4% in the B+ lactating group and 41.8% in the 'B+ pregnant' group (Figure 1). Death occurred in 6.3% of women in the 'own health' group, 2.7% in the 'B+ lactating' group and 1.2% in the 'B+ pregnant' group ( $P < 0.001$ ). B+ pregnant and lactating women were more likely to be LTFU in the first year (57% *vs.* 56.9% *vs.* 31.6%;  $P < 0.001$ ) and to have no follow-up after the first visit (42.4% *vs.* 29.2% *vs.* 16.4%;  $P < 0.001$ ) than women starting ART for their own health. Figure 2 shows the cumulative incidence of death and LTFU in the three study groups.

In adjusted analyses, the risk of LTFU was higher in B+ pregnant women (asHR: 2.77; 95% CI: 2.18–3.50;  $P < 0.001$ ) and B+ lactating women (asHR: 1.94; 95% CI: 1.37–2.74;  $P < 0.001$ ) than those who initiated ART for their own health (Table 2). Women who started ART at a peripheral type 2 HC were also more likely to be LTFU (asHR: 1.45; 95% CI: 1.17–1.80;  $P = 0.002$ ). The risk of NFU was higher in B+ lactating women (aOR: 2.36; 95% CI 1.23–4.52;  $P = 0.01$ ) and B+ pregnant women (aOR: 4.07; 95% CI 2.53–6.56;  $P < 0.001$ ) than women in the 'own health' group. A sensitivity analysis using the 90-day LTFU definition yielded similar results (Tables S1 and S2). A sensitivity analysis adjusted by individual health centre showed no differences between the two type 1 HC (Table S4).

When we compared the two groups of women starting ART under Option B+, B+ pregnant women tended to be more likely to have NFU (42.4% *vs.* 29.2%; aOR 1.73,

95% CI 0.95–3.17;  $P = 0.07$ ) and to be LTFU (67.5% *vs.* 55.4%; asHR 1.2; 95% CI: 1.03–1.96;  $P = 0.03$ ) than B+ lactating women.

### Comparison of outcomes with historical Option A cohort

Seventy-four pregnant women started ART under Option A between January 2011 and June 2013. Pregnant women under Option A were less likely to have started ART at a peripheral type 2 HC ( $P < 0.001$ ) but were more likely to have WHO stage III/IV ( $P < 0.001$ ) or an available CD4 cell count ( $P < 0.001$ ) than 'B+ pregnant' women (Table 1). B+ pregnant women had higher baseline CD4 cell counts ( $P < 0.001$ ) and a shorter time from HIV diagnosis to ART initiation (8 *vs.* 51 days;  $P < 0.001$ ). In adjusted analyses, B+ pregnant women were more likely to be LTFU (asHR: 1.91; 95% CI: 1.40–2.60;  $P < 0.001$ ) and to have NFU (aOR: 3.33; 95% CI 1.50–7.40;  $P = 0.003$ ) than pregnant women on ART under Option A (Table 3). A sensitivity analysis using the 90-day LTFU definition yielded similar results (Table S3).

We performed a subgroup analysis comparing pregnant women starting ART under Option A ( $n = 74$ ) with the subgroup of B+ pregnant women that fulfilled clinical and/or immunological criteria for starting ART for their own health (those with CD4 < 350 and/or WHO stage III/IV;  $n = 23$ ). In adjusted analyses, B+ pregnant women with clinical and/or immunological criteria for ART start were still more likely to have NFU (aOR: 3.61; 95% CI 1.15–11.33;  $P = 0.03$ ) than pregnant women on ART under Option A (Table S5).

### Discussion

In rural Mozambique, pregnant women who started ART under option B+ were three times as likely to be LTFU as women treated for their own health. A large proportion of those losses occurred early: close to half of them did not return to the clinic after the day of ART initiation. Compared to outcomes from a historical cohort of option A pregnant women on ART, the risk of NFU was more than three times higher in B+ pregnant women.

Less than half of the B+ women were retained in care during the first year after ART start. These estimates remained similar when using a more stringent definition of LTFU (90 days). High LTFU rates have been described in pregnant women under option A and B [30, 31], therefore suggesting that some of the factors underlying this poor retention may be a general problem of PMTCT and not specific to Option B+. However, the higher LTFU rate found in pregnant women starting ART under Option B+ compared to those starting under Option A

**Table 1** Characteristics of pregnant and lactating women starting antiretroviral therapy (ART) under Option B+, women of childbearing age starting ART for their own health and pregnant women starting lifelong ART under Option A

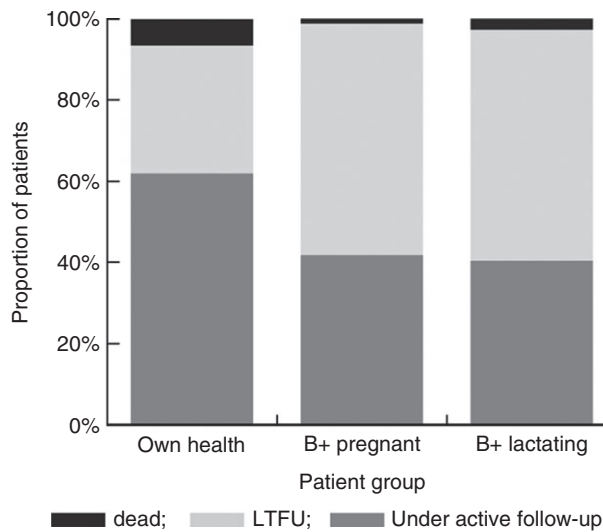
|   | B+ pregnant<br>( <i>n</i> = 243) | B+ lactating<br>( <i>n</i> = 65) | <i>P</i> * | Own health<br>( <i>n</i> = 317) | <i>P</i> † | A pregnant<br>( <i>n</i> = 74) | <i>P</i> ‡ |
|---|----------------------------------|----------------------------------|------------|---------------------------------|------------|--------------------------------|------------|
| Followed at a type 1 HC (%)                                     | 179 (73.7)                       | 45 (69.2)                        | 0.48       | 219 (69.1)                      | 0.24       | 71 (95.9)                      | <0.001     |
| HC  |                                  |                                  |            |                                 |            |                                |            |
| Ancuabe   | 53                               | 17                               | 0.45       | 119                             | <0.001     | 46                             | <0.001     |
| Metoro  | 126                              | 28                               |            | 100                             |            | 21                             |            |
| Meza  | 64                               | 20                               |            | 98                              |            | 3                              |            |
| NA  | 0                                | 0                                |            | 0                               |            | 4                              |            |
| WHO stage III/IV (%)  | 8 (3.3)                          | 4 (6.2)                          | 0.39       | 117 (36.9)                      | <0.001     | 27 (36.5)                      | <0.001     |
| CTX prophylaxis (%)   | 187 (77.0)                       | 40 (61.5)                        | 0.01       | 275 (86.8)                      | 0.002      | 58 (78.4)                      | 0.798      |
| Median age in years(IQR)  | 24 (20–30)                       | 25 (20–30)                       | 0.55       | 30 (24–37)                      | <0.001     | 26 (23–30)                     | 0.120      |
| Baseline CD4 available (%)                                      | 95 (39.1)                        | 37 (56.9)                        | 0.01       | 260 (82.0)                      | <0.001     | 48 (64.9)                      | <0.001     |
| Median CD4 count<br>in cells/mm <sup>3</sup> (IQR)              | 495 (373–664)                    | 593 (317–795)                    | 0.52       | 276 (158–395)                   | <0.001     | 358 (251–579)                  | <0.001     |
| Mean BMI at ART start<br>in kg/m <sup>2</sup> (SD)              | 22.21 ± 3.08                     | 21.25 ± 2.87                     | 0.07       | 20.02 ± 3.06                    | <0.001     | 23.10 ± 3.95                   | 0.059      |
| Mean Hb level in g/dl (SD)                                      | 9.97 ± 1.50                      | 10.48 ± 1.66                     | 0.13       | 9.86 ± 1.97                     | 0.61       | 10.79 ± 1.43                   | 0.173      |
| Median time from HIV<br>diagnosis to ART start in<br>days (IQR) | 8 (0–27)                         | 18 (4–120)                       | 0.001      | 44 (19–154)                     | >0.001     | 51 (23–114)                    | >0.001     |

BMI, body mass index; CTX, co-trimoxazole; Hb, haemoglobin; HC, health centres; NA, not available; IQR, interquartile range; SD, standard deviation.

\*Comparison of 'B+ pregnant *vs.* B+ lactating'.

†Comparison of 'B+ pregnant' *vs.* 'Own health'.

‡Comparison of 'B+ pregnant' *vs.* 'A pregnant'.

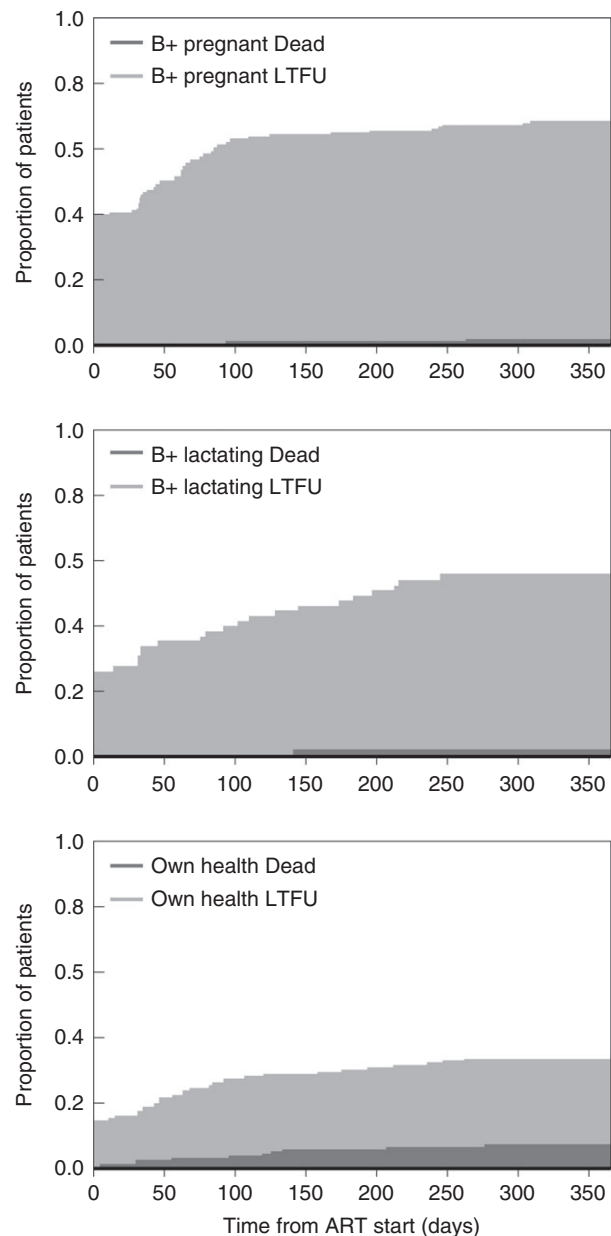


**Figure 1** One-year outcomes in women starting antiretroviral therapy (ART) for their own health, B+ lactating women and B+ pregnant women according to competing risk estimates. LTFU: lost-to-follow-up.

may suggest that there could be factors specific to this new strategy, such as the lack of sufficiently trained staff or the short time between HIV diagnosis and ART start (32% of B+ PLW were started on ART on the day of diagnosis). Improvement of the District HIV program (ART regimens, CD4 availability) with time should have in any case benefited retention of Option B+ women. Importantly, most LTFU were very early losses (NFU), possibly related to the short time between diagnosis and ART start, perhaps indicating that many of those women never started ART.

We found higher overall LTFU rates than other studies [14, 15] but similar to previous reports from this rural setting and from other regions in Mozambique, where a high and increasing attrition rate during the ART expansion process in the country has been reported [32]. Undocumented transfers [33] or deaths could also partly explain this very high LTFU rate. Health system factors such as high direct and indirect costs of receiving care and insufficient expansion in the number of health staff could also have played a major role [34]. Although capacity building and task shifting were implemented through various trainings, midwives still had very little experience in ART initiation and supervision was scarce.

Stigma and absence of community support may also have negatively contributed to attrition [35]. In Mozambique, a strategy of community ART distribution through self-forming groups of patients was shown to be quite successful [36–38], but pregnant women are excluded



**Figure 2** Cumulative incidence of lost-to-follow-up (LTFU) and death in B+ pregnant women, B+ lactating women and women starting ART for their own health. ART: antiretroviral therapy; LTFU: lost-to-follow-up.

from these groups as they need close clinical follow-up. Despite the common counselling policy for all groups, more experienced counsellors and longer time available for counselling in the Chronic Diseases Units/HIV clinics may have contributed to the lower attrition rate of women seeking HIV care for their own health and

**Table 2** Predictors of no follow-up (NFU) and lost to follow-up (LTFU) after start of antiretroviral therapy (ART) during the July 2013 and June 2014 period using a 180-day definition to consider a patient LTFU or NFU

|                                      |                   | Multivariable (adjusted) analyses |         |                  |         |
|--------------------------------------|-------------------|-----------------------------------|---------|------------------|---------|
|                                      |                   | NFU                               |         | LTFU             |         |
|                                      |                   | aOR (95% CI)                      | P-value | asHR (95% CI)    | P-value |
| ART group                            | Own health        | Reference                         |         | Reference        |         |
|                                      | B+ pregnant       | 4.07 (2.53–6.56)                  | <0.001* | 2.77 (2.18–3.50) | <0.001* |
|                                      | B+ lactating      | 2.36 (1.23–4.52)                  | 0.01*   | 1.94 (1.37–2.74) | <0.001* |
| WHO stage                            | I or II           | Reference                         | 0.14    | Reference        | 0.77    |
|                                      | III or IV         | 1.50 (0.87–2.60)                  |         | 1.05 (0.75–1.47) |         |
| Time from HIV diagnosis to ART start | >10 days          | Reference                         | 0.35    | Reference        | 0.13    |
|                                      | ≤10 days          | 1.22 (0.80–1.84)                  |         | 1.19 (0.95–1.50) |         |
| Age                                  | >25 years         | Reference                         | 0.97    | Reference        | 0.73    |
|                                      | ≤25 years         | 1.01 (0.69–1.47)                  |         | 0.96 (0.78–1.20) |         |
| HC type                              | Type 1            | Reference                         | 0.31    | Reference        | <0.001* |
|                                      | Peripheral type 2 | 1.23 (0.82–1.84)                  |         | 1.45 (1.17–1.80) |         |

HC, health centres.

\*Statistically significant.

**Table 3** Predictors of no follow-up (NFU) and lost to follow-up (LTFU) after start of ART when comparing pregnant women starting antiretroviral therapy (ART) under Option A and under Option B+ using a 180-day definition to consider a patient LTFU or NFU

|                                      |                   | Multivariable (adjusted) analysis |         |                  |         |
|--------------------------------------|-------------------|-----------------------------------|---------|------------------|---------|
|                                      |                   | NFU                               |         | LTFU             |         |
|                                      |                   | aOR (95% CI)                      | P-value | asHR (95% CI)    | P-value |
| Start of ART under                   | Option A          | Reference                         | 0.003*  | Reference        | <0.001* |
|                                      | Option B+         | 3.33 (1.50–7.40)                  |         | 1.91 (1.40–2.60) |         |
| WHO stage                            | I or II           | Reference                         | 0.29    | Reference        | 0.51    |
|                                      | III or IV         | 0.56 (0.19–1.67)                  |         | 0.86 (0.55–1.35) |         |
| Time from HIV diagnosis to ART start | >10 days          | Reference                         | 0.52    | Reference        | 0.12    |
|                                      | ≤10 days          | 1.18 (0.71–1.95)                  |         | 1.23 (0.95–1.60) |         |
| Age                                  | >25 years         | Reference                         | 0.58    | Reference        | 0.52    |
|                                      | ≤25 years         | 0.87 (0.53–1.42)                  |         | 0.92 (0.72–1.18) |         |
| HC type                              | Type 1            | Reference                         | 0.55    | Reference        | 0.16    |
|                                      | Peripheral type 2 | 1.19 (0.67–2.11)                  |         | 1.23 (0.92–1.63) |         |

HC, health centres.

\*Statistically significant.

Option A pregnant women. Active tracing was designed following national recommendations but was inconsistently done due to lack of transport and staff. No specific tracing strategy was designed for B+ women. Our results suggest that an improved and focused tracing strategy may be needed for Option B+ women.

We found better retention of B+ lactating women compared to B+ pregnant women. Other studies have also reported a higher attrition rate in pregnant women [15]. Women who start while lactating are probably a selection of those who are more motivated for ART so are more

likely to be retained, as opposed to those who start during pregnancy who would be more likely to just take treatment until the baby is born.

Our study is among the first ones to compare retention of pregnant women starting ART before and after Option B+ implementation. One of the main limitations of most studies assessing outcomes of Option B+ is their inability to compare results with those of pregnant women in option A during the same time period. We tried to address this gap by comparing our results with women under option A before B+ started. Protocols in terms of testing procedures,

notification of results or subsequent tracing did not differ between Option B+ and Option A women. The main differences between Option A and B+ were therefore the type of staff and clinic where they were attended as well as the recommendation to initiate early ART after diagnosis. We performed a subgroup analysis including only B+ pregnant women that would have been eligible for ART under Option A; differences in retention in that subgroup analysis may be mostly attributable to implementation and programmatic factors (such as limited and poorly trained staff or very early ART without proper counseling). However, residual confounding may still be important. Unfortunately, outcomes of Option A pregnant women not eligible for ART could not be assessed as only data from patients on ART were available. We also did not have data on women LTFU before ART initiation. In a large Mozambican study, only 31% of eligible individuals started ART within 90 days [39]; Option B+ may have reduced these pre-ART dropouts at the expense of higher rates of LTFU among patients in HIV care. Another limitation of our study was that we were not able to determine whether pregnant women were LTFU before or after birth. Other studies have suggested worse adherence in the post-partum period pointing out the need for retention measures adapted to post-delivery situations [30, 40]. Unfortunately, we could not analyse outcomes according to CD4 values as these were often missing. Information about education, ethnicity, marital status or household socioeconomic status of women, which could be a valuable addition to understanding potential reasons for LTFU, was not available. Finally, our cohort was limited to a single rural district, and therefore, our results may not be generalisable at the country level.

The high rate of LTFU described in our study could have severe consequences in terms of vertical transmission of HIV. Community-driven approaches or family-focused approaches could improve retention of pregnant women [41, 42]. Community ART dispensing programs have shown to improve retention of HIV-infected patients in many sub-Saharan African countries [43] but adapted solutions for PLW should be sought. Health system strengthening and ensuring that sufficient workforce is available are key for this PMTCT strategy in such settings. Although the one-stop strategy has unquestionable advantages for PLW, limited availability of trained health staff may hamper its success and lead to worse retention rates when compared to those in ART clinics [44]. Future research should evaluate bottlenecks in the HIV care cascade and factors affecting retention to help design strategies to address high attrition in these women.

## Conclusions

Our study shows very high proportions of early losses to follow-up in patients initiating ART under the option B+ strategy in rural Mozambique. These results underline some of the challenges related to the implementation of this strategy in settings with weak healthcare systems, insufficient ART counselling and retention measures. Our findings support the need for innovative strategies to improve retention as well as new service delivery models to address the barriers to successful HIV care for PLW.

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**Supporting Information**

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Lost-to-follow-up (LTFU) of pregnant and lactating women starting antiretroviral therapy (ART) under

option B+, women of childbearing age starting ART for their own health and pregnant women starting ART under Option A using a 90-days definition.

**Table S2.** Predictors of no-follow-up (NFU) and lost-to-follow-up (LTFU) after start of antiretroviral therapy (ART) during July 2013–June 2014 period using a 90-days definition for LTFU and NFU.

**Table S3.** Predictors of no-follow-up (NFU) and lost-to-follow-up (LTFU) after start of antiretroviral therapy (ART) when comparing pregnant women starting ART under option A and under option B+ using a 90-days definition for LTFU and NFU.

**Table S4.** Predictors of no-follow-up (NFU) and lost-to-follow-up (LTFU) after start of antiretroviral therapy (ART) during July 2013–June 2014 period adjusted by health center (HC) using a 180-days definition for LTFU and NFU.

**Table S5.** Predictors of no-follow-up (NFU) and lost-to-follow-up (LTFU) after start of antiretroviral therapy (ART) when comparing Option A pregnant women and Option B+ pregnant women with clinical and/or immunological criteria for starting ART for their own health. We used a 180-days definition for LTFU and NFU.

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