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# Adherence to ART and retention in care among HIV-infected pregnant women starting life-long treatment in Ifakara, Tanzania.

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**2014**
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# Adherence to ART and retention in care among HIV-infected pregnant women starting life-long treatment in Ifakara, Tanzania.

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**Student Number: 737395**

**A research report submitted to the faculty of Health Sciences, University of the Witwatersrand in partial fulfillment of the requirements for the Master of Science Degree in Epidemiology.**

# Declaration

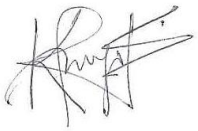
I declare that this research report is my own work to the faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.

It is submitted in partial fulfillment of the requirements for the degree of Master of Science in Epidemiology, in the field of Population Based Field Epidemiology.

I have been supervised by Dr. Charles Simion Chasela and Dr. Anna Gamell.

This work has not been submitted before for any examination or degree in any University.

Signature



26th September 2014

# Dedication

This report is dedicated to the girls attending public primary and secondary schools in rural Uganda.

In the face of all challenges, keep strong and read hard.

There is excellent value in education and keeping in school!

# Abstract

## Background

Antiretroviral therapy (ART) recommendations among HIV – infected pregnant women have been revised several times by the World Health Organization (WHO). Option B+, which is the latest recommendation continues to be rolled out in several countries across the globe but mostly in sub-Saharan Africa. Retention in care and adherence to antiretroviral (ARV) drugs taken by these women remains unclear in this new program. We assessed ability to stay in care (retention) and adherence to ART among HIV – infected women starting life-long treatment during pregnancy and after, at an HIV care and treatment clinic in Ifakara Tanzania. Our study provided an opportunity to understand the trends in adherence to ART and retention in care for this population.

## Methods

We analyzed data of HIV-infected pregnant women registered and starting ART for the first time in the Kilombero and Ulanga Antiretroviral Cohort in 2009 and 2010 with a follow up period of up to two years to 2011 and 2012 respectively. Adherence was by patient self-report (PSR) and was sufficient (good) if the woman took all the prescribed pills of the issued batch or insufficient (poor) if she missed two or more pills. Women that missed two or more consecutive scheduled visits to the clinic were not retained while those that honored their scheduled visits were retained in care. Two sample t test and Wilcoxon rank sum test were used to test predictor outcome associations for continuous variables while Pearson's and Fisher's exact tests were used for categorical ones. Hazard ratios of each predictor variable were calculated using Cox regression.

## Results

A total of 1,282 HIV – infected women were registered in KIULARCO between 2009 and 2010. Fifty (50) were pregnant and started life-long ART upon registration in this period. Of these, 25 (50%) were registered in 2009 and the other 25 (50%) in 2010. Slightly more than half, 52.2% had CD4 cell counts above 350cells/mm3. Almost half, 49% of the women were registered in their final (third) pregnancy trimester. About 82% were in WHO stage one and 60% of all the 50 women were initiated on AZT/3TC/EFV regimen. Only 5.7% had secondary education while the rest had primary or no education at all. Of the women that reported their partners HIV state, 54.5% had partners that had never tested for HIV.

Adherence for all participants was reported as sufficient (good) for the entire period the women were in care. No one had insufficient (poor) adherence. Retention in care was higher during pregnancy than after delivery. Generally, loss to follow up was 40%. About 30% were lost during pregnancy and the majority, 70% lost after they had delivered their babies. There was no evidence to prove that any of the factors studied independently predicted non retention. The most likely time to non retention was six months after delivery.

## Conclusions

Our study, despite small sample size, shows that among women diagnosed HIV – infected and starting life-long ART during pregnancy (Option B+), adherence to ART is sufficient and retention in care similar during and after pregnancy. Counseling on the importance of staying in care especially around the first few months after delivery should be emphasized at ANC.

## Acknowledgement

I am forever grateful to Indepth Network for sponsoring my studies. Please continue extending this to far more people.

My most sincere appreciation to my supervisors; Dr. Charles Simion Chasela and Dr. Anna Gamell for the guidance, direction and tireless effort rendered during this research journey.

To Dr. Rose Nathan, Emili Letang, Tracy Glass and the entire staff at the Chronic Diseases Clinic of Ifakara, thank you so much for welcoming me and providing a very conducive environment for me to carry out this research. It wouldn't have been possible without you.

I convey my heartfelt gratitude to Michael and Vicky Muyanja Njuba. You made my stay in South Africa comfortable.

I thank so much my parents, in-laws and siblings for the encouragement and support but most importantly comfort rendered to my wife and children the time I was away. I remain heavily indebted to you.

A big thank you my lecturers and classmates.

To my wife, Irene Patience Nabwire Jingo, mentioning you last was a trick!

I sincerely thank you for superbly undertaking mother and father duties to our little ones. All the social, economic and emotional effort sunk into this struggle has gone noticed. May the good Lord reward you abundantly!

Finally, thank you Lord for enabling me get this far!

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# Acronyms

**ANC:** Ante-natal care

**ART**: Antiretroviral therapy

**ARV:** Antiretroviral

**CDCI:** Chronic Diseases Clinic of Ifakara

**CI:** Confidence interval

**HIV:** Human Immune Virus

**HR:** Hazard ratio

**IQR:** Inter-quartile range

**MTCT:** Mother to Child Transmission.

**NACP:** National Aids Control Program

**PSR:** Patient self-report

**PLHIV:** Persons living with HIV

**PMTCT:** Prevention of Mother to Child Transmission.

**RCHC:** Reproductive and child health clinic

**SFRH:** St. Francis referral hospital

**WHO:** World Health Organization

# Chapter One: Introduction

## Background

Adherence to antiretroviral therapy (ART) and retention in care among persons living with HIV (PLHIV) started on this life-long treatment are very important in curbing the mortality and morbidity registered in this population [1]. By the end of 2011, approximately 34 million people were living with HIV [1]. Sub-Saharan Africa contributes to 69% of this global burden with the majority (58%) being women[1]. Many of these women are getting or will get pregnant at some point while they're HIV infected.

Due to overwhelming evidence that ART among HIV- infected pregnant women prevents transmission of HIV to the un-born babies [2, 3] the need to emphasize adherence to ART and retention in care for these women is highly important. This is the only way to achieve proper treatment outcomes [4-6]. More so, even if they don't get ART for prevention of mother to child transmission of HIV (PMTCT) they will need it for their own health when the CD4 cell counts drop [7].

In an effort to get more and more pregnant women to know their HIV status, several countries have implemented a number of pregnant women targeted testing strategies and approaches [8]. One of these strategies is routine HIV testing to all pregnant women attending ante-natal care (ANC) clinics [8, 9]. Women coming to attend ANC services and have a negative HIV test result more than three months prior to the current visit or are not aware of their HIV serostatus are offered an HIV test [9].

Tanzania is one of the countries that have embraced this strategy [10]. This integration of HIV testing into ANC services has led to an increased number of newly diagnosed HIV-infected pregnant women and several of them are eligible to start antiretroviral treatment [10]. The current WHO recommendations for PMTCT state that every woman diagnosed HIV – infected in pregnancy starts life-long ART [5, 11]. Adherence to ART and retention in care after treatment initiation is crucial among this population since both insufficient (poor) adherence and none retention in care can lead to drug resistance [12], sicker states and several other undesirable treatment outcomes [13, 14]. HIV-infected pregnant women starting ART may also not be able to protect the babies in the subsequent pregnancies [11, 13] if adherence to treatment and retention in care are not addressed.

The Kilombero and Ulanga Antiretroviral Cohort (KIULARCO) is run by the Chronic Diseases Clinic of Ifakara (CDCI) at St. Francis referral hospital (SFRH). Care and treatment of HIV-positive patients is provided at SFRH according to the National Aids Control Program (NACP) through the CDCI. SFRH is the most important health care facility in Kilombero and Ulanga districts, in the Morogoro region of southern Tanzania. The CDCI, a clinic with-in the hospital, works in cooperation with the Ifakara Health Institute (IHI), the Swiss Tropical and Public Health Institute and the Department of Infectious Diseases and Hospital Epidemiology of the University Hospitals of Basel and Bern, Switzerland. Since late 2004, all HIV-infected patients attending the CDCI are asked for informed consent to be enrolled in the Kilombero and Ulanga Antiretroviral Cohort (KIULARCO). This cohort comprises more than 6,000 people living with HIV (PLHIV) and is the largest rural HIV cohort in Tanzania [15]. This offers an opportunity to study the intended outcomes among HIV-infected pregnant women starting life-long treatment.

## Statement of the problem

In order to maximize the benefit of starting ART, PLHIV must be retained in care to ensure regular follow up that enables clinical monitoring of CD4 counts and viral loads and good drug adherence [3, 4, 16].

Unfortunately, adherence and retention rates among PLHIV are still low [1]. The Centers for Disease Control estimates that only 56% of all PLHIV linked to care are retained [1]. Worse still, to our knowledge, evidence on adherence and retention in care including predictors of these two outcomes among HIV-infected pregnant women starting ART is lacking.

## Justification of the study

The results from this study would allow for a better understanding of which period (during pregnancy or afterwards) HIV-infected pregnant women starting ART are at risk of poor adherence and loss to follow up.

Furthermore, the assessed predictive factors of adherence to ART and retention in care would allow us to know determinants of adherence to ART and retention in care for this population and as such offer a basis for potential counteractive measures to mitigate these problems.

Assessing adherence to ART and retention in care among HIV-infected pregnant women starting life-long treatment would also offer a concise understanding of the adherence and retention trends in this population. This makes Option B+ and other ART programs among HIV – infected pregnant women significantly improve PMTCT outcomes, women livelihoods and curtail transmissions from the women to their sexual partners.

# Literature review

## HIV burden

By the end of 2011, approximately 34 million people across the globe were living with HIV [1]. Majority of these (69%) were in Sub-Saharan Africa [1] with the bigger proportion of them (58%) being women. With such huge numbers of infected women, unborn babies are prone to HIV if nothing to prevent the infection is done [4]. This in turn leads to more new infections.

## ART among pregnant women

For over a decade, several studies have shown that using ART during and after pregnancy is effective in preventing MTCT of HIV [2, 3, 17].

Since the release of the first guidelines on PMTCT, the World Health Organization (WHO) has published several revisions and updates [1, 5, 11]. New evidence supporting safety and effectiveness of antiretroviral (ARV) drugs among pregnant women [14, 16, 18], the increase in availability of drugs [1, 19], the decrease in cost [19] and the ambitious goals of elimination of pediatric HIV infection by 2015 have driven this constant change in guidelines [4].

In 2010, WHO issued PMTCT guidelines recommending two PMTCT options; Option A and Option B [6, 20]. These two options include both treatment and prophylaxis components. In both options, CD4 cell count is necessary to decide the eligibility of HIV-infected pregnant women for life-long ART. For all women who have CD4 $\leq$ 350 cells/mm3 initiation of lifelong ART is recommended [20]. For those women not eligible for lifelong ART, Option A recommends antenatal prophylaxis with zidovudine followed by intrapartum and postpartum prophylaxis with

single doze nevirapine and zidovudine plus lamivudine [6]. Option B recommends triple ARV prophylaxis until after finishing breastfeeding [20].

The most recent WHO PMTCT recommendation is Option B+ [5, 11]. This option advocates for initiation of life-long ART to all HIV-infected pregnant women regardless of CD4 count and clinical stage and administration of daily nevirapine or zidovudine to all HIV exposed infants until the age of 4 to 6 weeks regardless of the breast-feeding method [5, 11].

## PMTCT Guidelines in Tanzania

The first Tanzanian PMTCT guidelines were developed in 2004 [21]. In 2007, the Tanzania Ministry of Health revised them and moved from single dose nevirapine (sdNVP) to combination prophylaxis [22]. In June 2012, new guidelines recommending the WHO PMTCT Option A were published [22]. Option B+ was not standard of care among pregnant women in Tanzania during our study period.

## Adherence to ART

Sufficient (good) adherence to ART during pregnancy and postpartum contributes to improved livelihoods and good PMTCT outcomes among women [14]. Some studies [23, 24] including a systematic review and meta-analysis [25], have assessed adherence to ART among pregnant and breastfeeding mothers. However, most of these studies follow up the participants until six months postpartum. During this period, mothers are supposed to be highly motivated to protect their child from MTCT. Moreover, during the first year after delivery, mothers and infants will attend the health facilities to get the scheduled immunizations [26].

These two reasons might be driving factors to keeping them adherent and retained in care [26]. An extended follow-up period such as done by the Mitra Plus study in Tanzania [27] and another study in Malawi [28] offers a better chance to understand adherence patterns in this population.

Since the final infant's HIV serostatus is often known at 18 months [11] and all immunizations are completed by a year [29], adherence trends studied after this period will surely be due to the woman's own drive and willingness to get treatment for her own health and not for PMTCT [26]. The determinants of adherence trends observed are also less influenced by the child's scheduled clinic visits.

## Retention in Care

Retention in care offers HIV-infected people a chance to be seen and continuously monitored by health care providers contributing to improved treatment outcomes [11]. Among HIV – infected pregnant women, the monitoring contributes to improved PMTCT outcomes both during and after pregnancy [5, 30]. Non retention in care in Sub-Saharan Africa occurs both in pre ART and post ART initiation periods [28]. Some studies have registered rates of loss to follow up ranging from 30% to 50%, [27]. Non retention in care among HIV- infected pregnant women has only been studied recently in South Africa [31] with 57.5% lost between HIV testing in pregnancy and six months post delivery. The study however, included pregnant women eligible and non-eligible to start ART. Our study focuses on women starting life-long ART, so to understand better this outcome in such a population.

## Determinants of adherence to ART and retention in care

Factors determining adherence to ART or retention in HIV care are either socio-demographic or related to the system through which HIV care and treatment is provided [11].

Age, sex, race, education status, marital state, domestic violence and economic status have been observed in several studies as socio-demographic determinants of adherence to ART and retention in care among PLHIV [31, 35, 36].

The distance to the HIV care and treatment clinic, transport costs, drug stock outs and late procurement by specific clinics have also influenced the adherence and retention patterns among HIV- infected people [36].

The factors above have all been studied in general populations and not specifically among HIV-infected pregnant women. A study like ours, will clarify whether these factors determine adherence and retention in care for this population as well.

## Summary:

There is a high global HIV burden and infection rates are higher among women than men. The advent of ART use in pregnancy has reduced several new infections to un-born babies through recommendations by WHO like Option B+.

Understanding adherence to ART and retention in care trends for HIV- infected pregnant women starting life-long ART has the potential to improve Option B+ and HIV treatment success among care and treatment programs. This will save many lives of babies, improve livelihoods of their mothers and reduce transmissions to their sexual partners.

## Aims and Objectives

## Research Question

To understand public health implications of starting life-long ART among HIV infected pregnant women, we explored the questions.

- Is there a difference in adherence to ART during pregnancy and during two years after delivery among HIV-infected pregnant women starting life-long treatment at Ifakara between 2009 and 2010?
- Is there a difference in retention in care during pregnancy and during two years after delivery among HIV-infected pregnant women starting life-long treatment at Ifakara between 2009 and 2010?
- What factors are associated with adherence to ART and retention in care among HIV-infected pregnant women starting life-long treatment at Ifakara between 2009 and 2010?

## Study Aim

This study sought to establish whether there is a difference in adherence to ART and retention in care with associated factors during pregnancy and at two years after delivery among newly diagnosed HIV-infected pregnant women starting life-long treatment at Ifakara between 2009 and 2010.

## Study Objectives

1. To compare adherence to ART during pregnancy and during two years after delivery among newly diagnosed HIV-infected pregnant women started on ART enrolled in Kilombero and Ulanga Antiretroviral Cohort (KIULARCO) between 2009 and 2010.
2. To compare retention in HIV care during pregnancy and during two years after delivery among newly diagnosed HIV-infected pregnant women started on ART enrolled in KIULARCO between 2009 and 2010.
3. To estimate time to none retention among newly diagnosed HIV-infected pregnant women enrolled in KIULARCO starting ART between 2009 and 2010.
4. To determine factors associated with adherence among newly diagnosed HIV-infected pregnant women started on ART enrolled in KIULARCO between 2009 and 2010.
5. To determine factors associated with retention in care among newly diagnosed HIV-infected pregnant women started on ART enrolled in KIULARCO between 2009 and 2010.

# Chapter Two: Methodology

## Introduction

This chapter elaborates the study methods used for the study right from the design and explains in detail the study setting of the Chronic Diseases Clinic of Ifakara (CDCI) at St. Francis referral hospital (SFRH). The chapter further explains the Kilombero and Ulanga ART cohort and how clients including pregnant women got enrolled. The population studied, together with the inclusion and exclusion criteria are explicitly laid out together with proper definition of retention in care and adherence to ART. Common methods of adherence and retention measurement are explained in depth and the chapter ends with a precise explanation of how the data was cleaned and analyzed to generate the results presented in this research report.

## Study design

This study was a secondary analysis of data that was collected longitudinally among participants attending the CDCI and being enrolled in the Kilombero and Ulanga Antiretroviral Cohort.

## Study setting

Pregnant women attend antenatal care (ANC) at the reproductive and child health clinic (RCHC) in SFRH. All women attending ANC services whose serostatus is unknown or had a negative test result more than 3 months prior to the visit are offered an HIV test. HIV-infected women diagnosed in the RCHC are referred to the CDCI for HIV care and treatment.

At the CDCI, HIV-infected pregnant women are counseled, CD4+ cell count is done and a baseline clinical visit with an HIV clinician takes place. HIV-infected pregnant women eligible

to start ART according to the national guidelines of the NACP are started on ART and subsequently followed up.

After initiation of ART, women are scheduled for clinical visits, drug refill and laboratory monitoring. Also, in case they present with any complaint, they attend the CDCI to be reviewed by a clinician (un-scheduled visits). Every time a woman is seen by the clinician, a detailed health history, pregnancy status and adherence are assessed and filled in a follow-up form. Blood samples are drawn during the follow-up period for subsequent CD4+ cell count and other organ function monitoring.

## Study population

We studied women that were diagnosed HIV positive registered in KIULARCO and started on ART during pregnancy between January 2009 and December 2010. All these women came from Kilombero and Ulanga districts in the Morogoro region of southern Tanzania.

## Inclusion criteria

- Newly diagnosed HIV-infected pregnant women starting life-long ART according to the Tanzanian NACP guidelines enrolled in KIULARCO between 2009 and 2010.
- Newly diagnosed HIV-infected pregnant women that without meeting the CD4 and WHO stage criteria to start ART were willing to and were started on life-long ART enrolled in KIULARCO between 2009 and 2010.

## Exclusion criteria

- Newly diagnosed HIV-infected woman and not pregnant
- Newly diagnosed HIV –infected pregnant women and not started on life-long ART during pregnancy.
- Women previously diagnosed HIV-infected but currently pregnant.

## Outcome measurements

## Adherence to ART

Adherence to ART for this study was defined as taking the prescribed pills in the right amount. We used the patient self-report (PSR) method which allows the participant to recall the pills taken and missed for the last issued batch. This method of assessment has been used in other studies and proved to be an effective tool of measuring adherence [32, 33].

It was dichotomized into two different measures as; sufficient (good) and insufficient (poor) adherence [12, 25]. Insufficient (poor) adherence was missing two or more days without taking ART of the last issued batch. If a woman missed less than 2 days without taking ART of the last issued batch, she was deemed to have sufficient (good) adherence to treatment. This information in the dataset formed our assessment to adherence levels during pregnancy and at 2 years after delivery.

## Retention in care

One was either in care or not at any point during the study period. Retention in care was honoring every scheduled clinic visit to the CDCI for two years from the date registered. Those

not retained in care were participants that had missed attending two or more consecutive scheduled visits to the clinic. We censored as being in care, all those that made two years in the cohort since registration. Women not meeting this criterion were censored as not retained in care. The dataset records were assessed on whether the woman honored scheduled visits to the CDCI and this provided basis for assessment of retention in HIV care. These numbers were compared for the two time periods; during and after pregnancy.

## Exposure measurements

The primary exposure variable was the period when the woman was pregnant and after pregnancy. The period during pregnancy spanned from the time of registration into the cohort until delivery while the period after pregnancy stretched from delivery to the mark of two years of follow up (at two years after delivery). The secondary exposure variables for this research were:-

## Socio-demographic variables

- Age at the time of registration was measured in years and was categorised during analysis to find out if specific age bands had different trends in respect to the two studied outcomes among the study group.
- Level of education was taken to be none; if a woman had never gone to school, primary; if she had gone to primary school but not secondary school and higher; if she attended secondary school or any tertiary institution or both.

- The year of registration was a factor we also considered in this research. Women were registered over two years from 2009 to 2010 but had to have a follow up of up to 2 years by 2012. This excluded those registered in 2011 and 2012.
- Parity was the number of living children that the mother reported to have at registration.
- Disclosure of HIV status. Women were asked if they had disclosed to anyone their HIV status.
- Marital status. Women were asked if they were single, married, divorced or separated. The ones that were divorced or separated were put in the same category as the single.
- Gestation age at registration. Women were asked for their last normal menstrual period and gestation of the current pregnancy calculated. This was recorded as weeks but for our analysis it was changed to months.
- Partner tested. Women were asked if their partners had been tested for HIV to find out if their being sero-negative or positive for HIV affected the woman's outcome.
- Occupation. Source of income was farming, employment in government and employment in private sector. Women that were employed in the both government and private sectors were considered non-farmers.

## Clinical variables

- CD4 cell counts were measured at baseline and at subsequent follow-up visits when the clinician wanted to monitor response to ART. The measurement was done in cells/mm3. We used baseline CD4 counts and categorised them into >350 cells/mm3 or below to ascertain their relation to the two outcomes of interest.

- WHO stage at registration was the baseline WHO stage of the woman. It was classified according to the WHO classification as 1, 2, 3 or 4 [34]
- Any opportunistic infection
- ART regimen was the type of combination antiretroviral drugs the woman was started on.

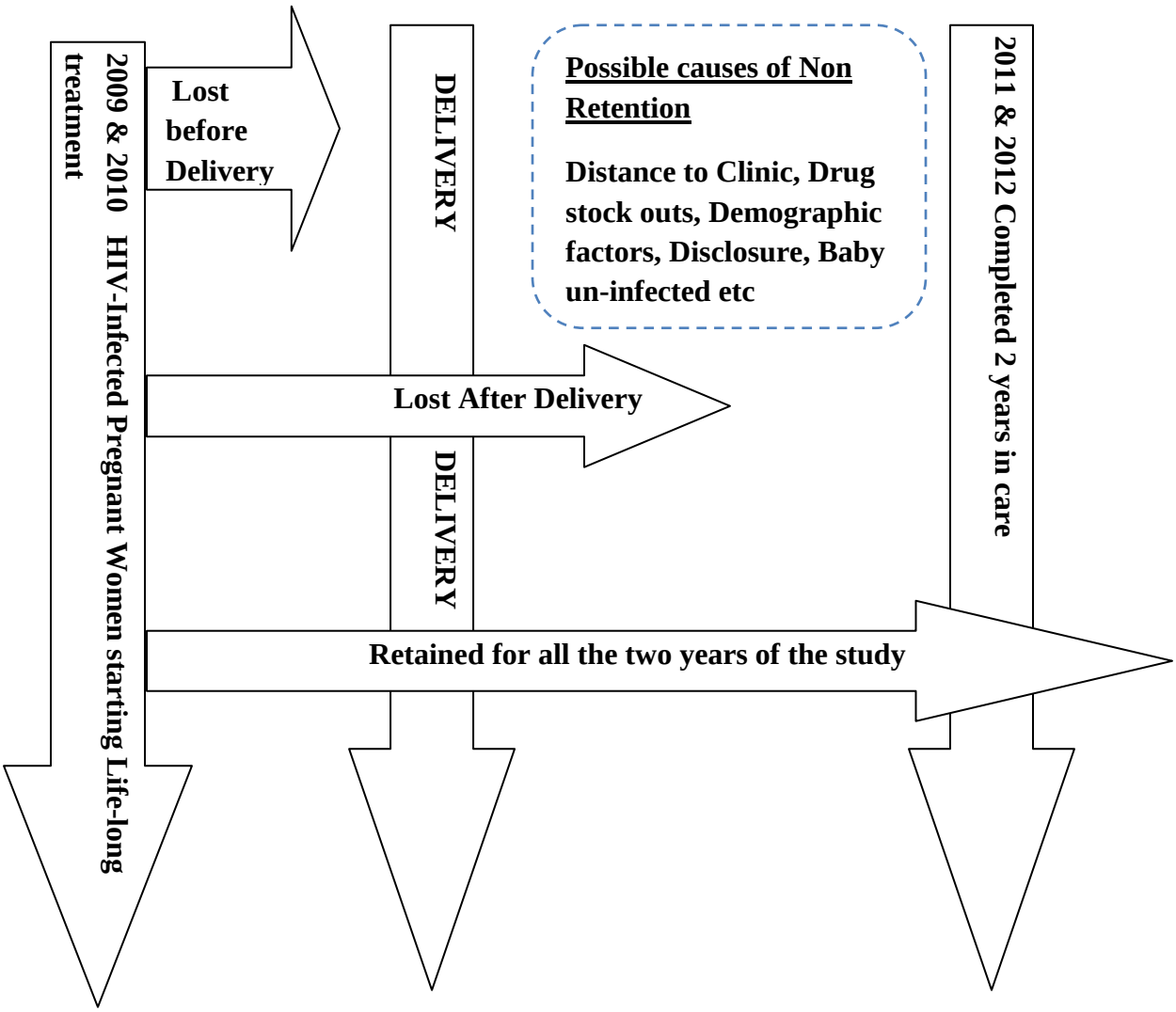



**Figure 1: Follow-up patterns in the Cohort**

## Data management and statistical analysis

The collected information on the baseline and follow-up forms and the laboratory results are double entered into the KIULARCO database. This is done by trained data entry clerks supervised by a data manager.

## Data cleaning and management

A dataset was provided containing de-identified particulars, baseline and follow-up information of participants that had been enrolled in KIULARCO from 2004 to 2012. Using Stata TM statistical package, we checked and cleaned firstly the participant registration dates for duplicates and missing dates among those that had a pregnancy ever reported. The observations that had registration date missing and had no pregnancy reported were dropped together with all those registered before January /1 /2009 (Study Period start). We also generated year of registration without month or day for each participant from their respective date of registration.

Participant's gender was checked for missing information at all follow-ups but also to filter out any mixed gender on subsquent visits. We dropped observations of all males in the data set since our study was on females.

Duplicates in the participant baseline and follow-up forms were deleted and follow-up numbers generated for every follow-up observations in ascending order according to the date the participant visited the clinic.

We coded 1 if a woman had a pregnancy ever reported either at baseline or any follow-up visit observation and code 2 if a woman had no observation during follow-up with pregnancy reported. Those with no pregnancy ever reported at any visit during follow up were dropped

from the dataset. Among those that had a pregnancy ever reported at anytime during follow-up, we retained women that were pregnant at registration into KIULARCO and dropped the ones that were not pregnant by the time of registration and only got pregnant later during follow-up. They were dropped because they got pregnant during care but were not pregnant at registration. Among women that were pregnant at registration, we kept those that started ART during that pregnancy and dropped the ones that didnot start ART while pregnant.

To be able to analyze time to non-retention, censoring occurred at two years since registration. This was 2011 for those registered in 2009 and 2012 for those registered in 2010. Participants that didn't get to two years either through death, transfer out, lost or any other means, were considered to have the event of interest (not retained). This censoring generated the woman's status at follow up as either retained in care if she had follow up visits up to two years since registration (censored) or not retained in care if her last visit didn't go up to two years since registration into the cohort (event). We also generated total length of follow-up (time) in months by subtracting the last date at censoring from the registration date in the cohort.

## Statistical analysis

## Descriptive statistical analysis

We assessed for normality in distribution of all continuous variables like age and CD4 counts using skewness and kurtosis tests, normal quantile plots, normal probability plots and normal distribution histogram graphs.

Normally distributed baseline continuous characteristics were summarized to obtain their means together with the standard deviation. We also tested for association of these characteristics with

the outcome variables by running the parametric; two sample t test to accord presence or lack of associations.

Continuous variables that were not normally distributed like mothers' baseline CD4 counts were summarized to obtain their median together with the inter-quartile range. We also tested for association of these characteristics with the outcome variables by running the non-parametric; Mann-Whitney test (Wilcoxon rank sum) to accord presence or lack of associations.

We carried out two way tabulations of frequencies of categorical baseline characteristics using Pearson's Chi Square test and Fischer's Exact test where observations of any cell were sparse. Proportions of mothers in each category with the respective percentages (%) were obtained.

## Inferential statistical analysis

Kaplan Meier estimates were used to compare retention in care between the two periods. The log rank test for equality of survival functions was used to test for statistically significant differences in retention in care between these two periods at the 5% level of significance. From Pearson's Chi Square, Fisher's exact, Mann-Whitney and two sample t tests, baseline characteristics that were found significantly associated with retention in care were fit in univariable Cox regression models to ascertain the strength of association. This was also done for baseline characteristics that were not significantly associated with retention in care but had biological or sociological plausibility. Hazard ratios and their respective 95% confidence intervals were generated.

Baseline exposure characteristics that generated associations with outcomes and had a P value less than 0.1 at univariable Cox regression were fit into multi-variable Cox regression analysis models. Biologically and sociologically plausible characteristics were also included in the multi-

variable Cox regression models to determine if they were independent predictors of retention in care.

Person time for participants was determined from the day of registration into the cohort to the date censorship. Kaplan Meier survival estimate curves were plotted to depict the median time to non-retention. Non-retention rates were generated for the two periods after survival time setting the data.

Confounding and interaction between starting ART in pregnancy and retention in care was also tested. The categorical variables were stratified and Mantel-Hanzsel odds ratios determined. Baseline characteristics that caused a change of less than 10% had strata specific odds ratios assessed for similarity or difference to rule out confounding.

We were unable to run model diagnostics for the assumptions of linearity and equal proportions because there was no evidence to show that the factors modeled explained retention in care.

## Ethical considerations

The KIULARCO project obtained ethical clearance from the IHI Ethical Review Board and the National Institute for Medical Research from Tanzania.

Permission to use the KUILARCO dataset for this research was obtained from the management of IHI and CDCI in Tanzania.

Ethics clearance to carry out the research was approved by the University of the Witwatersrand human research ethics committee (medical).

# Chapter Three: Results

## Introduction

In this chapter, we detail the results of the study. From the accrual of total numbers of pregnant women studied to the qualities of their baseline socio-demographic and clinical characteristics. The chapter explains in detail the differences in retention in care both during pregnancy and after pregnancy, elaborating clearly the evidence generated towards ascertaining predictors of non-retention. The time to non-retention together with adherence trends are made mention of.

## Study participants

In 2009 and 2010, a total of 2,016 HIV positive clients were registered into KIULARCO. The number of males was 734 while females were 1,282. Of these females, 836 women were registered between January and December 2009 while between January and December 2010, 446 women were registered. Out of 1,282 women registered in the two years, 106 (8.3%) women had a pregnancy within two years of follow up since registration into the cohort. The remaining 1,176 (91.7%) women did not get pregnant within the 2 years of follow up since registration into the cohort. As shown in the figure 1 below, 55 (51.9%) of the total 106 pregnant women were pregnant at the time of registration into the cohort. The remaining 51 pregnant women (48.1%) got pregnant much later after registration into the cohort i.e.; got pregnant while already in care.

Five women (9.1%) of the 55 women pregnant at the time of registration didn't start ART during pregnancy. The 50 women (90.9%) that started ART while still pregnant were the sample that met the inclusion criteria for the study.

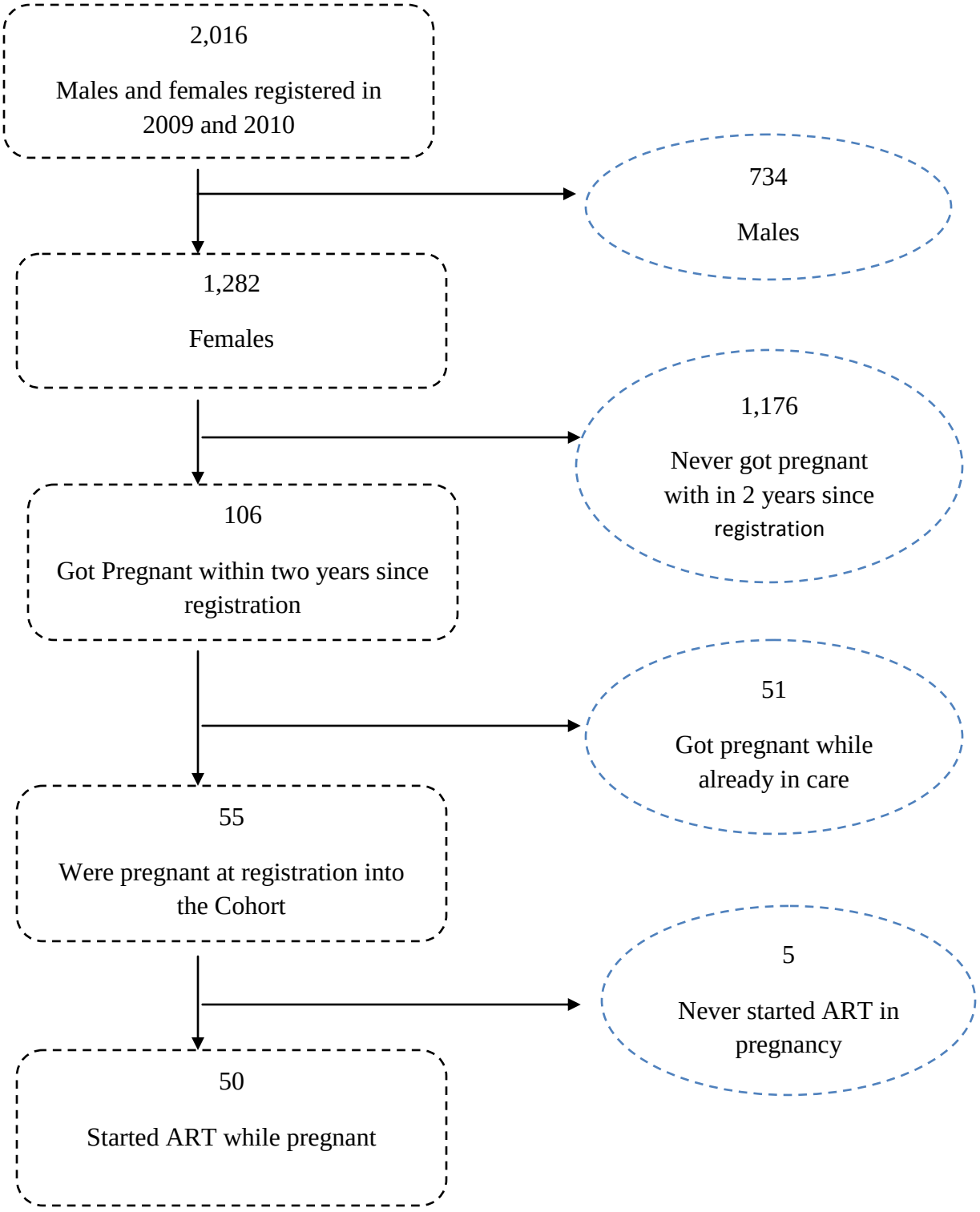



**Figure 2:** Consort diagram showing the accrual of number of study participants.

## Baseline characteristics

The proportions, means and medians of socio-demographic and clinical characteristics of study participants at the time of registration are summarized in table 1 below.

Our results show that 25 (50%) of the women were registered in 2009 while the other 25 (50%) were registered in 2010. Women registered in 2009 and 2010 were followed up until 2011 and 2012 respectively.

The mean age at registration was 29 years with a standard deviation of 6 years. Baseline CD4 cell counts were documented for 46 women. Twenty two women (47.8%) had CD4 cell counts less or equal to 350 cells/mm3 at registration while 24 women (52.2%) had CD4 cell counts more than 350 cells/mm3.

AZT/3TC/EFV was the most prescribed ART regimen with 30 women (60%) initiated on it. Ten women (20%) were initiated on d4T/3TC/NVP, 3 women (6%) on AZT/3TC/NVP and 7 women (14%) on other ART combination regimens. The majority of women were in WHO stage 1 (41 women 82%). Those in WHO stage 2 were 5(10%), while the ones in WHO stage 3 were 2(4%). Only 2(4%) women were in WHO stage 4.

Almost half of the total number of women had been registered in their third trimester of pregnancy (24 women 49%). The women in the second trimester at the time of registration were 11(22.4%) and 14 (28.6%) were in the first trimester at the time of registration. Eleven women (29.7%) had no child while 26 women (70.3%) had either one or more children at registration. Thirty six women (72%) had disclosed their HIV status to either their partner or someone else

and 14 (28%) had never disclosed their HIV status to anyone. Thirty two women (80%) of the 40 women that reported their marital status were married while the rest were single.

Only 9 women (18.4%) of the 49 women that had answered the alcohol intake question had a history of alcohol use. Among the 35 women whose education status was recorded in the dataset, 28 (80%) had attained primary school level of education, 2 women (5.7%) had secondary school level of education and 5 women (14.3%) had no school education at all. Occupation status was recorded for 33 women of whom 31 (94%) were farmers. The 2 women (6%) were involved in either private or government work which was categorized as non farmers. Thirty three women reported their partner's HIV test status and 18 (54.5%) had partners who had never tested for HIV. The remaining 15 women (45.5%) had partners who had tested for HIV before.

**Table 1: Characteristics of HIV- infected pregnant women starting ART.**

| **Factor** | **Level** | **Freq (%)**<br>**Mean (+/- St.dv)**<br>**Median(IQR)** |
|---|---|---|
| Year of Registration | 2009 | 25 (50%) |
| | 2010 | 25 (50%) |
| Age at baseline | Continuous | 29 (+/- 6) |
| CD4 category | Below 350 | 22 (47.8%) |
| | Above 350 | 24 (52.2%) |
| Start Regimen | AZT/3TC/EFV | 30 (60%) |
| | AZT/3TC/NVP | 3 (6%) |
| | d4T/3TC/NVP | 10 (20%) |
| | Other | 7 (14%) |
| Baseline WHO stage | 1 | 41 (82%) |
| | 2 | 5 (10%) |
| | 3 | 2 (4%) |
| | 4 | 2 (4%) |
| Gestation at registration | Trimester 1 | 14 (28.6%) |

| | | |
|---|---|---|
| | Trimester 2 | 11 (22.4%) |
| | Trimester 3 | 24 (49%) |
| Parity | No Child | 11 (29.7%) |
| | One & More | 26 (70.3%) |
| Disclosure | Yes | 36 (72%) |
| | No | 14 (28%) |
| Marital status | Married | 32 (80%) |
| | Single | 8 (20%) |
| Alcohol | Yes | 9 (18.4%) |
| | No | 40 (81.6%) |
| Education | None | 5 (14.3%) |
| | Primary | 28 (80%) |
| | Secondary | 2 (5.7%) |
| Occupation | Farmers | 31 (94%) |
| | Non-farmers | 2 (6%) |
| Partner tested | Yes | 15 (45.5%) |
| | No | 18 (54.5%) |

## Outcomes

## Adherence to ART

No woman in this study had reported having failed to take the right amount of the antiretroviral drugs prescribed by the attending clinician. The findings of this study, therefore, show that adherence to ART for these enrolled HIV – infected pregnant women was sufficient (good) for all the participants during the entire period they were followed up.

## Predictors of adherence to ART

Predictors to adherence could not be ascertained as all the HIV – infected pregnant women starting life-long ART reported sufficient adherence.

## Retention in care

Although the absolute numbers suggest a difference in retention during pregnancy and during two years after delivery, statistical evidence shows that **retention in care was similar for these two periods**. Although our sample size was small, the log rank test for comparison of retention showed statistical evidence of no difference between these two periods **(P = 0.491).** Thirty (30) of the 50 HIV – infected pregnant women starting life-long ART included in the study were still in care by 2 years since registration into the cohort. Thus, twenty women (40%) were lost to follow up by 2 years since their registration into the cohort. Among these women not retained in HIV care, 14 (70%) were lost during the period after pregnancy and 6 women (30%) lost during pregnancy as seen in figure 2 below.

Figure 3 shows Kaplan Meier estimates of retention in care both during pregnancy and after pregnancy. The log rank test for the comparison between the two periods showed no evidence of a difference in retention between the two periods**.** The analysis involved taking follow up time into consideration.

The incidence rates of non retention during pregnancy were 47 per 1,000 person months of follow up while after pregnancy incidence was 18 per 1,000 person months of follow up. The HR for non retention were reduced by half after pregnancy compared to during pregnancy although this evidence was not statistically significant **(HR: 0.5, 95%CI: 0.07-3.57)**.

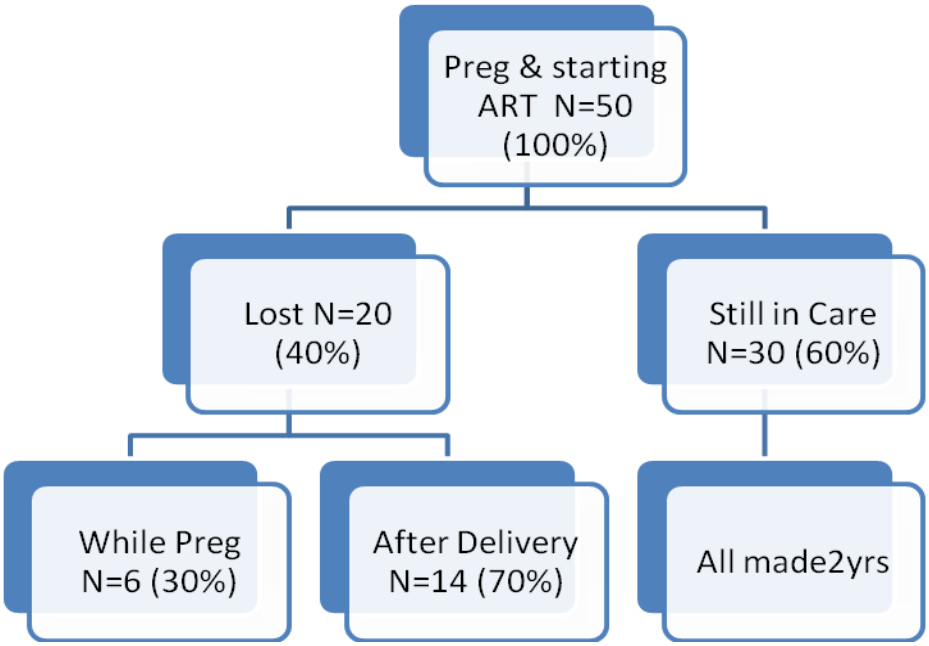



**Figure 3:** Females not retained in care and periods when they were lost from care.

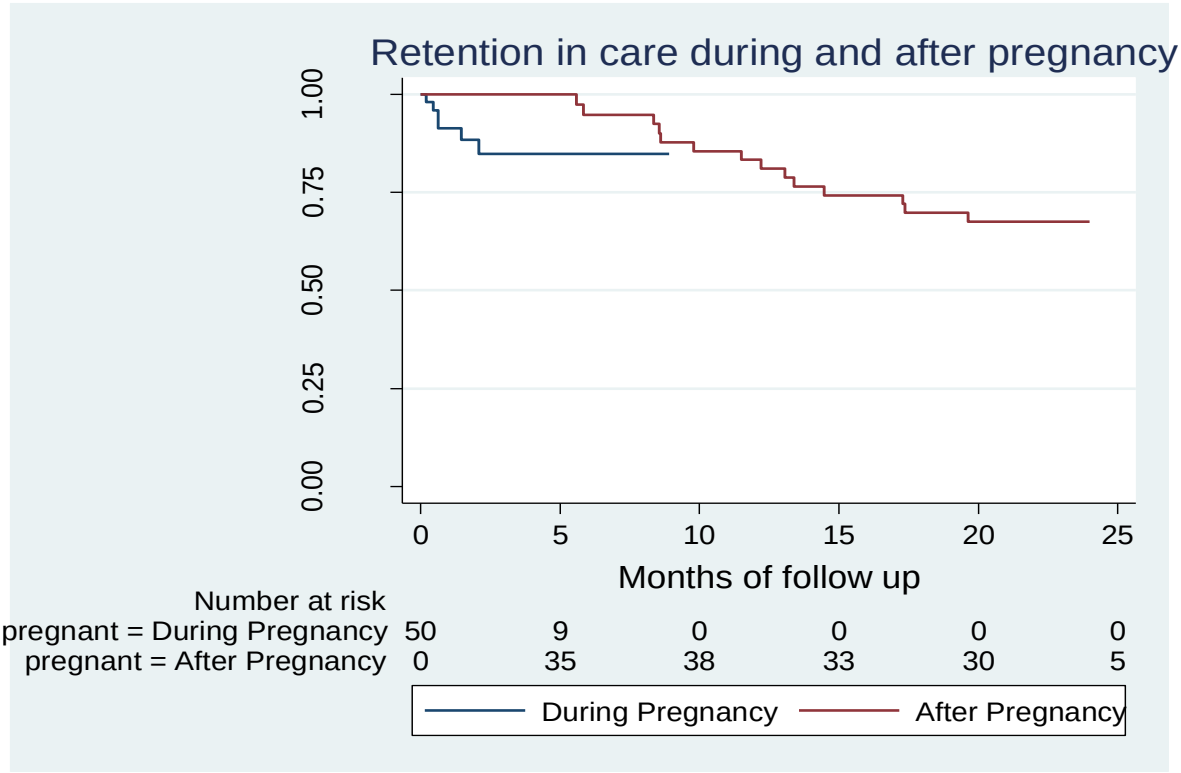



**Figure 4:** Kaplan Meier estimates of retention in care during and after pregnancy.

## Predictors of retention in care

Baseline CD4 cell counts and the type of ART regimen started showed statistically significant associations with retention in care (P=0.016 and P=0.022 respectively).

Among women with CD4 cell counts below 350cells/mm3, 81.3% were still in care by 2 years while 18.7% of them were not retained. Among the women with CD4 cell counts above 350cells/mm3, 45.8% were still in care by 2 years while 54.2% were not retained. At univariable Cox regression, there was statistical evidence that CD4 cell counts significantly predict retention in care among HIV-infected pregnant women. Women with CD4 cell counts above 350cells/mm3 were three times more likely to be lost compared to those with CD4 cell counts below 350cells/mm3 **(HR: 3.16, 95% CI: 1.00-9.97 P= 0.049).** However, after adjusting for other variables in multivariable Cox regression and given the small sample size, there was no statistical evidence that CD4 cell counts predicted retention in HIV care among these women starting life-long treatment **(HR: 3.12, 95% CI: 0.3-31.86 P= 0.34).**

Among women initiated on AZT/3TC/EFV regimen, 53.3% were lost while 46.7% were still in care by two years. Women initiated on regimens including; AZT/3TC/NVP, d4T/3TC/NVP and other combination ART, 80% were still in care and 20% lost during the study period. Initiation on ART regimens other than AZT/3TC/EFV, made women 64% more likely to stay in care but this evidence was only marginally significant at univariable Cox regression **(HR: 0.36, 95% CI: 0.12-1.09 P= 0.073).** When other variables were adjusted for in multivariable Cox regression, there was no evidence that the type of regimen started predicted retention in HIV care among women **(HR: 1.4, 95% CI: 0.12-15.74 P= 0.784).**

There was only marginal statistical evidence (P= 0.062) of association between retention in care and the gestational trimester of the woman at the time of registration. So was the association between the woman's school education level and retention in care (P= 0.067).

Women that were registered into the cohort while in the last trimester of their pregnancy were almost three times more likely to be lost from care as compared to women registered while in their first or second trimester. However, there was only marginal statistical evidence to support this finding on univariable Cox regression analysis **(HR: 2.56, 95% CI: 0.96-6.84 P= 0.061).** When other variables were adjusted for in multivariable Cox regression, there was no evidence that the trimester at registration predicted retention **(HR: 4.17, 95% CI: 0.41-41.92 P= 0.225).**

There was marginal statistical evidence that women with any school education compared to those with no level of school education, were less likely to get lost to follow up **(HR: 0.24, 95% CI: 0.06-1.03 P= 0.055).** Upon adjusting for other variables in the multiple variable Cox regression model, this effect lost significance **(HR: 1.01, 95% CI: 0.06-17.74 P= 0.996).**

There was no statistical evidence to support any associations between retention in care and all the other factors studied; age at baseline (P=0.468), year of registration (P=0.564), baseline WHO stage (P=0.724), number of children the woman had (P=0.695), distance to clinic (P=0.734), disclosure of HIV status (P=0.797), marital status (P=0.677), alcohol use (P=0.720), occupation(P=1.000), and knowing the partner's HIV test (P=0.722) as noted in the table 2 below.

Table 3 shows all univariable and multivariable Cox regression analyses and the hazard ratios generated.

**Table 2: Bivariable analysis of factors associated with retention in care among HIV infected pregnant women starting ART.**

| Factor | Level | Lost | Still in care | P-value |
|---|---|---|---|---|
| | | Freq (%) Mean(St.dv) | Freq (%) Mean(St.dv) | |
| Age at baseline | Continuous | 28 (+/- 7) | 29 (+/- 5) | 0.4608* |
| CD4 category | Below 350 | 4 (18.2%) | 18 (81.8%) | 0.016# |
| | Above 350 | 13 (54.2%) | 11 (45.8%) | |
| Year of Registration | 2009 | 11 (44%) | 14 (56%) | 0.564¶ |
| | 2010 | 9 (36%) | 16 (64%) | |
| Start Regimen | AZT/3TC/EFV | 16 (53.3%) | 14 (46.7%) | 0.022# |
| | Other regimens | 4 (20%) | 16 (80%) | |
| Baseline WHO stage | Stage 1 | 17 (41.5%) | 24 (58.5%) | 0.724# |
| | Other stages | 3 (33.3%) | 6 (66.7%) | |
| Gestation at registration | Trimester 1&2 | 7 (28%) | 18 (72%) | 0.062¶ |
| | Trimester 3 | 13 (54.2%) | 11 (45.8%) | |
| Parity | No Child | 2 (18.2%) | 9 (81.8%) | 0.695# |
| | One/more | 7 (26.9%) | 19 (73.1%) | |
| Disclosure | Yes | 14 (38.9%) | 22 (61.1%) | 0.797¶ |
| | No | 6 (42.9%) | 8 (57.1%) | |
| Marital status | Married | 9 (28.1%) | 23 (71.9%) | 0.677# |
| | Single | 3 (37.5%) | 5 (62.5%) | |
| Alcohol | Yes | 4 (44.4%) | 5 (55.6%) | 0.72# |
| | No | 15 (37.5%) | 25 (62.5%) | |
| Education | None | 3 (60%) | 2 (40%) | 0.067# |
| | Any | 5 (16.7%) | 25 (83.3%) | |
| Occupation | Farmers | 7 (22.6%) | 24 (77.4%) | 1# |
| | Non-farmers | 0 (0.00%) | 2 (100%) | |
| Distance to clinic | less than 5km | 4 (28.6%) | 10 (71.4%) | 0.734# |
| | More than 5km | 10 (37%) | 17 (63%) | |
| Partner tested | Yes | 4 (26.7%) | 11 (73.3%) | 0.722# |
| | No | 6 (33.3%) | 12 (66.7%) | |

**¶ ( Pearson's Chi square test ) * (ttest ) # (Fisher's exact test)**

**Table 3: Univariable and Multivariable analysis of factors associated with retention in care among HIV infected pregnant women starting ART.**

| Factor | Level | UNIVARIABLE ANAYSIS | | | MULTIVARIABLE ANAYSIS | | |
|---|---|---|---|---|---|---|---|
| | | Un-adjusted HR | Confid Interval | P value | Adjusted HR | Confid Interval | P value |
| Age at baseline | Continuous | **0.94** | **0.87 1.03** | **0.205** | | | |
| CD4 category | Below 350 | Base | | | Base | | |
| | Above 350 | **3.16** | **1.00 9.97** | **0.049 *** | **3.12** | **0.3 31.86** | **0.34** |
| Start Regimen | AZT/3TC/EFV | Base | | | Base | | |
| | Other regimens | **0.36** | **0.12 1.09** | **0.073 *** | **1.4** | **0.12 15.74** | **0.784** |
| Gestation at registration | Trimester 1&2 | Base | | | Base | | |
| | Trimester 3 | **2.56** | **0.96 6.84** | **0.061 *** | **4.17** | **0.41 41.92** | **0.225** |
| Education | None | Base | | | Base | | |
| | Any | **0.24** | **0.06 1.03** | **0.055 *** | **1.01** | **0.06 17.74** | **0.996** |
| Baseline WHO stage | Stage 1 | Base | | | | | |
| | Other stages | **0.82** | **0.24 2.84** | **0.756** | | | |

* Included in the final multivariable model

## Time to non retention

Total follow up time from all women included in the study was 901 person months for the entire study period. Women that were retained in care by two years contributed 730 person months of follow up time while those that were not retained contributed 171 person months.

Women that were not retained in care both during and after pregnancy had a median follow up of 9 months and IQR [1.5-13] months. Hence, time to non retention as generated by this data was approximately 9 months since registration in the cohort.

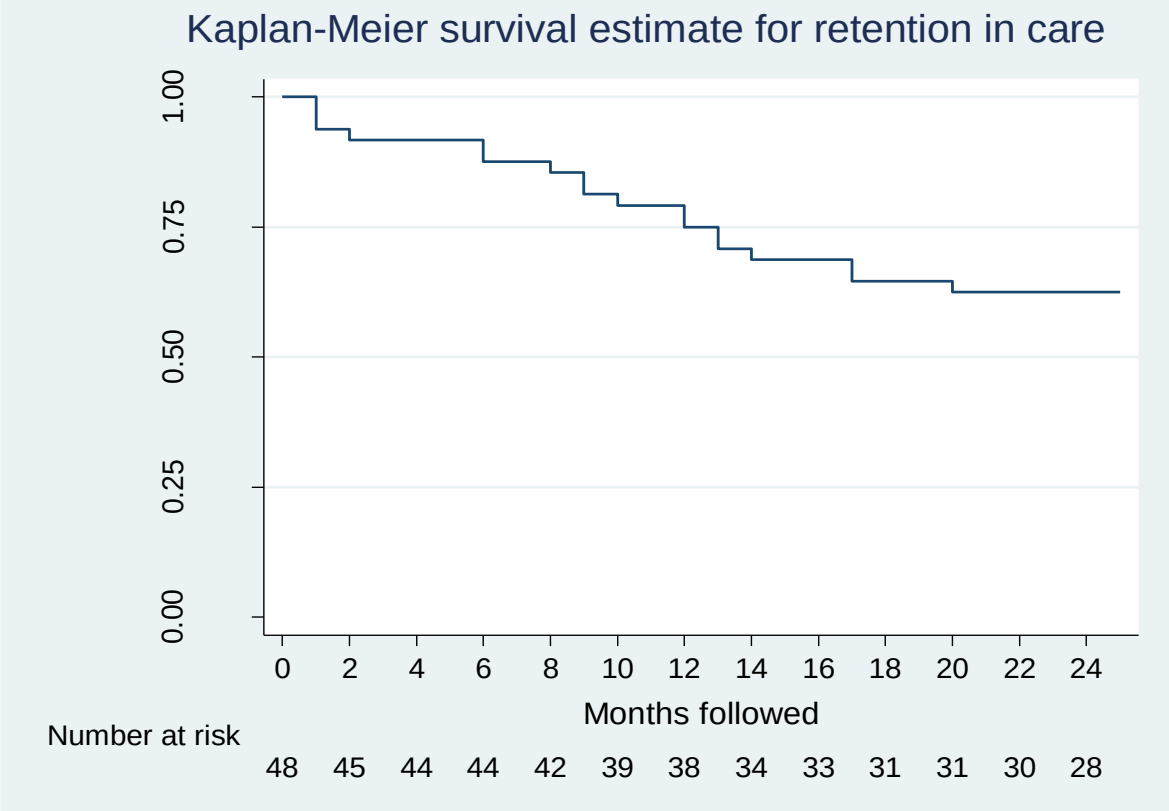



**Figure 5:** Kaplan Meier estimates of time to non retention in care

# Chapter Four: Discussion

## Introduction

This chapter explains the findings of our study with key comparison to other close studies elsewhere. Each finding is assessed in detail with the outcomes studied and related to existing literature attaching careful relevance to public health value of HIV clinical care of the pregnant women starting ART. It ends with the limitations that we faced during the study.

## Discussion

Our research aimed at establishing the difference in adherence to ART and retention in care, during pregnancy and after pregnancy including the predictive factors to these two outcomes. We also assessed the median time (in months) to non retention. The study was among HIV-infected pregnant women starting life-long treatment at Ifakara between 2009 and 2010. They were followed for two years to 2011 and 2012 respectively.

Our findings show that adherence was sufficient (good) for all women as long as they participated in the study. Although there was no statistical evidence to show differences in retention in care between the two periods, absolute numbers retained were more during pregnancy than after pregnancy. None of the clinical and socio-demographic factors studied independently predicted retention in care or adherence to ART. Median time to non retention was 9 months upon registration with an IQR of 1.5-13 months.

The above summary of results is discussed below per stated study objective with comparison to results from other studies.

## Adherence to ART

Adherence to ART was sufficient (good) for all the HIV-infected pregnant women in the study. Contrary to what is seen elsewhere [23, 25, 35]all participants reported 100% adherence. None of them had adherence reported as insufficient (poor) in the dataset. We believe this was so because the CDCI thoroughly counsels the women before they are started on ART. This could be a good practice that other programs might want to adopt. This result could also have arisen due to reporting bias since we used patient self report to assess this outcome. This bias could not be dealt with since our data was secondary. Otherwise, other ways of assessment including unannounced home pill count [33]and plasma drug concentrations could have offered a better option. Fortunately, PSR has been seen not to differ much from these two other measurements of adherence [32, 33]. The presence of viral load counts for these women would have been a perfect proxy for adherence in this population for comparison with the PSR as was done in another study [14].

The need to understand adherence trends in this population cannot be over emphasized as the benefits to sufficient (good) adherence to ART during pregnancy and postpartum are enormous including improved livelihoods and good PMTCT outcomes [13, 14, 24]. A finding with differences in adherences between the two periods for our group would have provided a background for a better understanding of which period (during pregnancy or afterwards) HIV-infected pregnant women starting ART are at risk of insufficient (poor) adherence.

## Predictors of Adherence to ART

The fact that all women had sufficient adherence to ART for both periods compared, we were unable to tease out how the studied socio-economic, demographic and clinical factors predicted adherence to ART. Stigma, poverty and successfully protecting the baby had been seen elsewhere [23, 27] as predictors but our dataset didn't have them recorded.

## Retention in care

Retention in care was similar when compared between the two periods during pregnancy and after pregnancy. However absolute numbers showed more people getting lost to follow up after pregnancy than during pregnancy. This could have been due to the longer follow up period after pregnancy. Women were followed up until two years since the day of registration yet most of them were registered in their second and third trimester which means their follow up time while pregnant was approximately six months for the majority allowing for over fourteen months of follow up after pregnancy.

Taking follow up time into consideration, incidence rates of loss to follow up during pregnancy were 47 per 1,000 person months of follow up while after pregnancy incidence was 18 per 1,000 person months. This trend suggests that loss to follow up is reduced by almost half if a woman was kept into care until delivery.

Although not many studies exist that have assessed retention in care among HIV – infected pregnant women starting ART, one done in South Africa recently [31] has findings different from the ones we got in our study. Women that tested HIV positive during pregnancy in the South African study, those eligible to start ART had 40% non retention.

Among women that were not eligible, 22% were lost. Including pregnant women that were both eligible to start ART and not eligible put general non retention levels at about 50% for this population.

## Predictors of retention in care

We didn't find any independent predictors of retention in care among the factors studied. This could have been due to the smaller sample of participants we registered that may not have been significant in the multivariable models run. However, when univariable models were run, the trend was that women with CD4 cell counts above 350cells/mm3 at registration had higher hazards of non retention in care than their counterparts who got registered with CD4 cell counts less than 350cells/mm3. This finding suggests that sicker HIV – infected pregnant women at registration (as depicted by lower CD4 counts) tend to stay in care more compared to those that don't feel that sick at registration. This same finding has been shown in other studies across Africa looking at both eligible and non-eligible for ART female populations [28, 35-37].

Similarly, more women initiated on AZT/3TC/EFV were lost to follow up compared to women initiated on other regimens. Much as it could have been due to the larger numbers on this regimen, it is also likely that side effects due to EFV could have accounted for the losses. Our study didn't capture side effects to the drugs initiated.

Women that were registered into the cohort while in the last trimester of their pregnancy were almost three times more likely to be lost from care as compared to women registered while in their first or second trimester. Likewise, women with any education compared to those with no

level of education, were less likely to get lost to follow up. These findings were consistent with what was found elsewhere [31, 37]

## Time to non retention

Among women not retained in care over the 2 year period of follow up, the median time to non retention was 9 months. In our review of available studies, none mentions time to non retention among HIV – infected pregnant women starting life-long ART. Considering that majority of the women are registered in their second or third trimester, this puts the danger period to non-retention at about six months after the baby is born. This could however have been affected by our small sample size.

## Limitations

While considering the findings of this study we acknowledge the fact that the dataset used was from only one HIV care and treatment center. This sample may not be representative of the vast numbers of HIV-infected pregnant women starting ART. Other sites might have a completely different experience and hence the need to do such studies elsewhere. Our study design was secondary data analysis and hence limited in the scope of factors to study. The ones included were those that had been collected during that study period. For future research, prospective studies should be designed to include and measure all factors exhaustively.

The findings of the study need a cautious interpretation due to the small sample size. Even though we included everyone who met the eligibility criteria, the number of study participants remained small. We were also unable to rule out mortality and transfers among those considered lost and this might have led to a slight increase in estimation of the outcome.

# Chapter Five: Conclusions and Recommendations

## Introduction

This chapter has conclusions based on the evidence generated and comparison with other studies as discussed earlier. It ends with the recommendations plus suggested further research to answer more questions generated out of this study.

## Conclusions

Our findings demonstrate that overall, adherence to ART was more than 95% while retention in care was 60%. Retention in care was similar for the 2 periods when HIV-infected pregnant women starting life-long ART were pregnant and after pregnancy. Adherence to ART was sufficient throughout the follow up period. This delivers more hope for the Option B+ program. It also reassures those countries that have rolled out and many that are still rolling out this program. We can have some confidence that these women started on ART during pregnancy will stay in care.

There were no independent predictors of retention in care among the factors studied in this study. However, we believe implementing programs need to assess critically women;

- With CD4 cell counts above 350 cells/mm3
- Registered in late pregnancy
- With no education, for aggressive counseling to attain a better public health outcome and clinical benefit to the women starting ART in pregnancy.

The study also found that after registration into care, the HIV-infected women who start life-long ART will have a median time to non retention in care of about 9 months since registration. Our sample size could have had an effect on the results we got and thus recommend bigger numbers in further studies as put below.

## Recommendations

Since we worked with just one care and treatment centre, we recommend that similar studies be done elsewhere with bigger sample sizes to compare outcomes for different locations. The larger sample sizes would give more conclusive results regarding adherence to ART and retention in care among HIV-infected women starting ART in pregnancy.

Involvement of local leadership and other partners is needed to send pregnant women to care and treatment centers before late pregnancy. This will ensure more women coming into care early and increasing the chances of retaining them into care. The impact on public health outcome will increase since being in care will result in taking their prescribed ART and preventing HIV infection to their sexual partners and babies in the forthcoming pregnancies.

We also recommend that for this population, counseling on the importance of staying retained in HIV care be emphasized at ANCs. This would mitigate the losses from care seen a few months after giving birth.

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# Appendices

## Appendix One: University ethics approval

Approval from the ethics committee (medical) of the University of the Witwatersrand

R14/49 Dr Jingo JohnPaul Kasule

# HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

## CLEARANCE CERTIFICATE NO. M131157

| | |
|---|---|
| **NAME: (Principal Investigator)** | Dr Jingo JohnPaul Kasule |
| **DEPARTMENT:** | Biostatistics and Epidemiology<br>Ifakara Health Institute, Tanzania |
| **PROJECT TITLE:** | Adherence to Antiretroviral Therapy and Retention in Care among HIV-Infected Pregnant Women starting Life-Long Treatment in Ifakara - Tanzania |
| **DATE CONSIDERED:** | 29/11/2013 |
| **DECISION:** | Approved unconditionally |
| **CONDITIONS:** | |
| **SUPERVISOR:** | Dr Charles Chasela |
| **APPROVED BY:** | Professor PE Cleaton-Jones, Chairperson, HREC (Medical) |
| **DATE OF APPROVAL:** | 02/12/2013 |

**This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.**

**DECLARATION OF INVESTIGATORS**

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

**PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES**

## Appendix Two: Permission to use dataset by Ifakara Health Institute

Permission from the Ifakara Health Institute head to use the dataset.

IFAKARA HEALTH INSTITUTE
research | training | services

ST FRANCIS
DESIGNATED DISTRICT HOSPITAL

Swiss TPH

# Data Use Agreement

## KIULARCO cohort

This document certifies that the primary investigator (PI) listed below has a research project that has been approved by the Scientific Committee of KIULARCO. Within the context of the approved research project, permission has been granted to use KIULARCO data. An anonymized dataset will be provided with the requested variables within a reasonable time period once clear specifications are provided.

The following guidelines apply:

- Data may only be used for the analysis of the approved research project.
- Intended publications, presentations, or abstracts must be clearly stated as part of the project proposal.
- Guidelines for authorship and publication must be followed.
- Data may not be shared with anyone not listed on the approved project proposal.
- The PI is responsible for ensuring that guidelines are followed by the study team and partners.
- Once the project is completed, the data should be deleted – new datasets will be provided for each approved project.

If any of the above guidelines are violated, authorization for data use will be immediately withdrawn and relevant third parties or journals notified as necessary.

**I agree to the data use conditions as specified above.**

Name of approved project: ***"Adherence to ART and retention in care among HIV-infected pregnant women starting life-long treatment in Ifakara, Tanzania"***

Printed name of PI: **Jingo Johnpaul Kasule**

Signature of PI _____

Date 2/October/2013.

Authorization given by _____

Date of authorization 02/10/2013