# Article Type: Original Article

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

Jara Llenas-García<sup>1</sup>, Philip Wikman-Jorgensen<sup>1</sup>, Michael Hobbins<sup>2</sup>, Manuel Aly Mussa<sup>3</sup>, Jochen Ehmer<sup>2</sup>, Olivia Keiser<sup>4</sup>, Francisco Mbofana<sup>5</sup>, Gilles Wandeler<sup>4,6</sup>, for SolidarMed and IeDEA-Southern Africa

<sup>1</sup>SolidarMed, Ancuabe, Mozambique
 <sup>2</sup>SolidarMed, Luzern, Switzerland
 <sup>3</sup>Health Provincial Directorate, Operational Research Nucleus of Pemba, Pemba, Mozambique
 <sup>4</sup>Institute of Social and Preventive Medicine, University of Bern, Switzerland
 <sup>5</sup>National Health Institute, Maputo, Mozambique
 <sup>6</sup>Department of Infectious Diseases, University Hospital Bern, Switzerland

# 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 analyzed 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 after 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 center), age, WHO stage and time from HIV diagnosis to ART.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/tmi.12728

**Results:** Over 333 person-years of follow-up (of 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 center was the only additional significant risk factor for loss to follow-up.

**Conclusions:** Retaining pregnant and lactating women in option B+ ART was poor; losses to followup were mainly early. 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 counseling and retention measures, especially at the beginning of treatment.

Keywords: Option B+; PMTCT; HIV; retention in care; rural Southern Africa; women's health

#### INTRODUCTION

Mozambique has one of the highest HIV prevalences in the world, reaching 10.8% among adults aged 15 to 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 motherto-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 AIDSrelated 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 centers 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 health care 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 analyzed retention in care from the start of the implementation of Option B+ in decentralized 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 5,600 persons are estimated to be infected with HIV (20). Ancuabe has no hospital but two big type 1 health centers (HC) and 4 peripheral type 2 HC, where two doctors and 48 health care providers work, including 12 midwives, 8 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 nonphysician 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 HCs 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 Option B+ started, 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. Nonpregnant nonlactating HIV-

infected women are attended at the Chronic Diseases Units/HIV clinics by a nonphysician 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 centralized at Ancuabe HC since mid 2012 where a PIMA® machine was located; CD4 samples from other HC were collected and transported to Ancuabe HC weekly. Adherence counselling was done 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 nonpregnant women (21). Active tracing was started two 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 1st July 2013 and 30th June 2014 in any of the three health centers 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 <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 done 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 anonymized 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 subsample of patient charts. Data analyses were done using SPSS 15.0 (SPSS inc, Chicago, Illinois) and the R© "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<sup>st</sup> 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:

- "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 ARVs) under Option A betweenJanuary 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 if 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 analyzed using cumulative incidence functions (CIF) and significance evaluated with Gray's test (27). Multivariable competing risk regression was used to model the adjusted sub-distribution hazard ratio (asHR) of CIF as proposed by Fine and Gray (28, 29). A second set of analyses using the same regression models were 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**

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 CD4cell counts (p<0.001) and were less likely to be inWHO 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 (interquartile range [ (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 days LTFU definition yielded similar results (Suppl. Tables 1 and 2; Supplemental Material). A sensitivity analysis adjusted by individual health center showed no differences between the two type 1 HCs (Suppl. Table 4, Supplemental Material).

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) or to have an available CD4 cell count (p<0.001) but were more likely to have WHO stage III/IV (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 (Suppl. Table 3; Supplemental Material).

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 be NFU (aOR: 3.61; 95% CI 1.15-11.33; p=0.03) than pregnant women on ART under Option A (Suppl. Table 5; Supplemental Material).

#### 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 triple 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, 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 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 the day they were diagnosed). Improvement of the District HIV program (ART regimens, CD4 availability) with time should have in any case benefited retention of Option B+ women. We would like to point out that most LTFU were very early losses (NFU), possibly related to the short time between diagnosis and ART start, and possibly indicating that many of those women never even got ART started.

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 was 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 retention (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 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 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. 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 an insufficient and not enough experienced staff or a very early ART start without proper counselling and address of adherence obstacles). 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 drop-outs 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 if pregnant women were LTFU before or after birth. Other studies have suggested worse adherence in the postpartum period pointing out the need for retention measures adapted to post-delivery situations (30, 40). Unfortunately, we could not analyze outcomes according to CD4 values as these were often missing. Information about education, ethnicity, marital status or household socioeconomic status of women, that 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 generalizable 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 availableare key for this PMTCT strategy in such settings. Although the one-stop strategy has unquestionable advantages for PLW, shortage of sufficient skilled 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 health care systems, insufficient ART counseling 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.

## ACKNOWLEDGEMENTS

We thank all the patients, doctors and nurses in the participating health centers. We would like to thank especially Dr. María Bolacha, medical chief officer of Ancuabe district and Agira laquite, SolidarMed maternal and neonatal health nurse for their support in the field. Parts of the data were presented at the 8th IAS Conference, Vancouver, 19-22 July 2015 and at the 9th ECTMIH, Basel, 6-10 September 2015.

# References

- 1. UNAIDS. Mozambique. Epidemiological Fact Sheet. 2013.
- 2. UNICEF. Preventing mother-to-child transmission (PMTCT) of HIV. Eastern and Southern Africa.
- Shapiro RL, Hughes MD, Ogwu A, Kitch D, Lockman S, Moffat C, et al. Antiretroviral regimens in pregnancy and breast-feeding in Botswana. N Engl J Med. 2010;362 (24):2282-94.
- Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. N Engl J Med. 2015;373 (9):795-807.
- 5. WHO. Use of Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. : WHO Library Cataloging-in-Publication Data; April 2012.
- 6. Schouten EJ, Jahn A, Midiani D, Makombe SD, Mnthambala A, Chirwa Z, et al. Prevention of mother-to-child transmission of HIV and the health-related Millennium Development Goals:

3. 4 time for a public health approach. Lancet. 2011;378 (9787):282-4.

- Schouten EJ, Jahn A, Chimbwandira F, Harries AD, Van Damme W. Is Option B+ the best choice? Lancet. 2013;381 (9874):1272-3.
- O'Brien L, Shaffer N, Sangrujee N, Abimbola TO. The incremental cost of switching from Option B to Option B+ for the prevention of mother-to-child transmission of HIV. Bull World Health Organ. 2014;92 (3):162-70.
- Ishikawa N, Shimbo T, Miyano S, Sikazwe I, Mwango A, Ghidinelli MN, et al. Health outcomes and cost impact of the new WHO 2013 guidelines on prevention of mother-to-child transmission of HIV in Zambia. PLoS One. 2014;9 (3):e90991.
- 10. Gopalappa C, Stover J, Shaffer N, Mahy M. The costs and benefits of Option B+ for the prevention of mother-to-child transmission of HIV. Aids. 2014;28 Suppl 1:S5-14.
- Fasawe O, Avila C, Shaffer N, Schouten E, Chimbwandira F, Hoos D, et al. Cost-effectiveness analysis of Option B+ for HIV prevention and treatment of mothers and children in Malawi. PLoS One. 2013;8 (3):e57778.
- Ciaranello AL, Perez F, Engelsmann B, Walensky RP, Mushavi A, Rusibamayila A, et al. Costeffectiveness of World Health Organization 2010 guidelines for prevention of mother-to-child HIV transmission in Zimbabwe. Clin Infect Dis. 2013;56 (3):430-46.
- Impact of an innovative approach to prevent mother-to-child transmission of HIV--Malawi, July
   2011-September 2012. MMWR Morb Mortal Wkly Rep. 2013;62 (8):148-51.
- Koole O, Houben RM, Mzembe T, Van Boeckel TP, Kayange M, Jahn A, et al. Improved retention of patients starting antiretroviral treatment in karonga district, northern Malawi, 2005-2012. J Acquir Immune Defic Syndr. 2014;67 (1):e27-33.
- 15. Tenthani L, Haas AD, Tweya H, Jahn A, van Oosterhout JJ, Chimbwandira F, et al. Retention in
   care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women
   ('Option B+') in Malawi. Aids. 2014;28 (4):589-98.
- 16. Wandeler G, Keiser O, Pfeiffer K, Pestilli S, Fritz C, Labhardt ND, et al. Outcomes of antiretroviral treatment programs in rural Southern Africa. J Acquir Immune Defic Syndr. 2012;59 (2):e9-16.
- Bhardwaj S, Carter B, Aarons GA, Chi BH. Implementation Research for the Prevention of Mother-to-Child HIV Transmission in Sub-Saharan Africa: Existing Evidence, Current Gaps, and New Opportunities. Curr HIV/AIDS Rep. 2015;12 (2):246-55.
- Health Mo. National Survey of Prevalence, Behavioral Risks, and Information about HIV and AIDS in Mozambique. Maputo: Ministry of Health; 2009.
- INE. Estatísticas do Distrito de Ancuabe. Maputo, Moçambique: Instituto Nacional de Estatística;
   2012. p. 1-32.

- 20. Abubacar A, Macurire Z, David L, Santana J, Mopola E, Nacir S, et al. Relatorio da supervisão específica dos programas de ITS/HIV/SIDA, PTV e TB. Pemba, Mozambique2012.
- Bastos R, Manuel R, Osman N, Nunes E, Fonseca T, Fernandes A, et al. Guia de Tratamento Antiretroviral e Infecções Oportunistas no Adulto, Adolescente e Grávida 2010/2011. Maputo: Ministério da Saúde. Direcção Naional de Assistência Médica; 2011.
- Egger M, Ekouevi DK, Williams C, Lyamuya RE, Mukumbi H, Braitstein P, et al. Cohort Profile: the international epidemiological databases to evaluate AIDS (IeDEA) in sub-Saharan Africa. Int J Epidemiol. 2012;41 (5):1256-64.
- 23. Team RC. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2014.
- 24. Gray B. cmprsk: Subdistribution Analysis of Competing risks. R package version 2. 2-7. 2014.
- 25. Chi BH, Yiannoutsos CT, Westfall AO, Newman JE, Zhou J, Cesar C, et al. Universal definition of loss to follow-up in HIV treatment programs: a statistical analysis of 111 facilities in Africa, Asia, and Latin America. PLoS Med. 2011;8 (10):e1001111.
- Johnson LF, Estill J, Keiser O, Cornell M, Moolla H, Schomaker M, et al. Do increasing rates of loss to follow-up in antiretroviral treatment programs imply deteriorating patient retention? Am J Epidemiol. 2014;180 (12):1208-12.
- Scrucca LS, A Aversa, F. Competing risk analysis using R: an easy guide for clinicians. Bone Marrow Transplant. 2007;40 (4):381-7.
- 28. Scrucca LS, A Aversa, F. Regression modeling of competing risk using R: an in depth guide for clinicians. Bone Marrow Transplant. 2010;45 (9):1388-95.
- 29. Fine J, Gray R. A proportional hazards model for the subdistribution of a competing risk. Journal of the American Statistical Association. 1999;94:496-509.
- 30. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. Aids. 2012;26 (16):2039-52.
- Wettstein C, Mugglin C, Egger M, Blaser N, Vizcaya LS, Estill J, et al. Missed opportunities to prevent mother-to-child-transmission: systematic review and meta-analysis. AIDS. 2012;26 (18):2361-73.
- 32. Auld AF, Mbofana F, Shiraishi RW, Sanchez M, Alfredo C, Nelson LJ, et al. Four-year treatment outcomes of adult patients enrolled in Mozambique's rapidly expanding antiretroviral therapy program. PLoS One. 2011;6 (4):e18453.
- 33. Caluwaerts C, Maendaenda R, Maldonado F, Biot M, Ford N, Chu K. Risk factors and true outcomes for lost to follow-up individuals in an antiretroviral treatment programme in Tete,

Mozambique. Int Health. 2009;1 (1):97-101.

- 34. Kieffer MP, Mattingly M, Giphart A, van de Ven R, Chouraya C, Walakira M, et al. Lessons
  Learned From Early Implementation of Option B+: The Elizabeth Glaser Pediatric AIDS
  Foundation Experience in 11 African Countries. J Acquir Immune Defic Syndr. 2014;67 (Suppl 4):S188-94.
- 35. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. J Int AIDS Soc. 2013;16 (1).
- 36. Decroo T, Telfer B, Biot M, Maïkéré J, Dezembro S, Cumba LI, et al. Distribution of antiretroviral treatment through self-forming groups of patients in Tete Province, Mozambique. J Acquir Immune Defic Syndr. 2011;56 (2):e39-44.
- 37. Pestilli S, Llenas-Garcia J, Larsson E, Hobbins M, Ehmer J, Wikman P. Self -help groups of HIV patients may increase retention in care in Northern Mozambique. 7th IAS; Kuala Lumpur2013.
- Decroo T, Koole O, Remartinez D, dos Santos N, Dezembro S, Jofrisse M, et al. Four-year retention and risk factors for attrition among members of community ART groups in Tete, Mozambique. Trop Med Int Health. 2014;19 (5):514-21.
- 39. Micek MAG-S, Kenneth Baptista, Alberto Joao Matediana, Eduardo Montoya, Pablo Pfeiffer, James Melo, Armando Gimbel-Sherr, Sarah Johnson, Wendy Gloyd, Stephen. Loss to follow-up of adults in public HIV care systems in central Mozambique: identifying obstacles to treatment. J Acquir Immune Defic Syndr. 2009;52 (3):397-405.
- 40. Phillips T, Thebus E, Bekker LG, McIntyre J, Abrams EJ, Myer L. Disengagement of HIV-positive pregnant and postpartum women from antiretroviral therapy services: a cohort study. J Int AIDS Soc. 2014;17 (1).
- Myer L, Abrams EJ, Zhang Y, Duong J, El-Sadr WM, Carter RJ. Family Matters: Co-enrollment of Family Members Into Care Is Associated With Improved Outcomes for HIV-Infected Women Initiating Antiretroviral Therapy. J Acquir Immune Defic Syndr. 2014;67 (Suppl 4):S243-9.
- 42. Hodgson I, Plummer ML, Konopka SN, Colvin CJ, Jonas E, Albertini J, et al. A Systematic Review of Individual and Contextual Factors Affecting ART Initiation, Adherence, and Retention for HIV-Infected Pregnant and Postpartum Women. PLoS One. 2014;9 (11).
- Bemelmans M, Baert S, Goemaere E, Wilkinson L, Vandendyck M, van Cutsem G, et al.
   Community-supported models of care for people on HIV treatment in sub-Saharan Africa. Trop Med Int Health. 2014;19 (8):968-77.
- 44. van Lettow M, Bedell R, Mayuni I, Mateyu G, Landes M, Chan AK, et al. Towards elimination of mother-to-child transmission of HIV: performance of different models of care for initiating

lifelong antiretroviral therapy for pregnant women in Malawi (Option B+). J Int AIDS Soc. 2014;17:18994.

**Corresponding author:** Jara Llenas-García, SolidarMed: Swiss Organization for Health in Africa, Obergrundstrasse 97, 6005 Luzern, Switzerland. Phone +34-65-2584257, email jarallenas@gmail. com

	B+ pregnant	B+ lactating	p1	Own health	p²	A pregnant	p³
	(n=243)	(n=65)		(n=317)		(n=74)	
Followed at a type	179 (73.7%)	45(69.2%)	0.48	219 (69.1%)	0.24	71(95.9%)	<0.001
1 HC (%)							
Ancuabe	53	17		119		46	
HC Metoro	126	28	0.45	100	<0.001	21	<0.001
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 avail- able (%)	95 (39.1)	37(56.9%)	0.01	260(82.0%)	<0.001	48(64.9%)	<0.001
Median CD4 count	495 (373-	593 (317-	0.52	276 (158-	<0.001	358 (251-	<0.001
in cell/mm <sup>3</sup> (IQR)	664)	795)		395)		579)	
Mean BMI at ART start 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 diagnosis to ART start in days	8 (0-27)	18 (4-120)	0.001	44 (19-154)	<0.001	51(23-114)	<0.001
(IQR)							

**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. <sup>1</sup>: for the comparison B+ pregnant vs. B+ lactating; <sup>2</sup>: for the comparison "B+ pregnant" vs. "Own health". <sup>3</sup>: for the comparison "B+ pregnant" vs. "A pregnant". BMI: body mass index; CTX: co-trimoxazole; Hb: hemoglobin; HC: health center; NA: not available; IQR: interquartile range; sd: standard deviation

-			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	l or ll	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	>10 days	Reference	0.35	Reference	0.13	
	to ART start	≤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*	
Y		Peripheral type 2	1.23 (0.82-1.84)		1.45 (1.17-1.80)		

**Table 2.** Predictors of no-follow-up (NFU) and lost-to-follow-up (LTFU) after start of antiretroviral therapy (ART) during theJuly 2013 and June 2014 period using a 180-days definition to consider a patient LTFU or NFU. HC: health center; \*: statistically significant

		Multivariable (adjusted) analysis					
		NFU		LTFU			
		aOR (95% CI)	p value	asHR (95% CI)	p value		
Start of ART under	Option A	Reference	0.002*	Reference	<0.001*		
	Option B+	3.33 (1.50-7.40)	0.003*	1.91 (1.40-2.60)			
WHO stage	l or ll	Reference	0.29	Reference	0.51		
	III or IV	0.56 (0.19-1.67)	0.29	0.86 (0.55-1.35)			
Time from HIV diagnosis	>10 days	Reference	0.52	Reference	0.12		
to ART start	≤10 days	1.18 (0.71-1.95)	0.52	1.23 (0.95-1.60)			
Age	>25 years	Reference		Reference			
	≤25 years	0.87 (0.53-1.42)	0.58	0.92 (0.72-1.18)	0.52		
HC type	Type 1	Reference		Reference			
	Peripheral type	1.19 (0.67-2.11)	0.55	1.23 (0.92-1.63)	0.16		
	2						

**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-days definition to consider a patient LTFU or NFU. HC: health center; \*: statistically significant





