Effectiveness of Lifelong ART for Pregnant and Lactating Mothers on Elimination of Mother to Child Transmission of HIV and on Maternal and Child Health Outcomes: Uganda 2013-2015

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LIST OF ABBREVIATIONS

MCH	Maternal and Child Health
AIDS	Acquired Immunodeficiency Syndrome
ANC	Ante-Natal Care
ART	Antiretroviral therapy
ARV	Antiretroviral
CDC	Centers for Disease Control and Prevention
CPHL	Center for Public Health Laboratories
DHO	District Health Officer
DHT	District Health Team
EID	Early Infant Diagnosis
eMTCT	Elimination of Mother-to-Child Transmission of HIV
FGD	Focus Group Discussion
HC III	Health Center level III
HC IV	Health Center level IV
HCT	HIV Counseling and Testing
HIV	Human Immunodeficiency Virus
HMIS	Health Management Information System
HSD	Health Sub-District
IDI	In-depth Interview
IP	Implementing Partner
IRB	Institutional Review Board
KI	Key Informant
M&E	Monitoring and Evaluation
MakSPH	Makerere University School of Public Health
PASS	Power Analysis and Sample Size
PCR	Polymerase Chain Reaction
PMTCT	Prevention of Mother-to-Child Transmission
PNC	Post-Natal Care
SMC	Safe Male Circumcision
UAC	Uganda AIDS Commission
UACP	Uganda AIDS Control Program
UNAIDS	Joint United Nation Program on AIDS
USG	United States Government
VHT	Village Health Team
WHO	World Health Organization

SUMMARY

Background: In September 2012, Uganda adopted the provision of lifelong combination antiretroviral therapy (ART) for all HIV positive pregnant and lactating mothers (called Option B+) in order to reduce mother to child transmission (MTCT) of HIV to less than 5%. By August 2013, the program had been scaled up in all the 112 districts of the country.

Objectives: We performed an evaluation to measure the effectiveness of the Option B+ strategy on elimination of MTCT of HIV and on maternal and infant health outcomes up to 18 months post-ART inititiation. Specifically, the objectives were to determine i) the rate of MTCT of HIV at 6 weeks after birth [1st polymerase chain reaction (PCR) test] and at 18 months postpartum (based on a final rapid HIV antibody test) among infants born to HIV positive mothers on Option B+, ii) retention of mothers in HIV care, iii) the mean change in CD4 cell count among mothers from ART initiation to 18 months post-initiation and iv) the reasons that mothers drop out of the program.

Methods: We identified a representative sample of 145 health facilities providing Option B+ in the 24 districts of the central region of Uganda. We abstracted available health facility record data of 2,169 pregnant or lactating mothers and their infants who had been enrolled on Option B+ between January and March 2013. We calculated MTCT rates and retention in care using survival analysis and evaluated factors associated with HIV transmission and with dropping out of care using cox-proportional hazards modeling. To explore reasons why women drop out of care, we performed 29 focus group discussions with peer mothers and village health team members, 27 in-depth interviews with mothers who were retained in care and 21 in-depth interviews with mothers who dropped out.

Results: Only 1,240 (57.2%) infants could be identified as having been in care and linked to their mothers. Of these, 1,089 (87.8%) had a 1st PCR test and 50 (4.6%) were identified as HIV positive. The rate of infection per month, based on the 1st PCR test was 3.2/100 person months (95% CI: 2.4-4.3). Only 352 (28.9%) infants had a final HIV antibody test and no new infections were identified. Poor adherence to antiretroviral (ARV) drugs by the mothers [adjusted Hazard Ratio (aHR) 1.89 (95% CI 1.30-2.73) and an infant receiving no ARV drugs (aHR 1.22 (95% CI 1.03-1.45) were associated with increased risk of MTCT of HIV. The proportion of mothers who were retained in care at 18 months post-ART was 62.0%. Only 58.5% of mothers had a baseline CD4 cell count test, and among these women, 69.3% had a repeat test performed. Among those with follow-up CD4 test at 18 months, the mean CD4 cell count increased from 532.6 cells/ µl (S.D 341.1) at baseline to 726.9 cells/ µl (S.D 365.6) ($p<0.001$) at 18 months post-ART initiation. MTCT, retention and proportion of women with baseline and follow-up CD4 cell count monitoring varied considerably by district as well as by health facility level; lower level facilities had higher HIV infection rates, lower retention of mothers and fewer women being monitored by CD4 tests.

Based on the focus group discussions and in-depth interviews, low levels of retention in care were the result of individual, interpersonal, institutional and community factors. The individual and interpersonal factors included fear of ART toxicities, concerns about disclosure and HIV-related stigma, insufficient partner support, domestic violence and belief in divine healing. The institutional and community factors included inadequate mobilization and tracking of mothers by the village health team members and peer mothers, client difficulty with facilitation to facilities, inadequate staffing at health care sites, poor provider attitudes and stock outs of ARV drugs.

Conclusion: These findings suggest that the implementation of the Option B+ program can reduce MTCT of HIV to less than 5%. However, HIV transmission during the postpartum period could not be accurately assessed because the majority of infants did not have a final HIV antibody test. High dropout rates, poor record keeping, failure to provide ARV prophylaxis to infants, poor provider attitudes, high levels of stigma and discrimination in the community, lack of partner support and stock-outs of ARV drugs are some of the factors that could undermine the program.

Recommendation: Measures to improve retention in care, availability of ARV drugs and adherence to treatment need to be multi-pronged, addressing not only the provider capacity and attitudes, and availability of medication, but also the social and economic realities of the environment in which women live.

Dissemination: The data for this evaluation are the property of the Government of Uganda. Results of the evaluation will be shared with key stakeholders including the Uganda Ministry of Health, Uganda AIDS Commission and the scientific community through reports, meetings, conference presentations and peer-reviewed publications. A final dissemination meeting for District Health Officers, district PMTCT focal persons, implementing partners, Development partners and the scientific community will be held in August 2015.

1.0 INTRODUCTION AND BACKGROUND

1.1 Introduction

Globally, an estimated 36.9 million people were living with HIV in 2014: Of these, 2.6 (7.0%) million were children less than 15 years of age [1]. More than 70% of the global HIV burden occurs in sub-Saharan Africa [2, 3]. In Uganda, an estimated 1.6 million people are living with HIV: About 15,000 new infections occurred in 2013 alone [2]. Vertical transmission of HIV from mother to child is the second most common route of transmission of HIV in Uganda, accounting for 18% of all new infections [4]. Without treatment, half of the children living with HIV would die before their second birthday [2]. The risk of HIV transmission from mother to child can be as high as 15-30% during pregnancy and 10-20% during breastfeeding if ARV drugs for the mother and infant are not provided [5, 6]. With programs for prevention of mother-to-child transmission (PMTCT) that include early HIV testing, special precautions during delivery and provision of antiretroviral treatment to the mother and infant, this risk can be reduced to less than 5% among infants who breastfeed and to less than 2% among infants who do not [6]. This approach has a huge potential to improve maternal and child health and survival [7]. In 2012, the WHO recommended that countries implement the Option B+ strategy, which, in addition to the above, includes providing lifelong antiretroviral therapy (ART) to HIV-infected pregnant and lactating mothers regardless of CD4 count [8]. This strategy was adopted by several priority countries in sub-Saharan Africa, including Uganda. By 2013, a considerable increase in the proportion of HIV-infected pregnant women who were started on ART in these countries was observed and the number of new HIV infections among children dropped drastically [3]. In Uganda, UNAIDS estimated a 40% reduction in new infant HIV infections.

1.1.1 Early infant diagnosis of HIV

The WHO recommends that infants born to HIV-infected mothers undergo a polymerase chain reaction (PCR) test to determine presence of viral RNA at or after 6 weeks of age [9]. This test identifies those infants who were infected intra-partum, or during or immediately after delivery. Serological assays suitable for HIV antibody detection in adults cannot be reliably used for confirmatory diagnosis of HIV in infants as the interpretation of a positive HIV antibody test is confounded by the persistence of maternal HIV antibody for up to 18 months. A repeat HIV antibody test should be performed among infants at this age or at the conclusion of breastfeeding, to identify those who may have seroconverted.

1.1.2 HIV-free survival in a breastfeeding population

Breastfeeding is recommended as the optimal feeding practice for all HIV-infected women in countries where significant numbers of children still die from diarrhoea, pneumonia, and malnutrition. However, 10-20% of breastfeeding infants may become infected unless preventive measures are taken [10]. A dramatic reduction in postnatal MTCT of HIV and in infectious morbidity can be achieved if i) HIV-infected mothers exclusively breastfeed for the

first six months, ii) they continue breastfeeding until twelve months while introducing complementary foods, and iii) mothers and infants are adherent to ART during this period. Adherence to these guidelines can reduce the risk of vertical transmission [11]. The term "HIV-free survival" emphasizes not only the importance of eliminating MTCT of HIV but also the promotion of breastfeeding to reduce the risk of death from infectious diseases [10].

1.1.3 Retention in HIV care

Retention in care is required to optimize clinical outcomes for those on ART. Retention is often defined as "being alive and receiving ART at the end of a follow-up period [12]. For HIV-infected mothers on ART, retention in care is essential for continued receipt of ART, evaluation of medication toxicities and early identification of treatment failure [13]. In addition, women who continue in care may receive additional services such as social support and secondary prevention messages that can help them cope with lifelong ART [12]. Failure to attend clinics has been associated with poor drug adherence, clinical deterioration and high risk of death. Interruption of ART leads to emergence of drug resistance, limiting future drug options and increasing mortality [14, 15]. Poor retention in care among HIV-infected individuals on ART has been reported to occur in many countries in Africa [16, 17], including Uganda [18-20]. Long distances to health facilities, financial constraints, food shortage and insecurity, ART toxicities, stigma, inadequate social support, fear of disclosure and belief in divine healing have all been reported as being associated with retention failure [20-22].

1.1.4 Monitoring response to ART

Response to treatment needs to be monitored to ensure that drug resistance does not occur. Treatment failure can be measured in three ways: i) clinically, by disease progression and WHO staging, ii) immunologically, using trends in CD4 counts over time; and iii) virologically, by measuring plasma HIV-1 RNA levels (HIV viral loads) [23]. After ART initiation, the CD4 cell count is expected to increase while viral load is expected to decrease; however, this does not occur among those who have drug-resistant HIV [24]. Immunological non-responders are defined as those having a CD4 count below 100 cells/ µl after 6 months of therapy; a return to, or a fall below, the pretherapy CD4 cell count after 6 months of therapy; or a 50% decline from the on-treatment peak CD4 value (if known) [23]. According to the 2012 Ugandan National Integrated Guidelines on ART and PMTCT, all HIV-infected pregnant/lactating mothers should have a CD4 cell count performed at ART initiation and every 6 months [6].

1.1.3 History of the PMTCT program in Uganda

Uganda issued its first PMTCT guidelines in 2000; these recommended provision of a single dose of Nevirapine (sdNVP) to HIV-infected mothers during delivery. In 2006, the treatment guidelines were updated and recommended the use of combination ARV regimens for the mother during pregnancy. In 2011, Uganda signed the Global Plan towards virtual elimination of new HIV infections among children by 2015, the targets of which are to reduce new pediatric HIV infections by 90% and to reduce MTCT of HIV to less than 5% at the population level

[25]. As a result of the global commitment to controlling the AIDS pandemic, services for prevention, treatment and care of HIV infections have been scaled up in the country. In 2012, the country shifted from the Option A strategy (combination ART for mothers with CD4 count <350 cells/µl or ARV prophylaxis from 14 weeks of gestation until delivery for mothers with a CD4 count >350 cells/µl) to Option B (combination ART irrespective of CD4 count until 1 week after cessation of breastfeeding) [6]. Uganda quickly transitioned to rolling out Option B+ in 2012 and by the end of 2013, Option B+ was rolled out in all the 112 districts in the country; 95% of the hospitals, Health Centers [HC] IVs, and HC IIIs were providing this service. In order to improve retention in care for mothers and infants, a critical component of the Option B+ strategy is to provide clinic appointments for follow-up on the same day for both mother and infant (mother-baby care points) [26].

To-date, there has been no comprehensive evaluation of the effectiveness of the Option B+ strategy in Uganda. This evaluation examined the rates of MTCT of HIV among infants, retention in care and reasons for dropping out.

1.2 Background to the META Project

The Monitoring and Evaluation Technical Assistance (META) project [now called the Monitoring and Evaluation Technical Support (METS) project] is a CDC-funded collaboration between the Makerere University School of Public Health and the University of California San Francisco. The mandate of the META project is to help strengthen national, district and health facility monitoring and evaluation systems for HIV/AIDS programs. The project collaborates with MoH and Implementing Partners.

In January 2015, META received approval of a protocol to conduct an evaluation of the effectiveness of Option B+ in Uganda.

2.0 OBJECTIVES OF THE EVALUATION

2.1 Main objective

To measure the effectiveness of Option B+ strategy on the MTCT rate and on maternal and child health outcomes up to 18 months postpartum.

2.2 Specific objectives

1. To determine the rate of MTCT of HIV at 6 weeks and 18 months postpartum, among infants born to HIV positive mothers on Option B+
2. To determine the retention of mothers in HIV care, up to 18 months post-ART initiation
3. To determine the mean change in CD4 cell count among mothers between ART initiation and up to 18 months post-ART initiation
4. To identify reasons for dropping out of care among mothers enrolled in the option B+ program.

3.0 METHODOLOGY

3.1 Setting

The evaluation was carried out in all the 24 districts of the central region of Uganda. The region was chosen for the evaluation because Option B+ was rolled out first in this area (October 2012), making it possible to follow mother-baby pairs for 18 months post-partum. The districts included 1) Kampala 2) Kiboga 3) Kalangala 4) Kayunga 5) Nakasongola 6) Luweero 7) Mpingi 8) Masaka 9) Mubende 10) Rakai 11) Mukono 12) Sembabule 13) Wakiso 14) Bukomansimbi 15) Butambala 16) Buikwe 17) Buvuma 18) Gomba 19) Kalungu 20) Kyankwazi 21) Lwengo 22) Lyantonde 23) Mityana and 24) Nakaseke (Figure 1). According to the 2014 census estimates, the region has a total population of 9,579,119, which comprises 27.5% of the national population [27].

Figure 1. Map of Uganda showing study districts

Considerable variations exist in the population of the districts in the region: Kalangala has the lowest number number of residents (53,406) while Wakiso has the highest (2,007,700). The regional adult HIV prevalence was estimated to be 9.8%, with women (11.1%) more likely to be infected than men (8.2%) [28, 29]. At the time of the evaluation, there were 358 health facilities accredited to provide Option B+ in the region. They comprised of 2 Centers of Excellence (COE), 35 hospitals, 45 HC IVs, 250 HC IIIs and 26 clinics.

3.1 Design

The evaluation involved both a quantitative and qualitative component. The quantitative component was based on a retrospective cohort analysis of data abstracted from records of pregnant or lactating mothers who were enrolled on option B+ between January and March 2013. A representative sample of health facilities in all the 24 districts, stratified by level of facility was identified for inclusion. Health facility records were reviewed and data abstracted from antenatal care registers, the pre-ART and ART registers, ART cards, the EID register and the Exposed Infant Clinical Chart. The qualitative component involved focus group discussions (FGDs) with peer mothers and village health team (VHT) members and in-depth interviews (IDIs) with HIV positive mothers lost to follow-up and those who were retained in care

3.2 Sampling strategy

3.2.1 Quantitative evaluation

Facility sampling: A stratified sampling design was adopted to select the health facilities. All the health facilities in each of 24 districts in the region that provide Option B+ services were stratified according to their level of care [COE, hospitals, HC IVs, HC IIIs and clinics]. Clinics were subsequently excluded from the sampling frame because they had not initiated Option B+ during the required time period. Based on sample size calculations and estimations of clinic population size, it was determined that one third (1/3) of the facilities in each district were required for inclusion. Within each district, 1/3 of facilities within each stratum were selected using systematic sampling. The sampling interval was obtained by dividing the total number of facilities with the number of facilities to be studied in each stratum (N/n). After obtaining a random start from a table of random numbers, the interval was followed until the required number of facilities in each stratum was identified.

Sampling of mother-baby pairs: Records of all HIV positive mothers enrolled on Option B+ between January and March 2013 and their live-born infants were reviewed in the selected facilities. Infants were linked to their mothers through the mothers' antenatal care (ANC) number and clinic number. Linkage was further confirmed by checking the consistency of the mothers' name and sex of the infant.

3.2.2 Qualitative evaluation

A theoretical sampling approach, in which participants were selected based on their relevance to the questions being asked [30-32], was used to identify the facilities and the participants in qualitative interviews. Since the qualitative evaluation focused on issues related to loss to follow-up and retention in care, the health facilities were selected based on low retention rates.

Facility sampling: In each of the 24 districts, the health facilities with the lowest retention rates among those already sampled for the quantitative assessment were selected for inclusion. The PMTCT focal persons in each district assisted in identifying the facilities.

Sampling of mothers: From each of the selected facilities, two mothers who were active in care and two mothers who had been lost to follow-up (LTFU) were purposively identified to participate in the IDIs. Mothers LTFU were defined as those not seen at the facility for three months since their last missed appointment, based on the ART register. VHT members or peer mothers attached to the selected facilities, along with the study team members attempted to trace and contact these mothers. Participants were contacted by phone, and if unsuccessful, by a home visit. If a mother could not be reached by either method, another eligible mother was selected. Because mothers LTFU are difficult to trace, and if found were reluctant to participate, efforts were ultimately made to contact all mothers not retained in care at each selected facility. The exact tracing and refusal rates were not documented. Because of the difficulty of recruiting mothers for IDIs, one mother retained and one mother LTFU were enrolled from selected facilities.

Sampling of VHTs and Peer Mothers: The in-charges of the sampled facilities contacted the VHT members and peer mothers affiliated with that facility and invited them to participate in FGDs. At each of the selected facilities, either one FGD for VHTs or for peer mothers was conducted.

3.3 Sample size

3.3.1 Quantitative evaluation

Sample sizes were calculated for each quantitative objective, using PASS software, and were based on assumptions about reductions in MTCT to less than 5%, and retention in care of mothers and infants. The maximum effective sample size required was 1500 women. Because women from one facility were not completely independent of one another, a design effect of 2 was applied to adjust for clustering; therefore, the maximum desired sample size of 3,000 maternal records. In this evaluation, a total of 2,169 (72.3%) records were obtained.

3.3.2 Qualitative evaluation

Overall, 29 FGDs and 48 IDIs from 18 districts were conducted. The districts included 1) Kampala 2) Kiboga 3) Kalangala 4) Kayunga 5) Nakaseke 6) Luweero 7) Mpigi 8) Masaka 9) Mubende 10) Rakai 11) Mukono 12) Wakiso 13) Bukomansimbi 14) Buikwe 15) Gomba 16) Lyantonde 17) Mityana and 18) Nakaseke. Each FGD comprised of 6-10 participants. Of the 29 FGDs, 11 were held with peer mothers and 18 with VHT team members. Of the 48 IDIs, 27 were held with mothers retained in care and 21 were held with mothers who dropped out.

3.4 Data collection

For both the quantitative and qualitative evaluation, data were collected by research assistants who had at least a basic knowledge of the PMTCT program, and who underwent training on research ethics and on the data collection procedures prior to going to the field. A total of 16 teams were assembled, each comprised of 5 research assistants and supervised by a senior staff member from the MOH, and by a member of the META project. Data from mother-infant

records in the selected facilities were abstracted using structured paper abstraction forms that were developed based on careful review of data collected on routine clinical records. Topic guides for FGD and IDI were used during interviews. For both the FGDs and IDIs, two research assistants were present, one to facilitate the discussion or the interview and the other to take notes. The IDI and FGDs were also audio-recorded with permission from participants. Data collection was an iterative process that allowed for new lines of questioning to arise so that issues that emerged during discussion could be pursued.

3.5 Measures

Quantitative evaluation: The main outcome variables were i) HIV status of the infant (positive or negative) based on 1st PCR test, ii) retention of mothers in care at the end of a follow-up period) and iii) change in mothers' CD4 count from ART initiation to last recorded CD4 test, as well as 18 months, post-ART initiation. The explanatory variables included mothers' CD4 count at baseline, WHO clinical stage, ART regimen at initiation, adherence to the 1st three clinic appointments, ART adherence of the mother at the last recorded clinic visit, health facility level, place of delivery, infants' adherence to the 1st three clinic appointments, infant ARV use, infant feeding practices and age of infant at HIV testing. The sociodemographic characteristics of the mothers and infants were also assessed.

Qualitative evaluation: The IDIs explored knowledge of and experience with the PMTCT program, perceptions of and attitudes towards the program, challenges in accessing care, reasons for loss to follow-up and suggestions for improving the program. The FGDs with the VHT members and peer mothers focused on their understanding of the PMTCT program, approaches used to fulfill their roles, experiences with following mothers, challenges with and perceived barriers to successful enrolment in the option B+ program and factors they believed to improve retention of clients.

3.5 Data management and analysis

Quantitative data: Completed paper abstraction forms were transported to the META offices in Kampala for double data entry into Epi Data software. Range and logic checks were performed, and the data were exported to STATA 12.0 for analysis. The proportion of infants who were HIV infected based on the 1st PCR was computed for the sample overall, and by district and health facility level. Differences in proportions of HIV infected infants across the health facility levels were compared using chi squared tests for categorical variables. Student's *t*-test was used to compare mean CD4 cell counts at baseline and at last test. The MTCT rates per 100 person months and mother retention rates were determined using Kaplan-Meier survival analysis. Factors associated with HIV transmission and maternal retention were evaluated using Cox proportional hazards modelling.

Qualitative data: Data from the FGDs and IDIs were stored in both soft copy form on tape recorders and hard copy form as paper notes. Transcription of the tapes from the FGDs and

IDIs was performed by the research assistants who translated them into English. Three META staff trained in qualitative analysis read through all transcripts and notes, and collectively identified recurrent themes and ideas, on the basis of which a code book was developed. The transcripts were entered into NVivo (version 10) software to determine the frequency of statements made relative to the identified codes, and to highlight those sections related to specific themes and subthemes. The data were interpreted based on internal consistency, extensiveness and specificity of responses and trends or concepts that cut across the various discussions. Analyzed data were presented in text form.

3.6 Quality control

Research assistants who collected data participated in a one-week training in both quantitative and qualitative data collection methods that included familiarization with health facility registers and forms. Standard operating procedures were developed that provided guidance on how to abstract data. Abstraction forms were pre-tested in non-study health facilities for purposes of clarity, validation, suitability and logical flow of the variables and revised accordingly, before being used in the field. Forms were checked for completeness by supervisors at the end of each day, before being sent to META for data entry.

Training on qualitative data collection included information on how to create rapport with the respondents, to listen attentively, to use prompts, and how to guide the respondents back to the topic. The FGDs and IDIs were conducted in a neutral place considered to be convenient and private as agreed to by the respondents.

3.7 Ethical considerations

The protocol was approved by the Makerere University School of Public Health Higher Degrees and Ethics Committee, the Uganda National Council for Science and Technology and the Center of Global Health (CGH) office of the Associate Director for Science (ADS), Division of Global HIV/AIDS (DGHA), CDC-Atlanta.

Participants in IDIs and FGDs completed written informed consent, with a separate signature for consent for audio-recording. For participants who could not write, thumb prints were obtained. Informed consent forms were translated into the local language of Luganda, and back-translated to English to ensure accuracy of translation. Participants were given copies of the consent forms to read in the local language, or had the forms read to them by the research staff. Participants in qualitative interviews received approximately 5 USD to compensate them for their transportation.

4.0 RESULTS

4.1 Sociodemographic characteristic of the mothers and infants

Sociodemographic characteristic of the mothers

Records from 2,169 HIV positive pregnant and lactating mothers initiated on lifelong ART between January and March 2013 were abstracted from a representative sample of 145 health facilities. The median follow-up time was 20.2 months (IQR 4.2-22.5). The greatest proportion of records (22.9%) were obtained from health facilities in Kampala (Figure 2). The highest proportion, 39.3% were abstracted from HC IIIs, 30.0% from Hospitals, 21.7% from HC IVs and 8.9% from one COE. The median age of mothers was 25 years (IQR, 22-29) (Table 1). Most women (44.3%) were enrolled in the ante-natal period, and only 12% in the post-partum period; however, time of enrolment could not be determined for 43% of the sample, because enrolment status was based on the date of birth of the infant, and a large proportion of infants could not be linked. Slightly less than two thirds of the mothers 58.5% had results of CD4 test at ART initiation. The mean CD4 count at ART initiation was 568 cells/µl (S.D 345.9). Nearly all the mothers (96.5%) were initiated on Tenofovir/Lamivudine/Efavirenz (TDF/3TC/EFV) regimen. Good adherence to ART (≥95% adherence to prescribed doses) was recorded for 1,504 (91.4%) mothers. The majority 1,592 (73.4%) kept all their monthly clinic appointments during the 1st three months post-ART initiation. Only 1,240 (57.2%) infants could be identified in the records and linked to their mothers (Table 1).

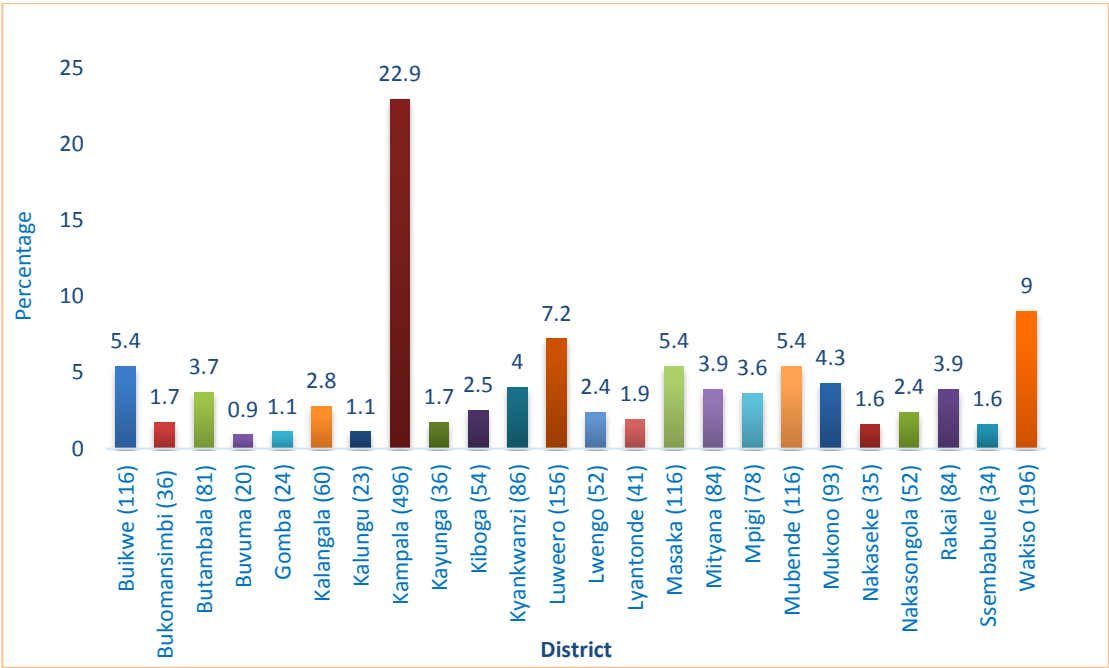

Figure 2. Proportion of the total number of records abstracted in each district

Table 1. Characteristics of HIV positive pregnant and lactating mothers whose records were evaluated

Characteristic	Frequency (N=2,169)	Percentage (%)
Median length of follow-up, months (IQR)	20.2 (4.2-22.5)	
Age in years [N=2,142]: Median (IQR): 25 (22-29)		
15-24	961	44.1
25-34	1,007	47.0
35-44	169	7.9
45-54	5	0.2
Facility level		
COE	194	8.9
Hospital	651	30.0
HC IV	471	21.7
HC III	853	39.3
Status at enrolment		
Pregnant	960	44.3
During delivery	9	0.4
Lactating	263	12.1
Unknown	937	43.2
Had a CD4 cell test at ART initiation		
Yes	1,269	58.5
No	900	41.5
Mean CD4 count at ART initiation	568 cells/µl (S.D 345.9)	
Adherence to ART at last clinic assessment (N=1,645)		
Good	1,504	91.4
Fair	52	3.2
Poor	89	5.4
Mothers seen for all 1st three clinic appointments		
Yes	1,592	73.4
No	577	26.6
Infant record linked to mother		
Yes	1,240	57.2
No	929	42.8

The proportion of mothers who had a CD4 test at ART initiation varied considerably by district: only 10% of mothers underwent CD4 testing in Kalangala, compared to 85% in Kampala district (Figure 3). Similarly, the proportion of mothers who had a CD4 test at ART initiation

varied by health facility level: 44.1% of mothers underwent CD4 testing at HC IIIs, 53.9% at HC IVs, 68.7% at hospitals and nearly all (99%) mothers at the COE had CD4 test performed at baseline.

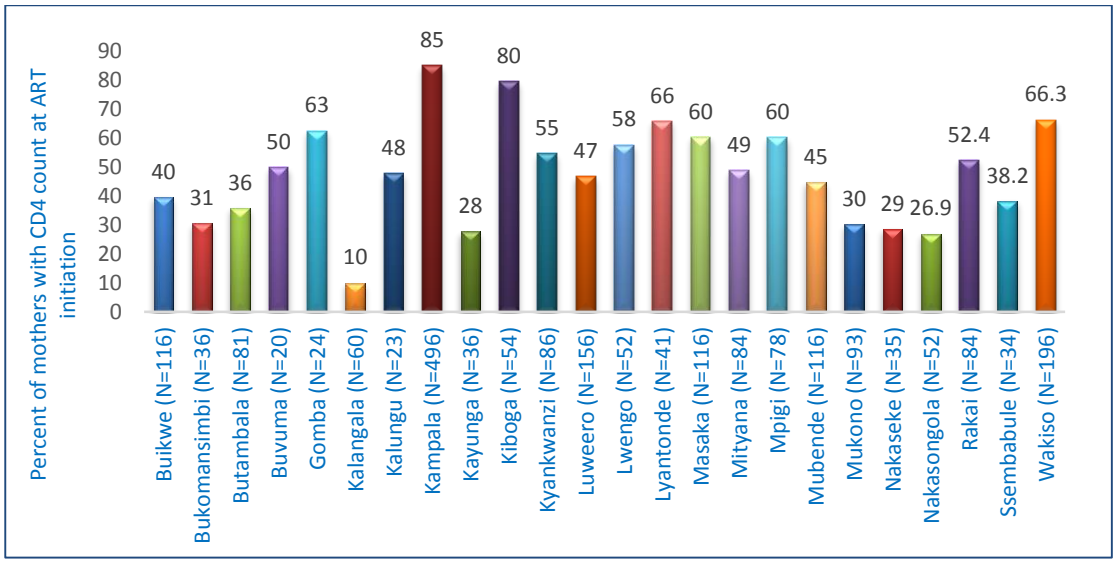

Figure 3. Proportion of mothers in each district who had a CD4 test at ART initiation

Sociodemographic characteristic of HIV-exposed infants

Only 1,240 (57.2%) of records of infants born to HIV infected mothers could be identified and linked to maternal records. Significant variations were observed in the proportion of mother-infant pairs who could be linked. These ranged from 23.8% in Bukomansimbi to 88.9% in Kiboga district (Figure 4).

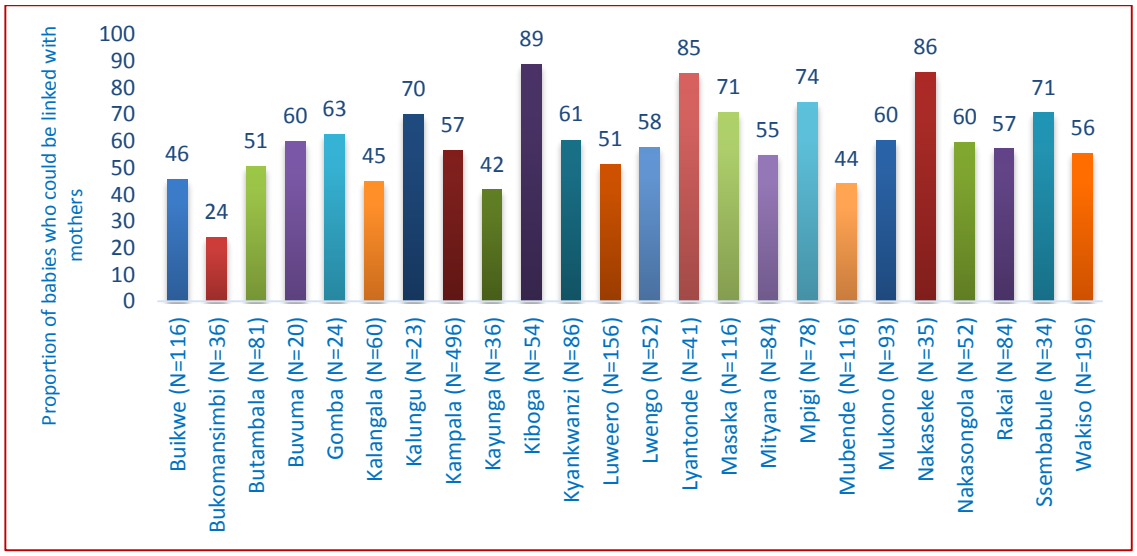

Figure 4. Proportion of HIV-exposed infants in each district who could be linked with mothers

Infants were enrolled at various times, with more than half being enrolled at 6 weeks of age. The median length of follow-up of infants was 9.0 months (IQR 2.6-13.6). The median age of infants at enrolment was 1.6 months (IQR 1.4-2.4) (Table 2).

Table 2. Characteristics of HIV-exposed infants whose data were abstracted

Characteristic	Frequency (N=1,240)	Percent (%)
Sex		
Male	593	47.8
Female	629	50.7
Not documented	18	1.5
Age at enrolment, months (N=1,167)		
0-1.5	582	49.9
1.5-3	409	35.1
4-6	85	7.3
>6	91	7.8
Median length of follow-up, months (IQR)	9.0 (2.6-13.6)	
Place of delivery		
Facility	1,009	81.4
Home	91	7.3
Not documented	140	11.3
Had 1st PCR performed		
Yes	1,089	87.8
No	151	12.2
Median age at 1st PCR (months)	1.5 (IQR 1.5-2.0)	
Had final HIV rapid test performed		
Yes	352	28.9
No	888	71.1
Median age at Rapid HIV test (months)	21.1 (IQR 19.1-23.7)	
Infant feeding practices at 1st PCR		
Exclusive breastfeeding	1,042	84.0
Replacement feeding	22	1.8
Mixed feeding	78	6.2
Complementary feeding	45	3.6
No-longer breastfeeding	13	1.0
Not documented	40	3.2
Received cotrimoxazole prophylaxis for 1st three months		
Yes	810	65.3
No	430	34.7

Most infants (81.4%) were born in a health facility. A large proportion (87.8%) of those who were linked had a 1st PCR test. A much smaller proportion (28.9%) had a final antibody test. The most common infant feeding method practiced at 1st PCR test was exclusive breastfeeding (84.0%). The majority (65.3%) of infants received cotrimoxazole at each clinic visit for the 1st

three months of their life. Three quarters (75.0%) of infants were reported to have received daily Nevirapine from birth to 6 weeks postpartum; 17% of infants received no ARV drugs for prophylaxis and 8% received a regimen that was no longer recommended (Figure 5). However, since half of the infants were enrolled after 6 weeks of age, it is not clear whether the health workers were recording what the infants may have received prior to being in care or whether they were unclear about the guidelines and gave the infants 6 weeks of NVP at the time of their enrolment.

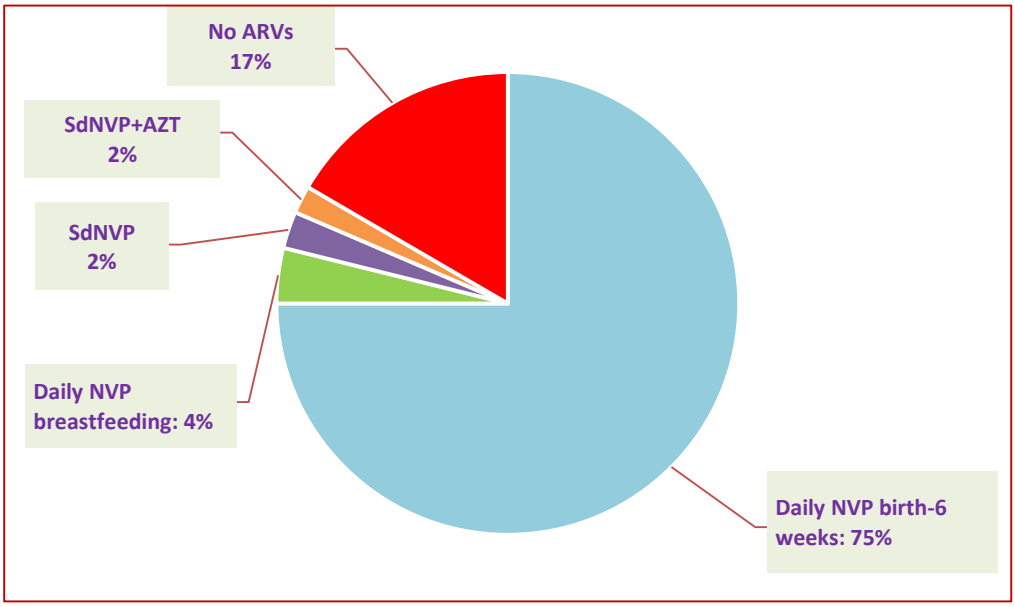

Figure 5. ARV regimens prescribed for HIV-exposed infants

4.2 MTCT of HIV at 1st PCR

The proportion of infants identified as HIV positive based on their 1st PCR test was 4.6% (95% CI: 3.3%-5.8%) (Table 3). Significant variation in the proportion of HIV-positive infants was observed across different levels of health facility, from 1.8% (95% CI: 0.2%-6.2%) among infants seen at the COE to 7.0% (95% CI: 4.6%-10.0%) (p=0.04) among infants seen at HC III level. The overall MTCT rate was 3.2/100 person months (PM) (95% CI: 2.4-4.3) and varied between 1.3/100 PM (95% CI: 0.3-5.1) at the COE to 5.0/100 PM (95% CI: 3.4-7.4) at HC III.

The proportion of infants who were HIV positive based on the 1st PCR test also varied considerably by district and ranged from 0.0% in Buvuma, Kayunga, Kiboga and Nakasongola to 20.0% in Kalungu district (Table 4). In 14 districts (58.3%), the proportion of infants who were positive was less than 5%.

Table 3. Proportion of HIV-exposed infants who tested positive at 1st PCR and the MTCT rate/100 person months by health facility level

Health facility level	Infants tested	Proportion of HIV+ infants (95% CI)	MTCT rates/100 person months (95% CI)	P-value
CEO	113	1.8 (0.2-6.2)	1.3 (0.3-5.1)	
Hospital	374	4.0 (2.2-6.5)	2.9 (1.7-4.8)	0.26
HC IV	252	2.4 (0.8-5.1)	1.7 (0.8-3.8)	0.73
HC III	350	7.0 (4.6-10.0)	5.1 (3.4-7.4)	0.04
Total	**1,089**	**4.6 (3.3-5.8)**	**3.2 (2.4-4.3)**	

P-value is based on differences in proportions of HIV+ infants

Table 4. Proportion of HIV-exposed infants who tested positive at 1st PCR and the MTCT rate/100 person months by district

No	District	No. of infants tested	Proportion of HIV-positive infants	MTCT rates/100 person months (95% CI)
1.	Buikwe	53	1.9	1.4 (0.2-9.7)
2.	Bukomansimbi	12	8.3	6.1 (0.9-43.0)
3.	Butambala	39	7.7	5.6 (1.8-17.3)
4.	Buvuma	13	0.0	0.0
5.	Gomba	13	15.4	11.2 (2.8-44.7)
6.	Kalangala	25	12.0	8.7 (2.8-27.0)
7.	Kalungu	15	20.0	14.5 (4.7-45.0)
8.	Kampala	227	2.6	1.9 (0.9-4.0)
9.	Kayunga	11	0.0	0.0
10.	Kiboga	44	0.0	0.0
11.	Kyankwanzi	39	2.6	1.9 (0.3-13.2)
12.	Luweero	66	6.1	4.4 (1.7-11.7)
13.	Lwengo	29	3.5	2.5 (0.4-17.8)
14.	Lyantonde	30	6.7	4.8 (1.2-19.4)
15.	Masaka	75	2.7	1.9 (0.5-7.7)
16.	Mityana	42	4.8	3.5 (0.9-13.8)
17.	Mpigi	55	1.8	1.3 (0.2-9.4)
18.	Mubende	47	6.4	4.6 (1.5-14.4)
19.	Mukono	45	4.4	3.2 (0.8-12.9)
20.	Nakaseke	23	4.4	3.2 (0.4-22.4)
21.	Nakasongola	24	00	0.0
22.	Rakai	46	4.4	3.2 (0.8-12.6)
23.	Ssembabule	20	10.0	7.3 (1.8-29.0)
24.	Wakiso	29	7.3	5.3 (2.5-11.1)

MTCT of HIV at final HIV test

The number of infants who had a documented final HIV test was 352 (28.9%). The median age at final HIV test was 21.1 months (IQR, 19.1-23.7). All those who had a final test had also undergone PCR testing (and tested negative). No infant was found to be HIV seropositive on the final antibody test.

Predictors of MTCT of HIV

Table 5. Factors associated with MTCT of HIV in unadjusted and adjusted cox-proportional hazards modeling

Variable	Unadjusted HR (95% CI)	*P*-value	Adjusted HR (95% CI)	*P*-value
Age of mother (years)				
15-24	1.00			
25-34	0.71 (0.61-0.81)	<0.001	--	--
≥35	0.63 (0.48-0.83)	0.001	--	--
Place of delivery				
Hospital	1.00			
Home	1.2 (0.94-1.64)	0.13	--	--
Health facility level				
COE	1.00			
Hospital	0.87 (0.66-1.11)	0.24		
Health Center IV	1.01 (0.77-1.32)	0.94		
Health Center III	1.26 (0.96-1.60)	0.07	--	--
CD4 count at ART initiation (cell/µl)				
< 200	1.00			
200-350	0.96 (0.63-1.43)	0.86		
>350-500	0.87 (0.57-1.32)	0.51		
>500	0.76 (0.52-1.10)	0.15	--	--
Infant feeding practice at 1st PCR				
Exclusive breastfeeding	1.00			
Replacement feeding	0.74 (0.24-2.30)	0.60		
Mixed feeding	2.0 (1.33-3.01)	0.001		
Complementary feeding	1.63 (0.91-2.93)	0.09		
Weaning	2.41 (0.34-17.20)	0.38		
No longer breastfeeding	1.34 (0.43-4.18)	0.62	--	--
Adherence to ARVs				
Good	1.00		1.00	
Fair	1.71 (1.09-2.69)	0.02	1.12 (0.71-1.98)	0.09
Poor	**3.53 (2.66-4.68)**	**<0.001**	**1.89 (1.30-2.73)**	**0.001**
Infant ARVs				
Daily NVP birth-6 weeks	1.00		1.00	
Daily NVP-breastfeeding	1.11 (0.61-2.04)	0.73	0.41 (0.22-1.69)	0.19
sdNVP	0.96 (0.43-2.17)	0.92	0.21 (0.19-1.54)	0.11
sdNVP+AZT	0.88 (0.32-2.40)	0.80	0.13 (0.11-1.33)	0.06
No ARVs	**1.76 (1.24-2.50)**	**0.001**	**1.22 (1.03-1.45)**	**0.02**

Cox proportional hazards modeling was used to determine predictors of MTCT of HIV based on the results of the 1st PCR test (Table 5). In unadjusted analyses, older age of mothers (25 years and above) was associated with less risk of infant HIV infection. Poor adherence of the mother to ART, mixed feeding and an infant not receiving any ARVs were associated with greater risk of MTCT. Independent predictors of infant HIV infection included poor maternal adherence to ART (adjusted hazard ratio [aHR] 1.88, 95% CI 1.30-2.73), p<0.001) and having no ARVs prescribed for the infant (aHR 1.22, 95% CI 1.03-1.45, p=0.02).

4.3 Retention of mothers in care up to 18 months post-ART initiation.

The overall median follow-up time of mothers was 20.2 months (IQR 4.2-22.5). Median follow-up time varied depending on the enrolment status of the mother and was considerably shorter among mothers whose enrolment status could not be established. Among all mothers, the proportion retained in care at 6 months was 74.2%, at 12 months was 66.7% and at 18 months was 62.0% (Table 6). Retention of mothers in care at each time period varied by level of health facility and was highest among women being seen at hospitals and lowest among those seen at HC IIIs.

Table 6. Proportion of mothers who were retained in care at 6, 12 and 18 months post-ART initiation by level of health facility

Facility level (No enrolled at baseline)	Time in months	Proportion remaining in care
Overall (N=2,169)	6 months	74.2
	12 months	66.7
	18 months	62.0
Hospital (N=845)	6 months	79.2
	12 months	71.9
	18 months	70.0
HC IV (N=471)	6 months	75.0
	12 months	66.8
	18 months	62.7
HC III (N=853)	6 months	68.7
	12 months	61.3
	18 months	56.6

Figure 6 below shows the Kaplan Meier curve of the probability of retention in care among mothers being seen at different levels of health facility over time.

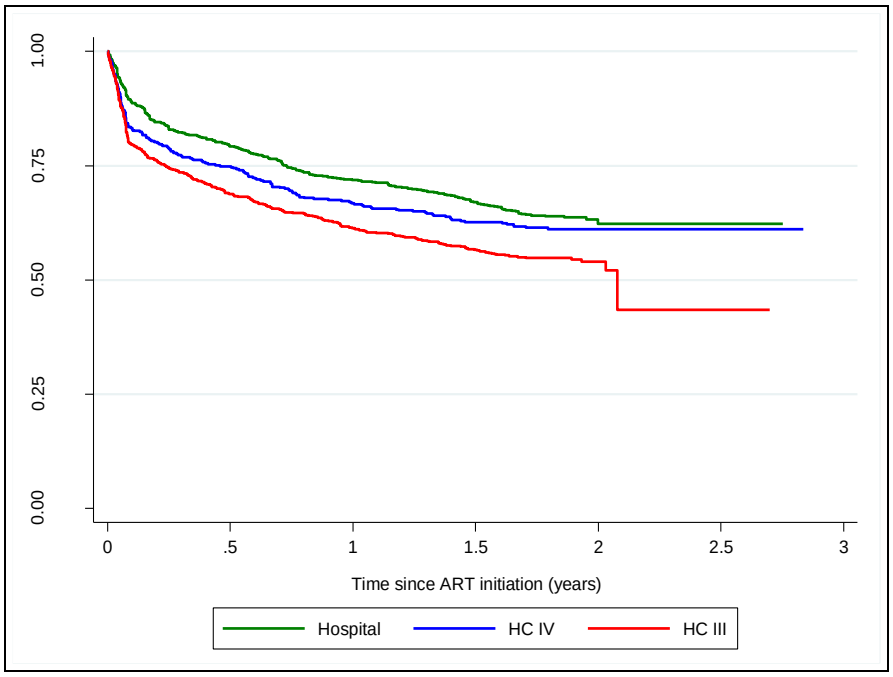

Figure 6. Kaplan-Meier curve for retention of mothers in care by health facility level

The proportion of mothers retained in care at 18 months post-ART initiation varied considerably by district, ranging from 36.1% in Bukomansimbi to 87.0% in Kiboga district (Figure 7)

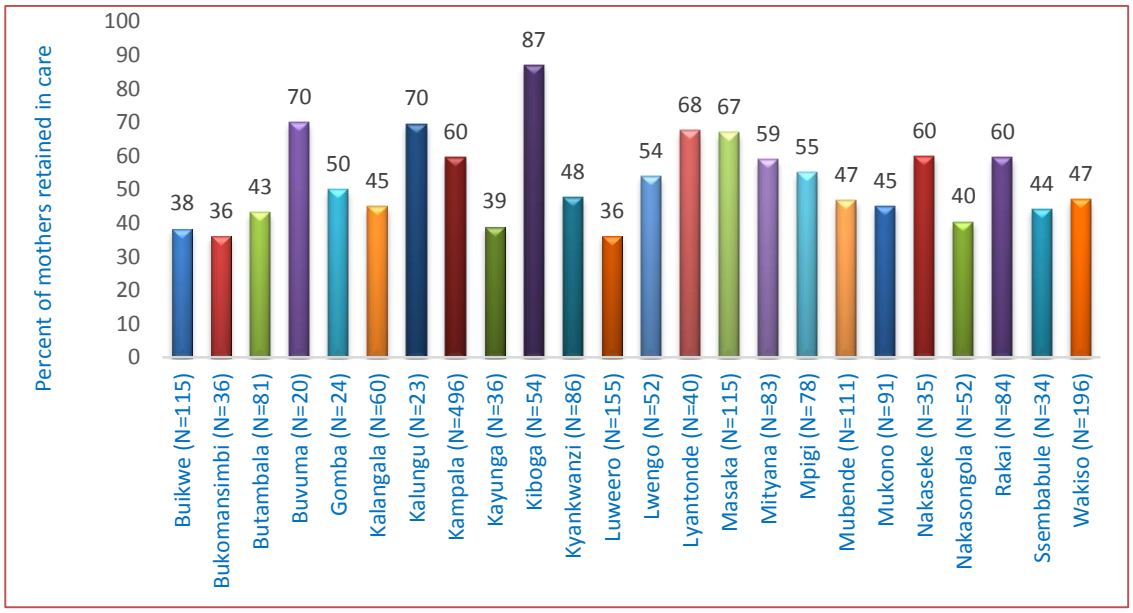

Figure 7. Proportion of mothers retained in care at 18 months in each district

Predictors of retention in care among mothers

Factors associated with retention in care of mothers at 18 months post-ART initiation in both unadjusted and adjusted cox-proportional hazard modeling are shown in Table 7. In the unadjusted analyses, older mothers were less likely to be retained. Mothers who kept their 1st three clinic appointments and those with fair to good adherence to ART were more likely to continue in care. Factors independently associated with retention in care included attending all the 1st three clinic appointments (aHR 1.17, 95% CI 1.01-1.92), p=0.04) and good adherence to ARVs (aHR 1.99, 95% CI 1.09-3.66, p=0.02).

Table 7. Factors associated with mother's retention in care; unadjusted and adjusted cox-proportional hazards modeling

Variable	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	*P*-value
Age group (years)				
15-24	1.00			
25-34	0.71 (0.61-0.81)	<0.001	--	--
≥35	0.63 (0.48-0.83)	0.001	--	--
Place of delivery				
Hospital	1.00			
Home	1.2 (0.94-1.64)	0.13	--	--
Health facility level				
COE	1.00			
Hospital	0.87 (0.66-1.11)	0.24		
Health Center IV	1.01 (0.77-1.32)	0.94		
Health Center III	1.26 (0.96-1.60)	0.07	--	--
CD4 cell count at ART initiation (cells/µl)				
< 200	1.00			
200-350	0.96 (0.63-1.43)	0.86	--	--
>350-500	0.87 (0.57-1.32)	0.51		
>500	0.76 (0.52-1.10)	0.15		
Adherence to all the initial 3 clinic appointments				
No	1.00			
Yes	1.79 (1.05-2.71)	0.02	**1.17 (1.01-1.92)**	**0.04**
Adherence to ARVs				
Poor	1.00			
Fair	1.71 (1.09-2.69)	0.02	1.22 (0.98-1.84)	0.08
Good	3.53 (2.66-4.68)	<0.001	**1.99 (1.09-3.66)**	**0.02**

4.4 Mean change in CD4 Cell Count

Of the 1,269 (58.5%) mothers who had a baseline CD4 test performed, 880 (69.3%) mothers had at least one follow-up CD4 test done: 122 (13.8%) had a repeat CD4 test at 6 months; 175 (19.9%) had a test at 12 months; 358 (40.7%) had a test done at 18 months and 234 (26.6%) mothers had their follow-up CD4 test done after 18 months, post ART initiation. Overall, 641 (72.8%) registered an increase in CD4 count, 192 (21.8%) had their follow-up CD4 count fall

below the pre-therapy count and 47 (5.3%) had their follow-up CD4 count return to the pre-therapy count (no change in CD4 count).

Among those with an increase in CD4 count; the mean CD4 cell count increased from 578.1 cells/ µl (S.D 299.1) to 648.4 cells/ µl (S.D 323.3) (p=0.08) at 6 months. Among mothers with a repeat CD4 test at 12 months, the mean CD4 cell count increased from 597.1 cells/ µl (S.D 298.1) to 729.2 cells/ µl (S.D 313.7) (p<0.001). Among those with CD4 test done at 18 months, the mean CD4 cell count increased from 532.6 cells/ µl (S.D 341.1) at ART initiation to 726.9 cells/ µl (S.D 365.6) (p<0.001).

Among mothers with a decrease in CD4 count, the mean count decreased from 755.9 cells/ µl (S.D 401.4) at baseline to 586.1 cells/ µl (S.D 286.5) (p<0.001) at 18 months post-ART initiation. Mothers with increased CD4 cell count and those with same/decreased CD4 cell count at 18 months post-ART initiation were comparable in terms of age, adherence to ART and adherence to the 1st three clinic appointments (P>0.05) (Table 9). However, the mean CD4 cell count at ART initiation among mothers with reduced CD4 cell count (755.9 cells/ µl) was significantly higher than among mothers with increased CD4 cell count (487.9 cells/ µl) (p<0.001) at follow-up.

Table 8. Characteristics of mothers with increased and reduced CD4 count at 18 months post ART initiation

Variable	Increased CD4 count (N=641)	Same/reduced CD4 count (N=239)	Test Statistic	P value
Mean age in years (S.D)				
	26.5 (5.2)	26.3 (5.2)	t = 0.508	0.61
Mean CD4 cell count at ART initiation (cells/µl) (S.D)				
	487.9 (269.7)	755.9 (401.4)	t = -11.372	<0.001
Adherence to ART (%)				
Good	567 (95.3)	208 (94.1)	χ^2 = 0.039	0.47
Fair	16 (2.7)	6 (2.7)	--	--
Poor	12 (2.0)	7 (3.2)	--	--
Mothers seen for all 1st three clinic appointments (%)				
Yes	610 (95.2)	233 (97.5)	χ^2 = 1.796	0.06
No	31 (4.8)	6 (2.5)		

4.5 Reasons for dropping out of care

Based on analyses of qualitative data, reasons for dropping out of care were grouped into four broad categories; individual, interpersonal, institutional and community factors. The individual and interpersonal factors underpinning retention in care included fear of ART toxicities especially when the drugs were taken on an empty stomach, fears around disclosure and stigma, including loss of confidentiality, inadequate partner support, concerns about domestic violence and a belief in divine healing. The institutional and community factors that were identified included inadequate mobilization and tracking of mothers by village health team members and peer educators, problems with transportation to the facilities, poor provider attitudes and stock outs of ARV drugs at health facilities.

Individual and interpersonal factors

Fear of toxicities experienced after taking ART

Concern about and fear of side-effects of ART were frequently mentioned in both the focus group discussions and in-depth interviews. Many mothers described the unpleasant side effects they experienced after taking ARV drugs:

> "I used to take drugs and I found out that I was getting worse. Whenever I took the drugs I would run mad, I can be like a crazy person. When I take it I get mental instability, I get uncoordinated speech and they have to tie me up like a mad person. Even when I take it at 8:00 pm it can continue affecting me until morning. I can be like a person who has taken alcohol, as if I am drunk" (Mother who dropped out of care – Mityana)

> I heard people that take HIV drugs get some mental problems. For example we have a man in the community who ran mad (mentally impaired) and people said that it was as a result of taking HIV drugs and I think this scares people from taking ARVs (Mother retained in care, Lyantonde district)

> "Some people fear to take ART because there are some people who die suddenly and others say it is because of the ART that they have been taking" (FGD with peer mothers, Luweero district)

> "One week into the constant swallowing, I started having a problem of swelling of my whole body (Mother who dropped out of care –Lyantonde district)"

> "I found challenges with the medicine, I used to feel dizziness, experience funny dreams and also feel like am drunk" (Mother retained in care, Mukono district)

The mothers expressed concern about taking drugs on an empty stomach. Because of the level of poverty in some areas, many women were unable to take the drugs with food:

> "The health workers tell us that we should feed well, eat green vegetables, eat porridge, milk and to take good care of our life so that we are not attacked by diseases yet some of us cannot afford that kind of food." (Mother who dropped out of care, Mubende District)

> "The problem is that the medication requires good feeding but some women in the community don't have food. For example a woman can take drugs on an empty stomach and the drugs will have a negative effect

> in the stomach or she might vomit the drugs and this is continuous and as a result people drop out of the program" (FGD with VHT members, Bukomansimbi district)

Disclosure and stigma

Fear of disclosing one's HIV status is a potential barrier to accessing care. Peer mothers in FGDs explained that mothers may drop out of care because they do not want their partners and children to know that they have HIV. As a result, they find it very difficult to access treatment as illustrated by the following quotes:

> "After women get their HIV positive results, we often ask them whom they will disclose to and often times they say that they will not talk to anyone about it. This means that if such women are married, they will not come for treatment for fear of their husbands and families knowing" (FGD with peer mothers, Lyantonde district).

> "Some mothers fear their husbands to know their HIV status while others fear community members such as their neighbors". They give wrong telephone numbers and wrong names as they register at the facilities and when we go to look for them in their villages, we fail to find them" (FGD with peer mothers, Luweero district).

> "Another challenge is that some of these mothers caution us not to go to their homes, they tell us that whenever we need them, we can only meet at some other places where there are no many people. Then you again wait for someone for over an hour to turn up for an appointment where you agreed to meet and we give up" (FGD with peer mothers, Bukomansimbi district)

Clients are fearful of going to the health facilities because they may be identified by the community, as well as their partners, as being HIV infected

> "Some people gossip a lot about their friends who are HIV positive and on treatment and this increases the stigma in the community which leads to dropping out of the program" (FGD with peer mothers, Kiboga district).

> "When some mothers are given drugs, they throw them away on their way back home because they don't want their husbands to chuck them after knowing their status" (Mother retained in care, Mukono district)

> "Most of the time am scared of coming to the health facility because of the people around my village whom I suspect to see me. "Why I stopped taking the drugs is because I wasn't swallowing it right, I was swallowing in hiding, not swallowing in time, I was afraid of my family members finding out and my husband too. I even got misunderstandings with my husband because he had seen me sometime swallowing the drugs and I would then hide the drug. One time he saw a tablet that had fallen on the floor, because I dropped it when I was in a hurry. He then asked me about it and we had a big argument" (Mother who dropped out of care, Buikwe district).

Inadequate partner support and domestic violence

Lack of partner support continues to be a critical barrier to retention in care and adherence to treatment. Limited male involvement and support were reported by village health team members and mothers who dropped out of the program. Participants discussed the difficulty

that mothers face when they are given HIV positive results; if they disclose to partners or their family, they may risk domestic violence, having their children taken away from them, and/or divorce:

> "The problem is that male involvement is very limited in this program and many men are not supportive at all. Most of the mothers do not come for antenatal with their husbands and this becomes a problem when we go there to make follow-ups. Some men want their women to use local herbs instead of tablets and when the women reveal that they are HIV positive, this causes domestic violence yet in the actual sense they (men) are also on HIV drugs without the knowledge of their women". (FGD with VHT members, Buikwe district)

> When some women disclose to their husbands, the husband can take the baby away and give it to another woman who is HIV negative (FGD with peer mothers, Mpigi district).

> "Most women who abandon the program have challenges in their homes. Many experience violence. Some may miss coming back on the appointment dates because of such challenges like fear of divorce. They decide to abandon the program. The next time they realize that they are pregnant and they do not even come back to deliver in hospital to save the child. They fear that when they go back to the hospital, they will be blamed (FGD with VHT members, Masaka district).

One of the mothers who dropped out of care indicated that domestic violence was the reason she abandoned the program:

> "We failed to agree with my husband because he was so violent. He chased me away from home. He is the one who tested first and he was positive but he abandoned the drugs. They have talked to him but he has failed to change. I fear to ask for a transfer to come back to this health center and yet I may get into the same problems." (Mother who dropped out of care, Mityana district)

Belief in divine healing

Myths and beliefs about spiritual healing are still prevalent in some areas. Religious leaders may preach about faith-healing, dissuading patients from being medically treated for HIV infection as reported below:

> "We have also a problem of certain religious sects that are misleading people. For example Born-Again Christians tell people that they can get spiritually healed if they are HIV positive and this has led to many people abandoning treatment" (FGD with VHT members, Mpigi district)

Institutional and community factors

Inadequate facilitation and motivation of VHT members and peer mothers

VHT members and peer mothers are charged with the responsibility of mobilizing communities for health interventions, providing health education, following up HIV-infected mothers and their infants in the community and promoting health seeking behaviours. However, the VHT members and peer mothers interviewed felt that they lacked the support needed to fulfill their roles:

> "We work here all day, but cannot even find some lunch to eat. So you reach a time when as a service provider, you feel you are exhausted and hungry. Remember that some of us live far from the health facility and we have to pay out of our own pockets to facilitate our selves. Ministry of Health should do something about it" (FGD with peer mothers, Buikwe District)

In addition to lack of support, the peer mothers reported that they are not respected and are discriminated against by the health workers. They felt that their contribution was not acknowledged, their time not compensated and they lack funds for transportation:

> "Peer mothers are not allowed to get leave, fall sick, no transport and no lunch. When you fall sick, that day is cut off. We are taken to be failures, we do not have a future because we are already HIV positive. For example, if a peer mother goes to office to ask for a key to the toilet, the nurse/health worker says go to the other one for the clients" (FGD with peer mothers, Kampala)

> "Sometimes when we are providing health education, a health worker comes and interrupts you, rubbishing what you are teaching in front of the clients, yet we base our health education on what we have been taught. So makes us look stupid in front of the mothers" (FGD with VHT team members, Kampala district)

> "VHTs have a big challenge of transport in trying to follow up these mothers. For example after discovering that the mother is lost and you think of walking for more than 4 km, you surely lose the morale" (FGD with VHT members, Bukomansimbi district)

Some community members perceive VHTs as salaried employees when they are actually volunteers:

> "The challenge is that some people think that we are paid for the work we do. When we gather people and decide to educate them about a certain topic, say about avoiding traditional birth attendants, people think that we have been given money to do that health education task" (FGD with VHT members, Mukono district)

Transportation to the health facilities

Long distances and high transport costs to the health facilities were reported as major barriers to retention in care. Mothers who were retained in care reported that living nearer to a health facility made it much easier to continue treatment:

> "I had moved out of care when I was living far from the health facility and I almost died. But when I started living near the facility I resumed care and I have never left. It is easier when you live near the facility" (Mother retained in care, Mukono District)

> "It is easy for me to access the facility since I don't have to walk very long distances. Even when I am unable to come, the health worker can easily check on me and bring me the medication when necessary" (Mother retained in care, Mpigi District)

> "Many women who stay closer to the hospital find it easy to access HIV treatment because they can decide to come to the facility at any time of their convenience without their husbands getting to know unlike women who come from very far because they have to wait for their husbands to travel on long journeys so that they walk to the health facility to get drugs."(FGD with VHT members, Lyantonde

district)

In FGDs, it was reported that mothers who lived in households located further away from the health facilities were more likely to drop out:

> "Mothers who live very far from the health facility and who do not have transport end up missing their appointments and eventually dropping out of care" (FGD with VHT members, Buikwe district)

Health facility barriers

Inadequate staff

A shortage of health staff in some facilities was reported as a key barriers to retention in care. Due to inadequate staffing, mothers had to wait for long hours to receive services and this discouraged them from returning to the facilities:

> "Health workers are also very few. You find that there only one person working on antenatal patients and yet she is the same one to help mothers on PMTCT" (FGD with peer mothers, Mukono district)

> "There is a lot of delay at the facilities, mothers take long before they are served and they become very hungry, Some mothers have even run away from the program because of that" (FGD with peer mothers, Luwero district)

Shortage of staff was reported to be worse at the hospitals than in the lower level health facilities:

> "Loss to follow up of both mothers and infants is very common at the hospitals because there isn't enough time to prepare women for the results. For instance, the day of testing is the same day for receiving results and health workers don't have enough time to counsel each patient. So the situation becomes very unbearable for the mother to take in at the same time and in most times, such mothers don't come back" (FGD with peer mothers, Lyantonde Hospital)

Provider attitudes

Provider attitudes played a central role in how patients perceive health services and whether they decided to continue receiving care or not. Mothers who were retained in care reported that provider attitudes are key factors influencing retention:

> The very first reason I am still in care is the health workers; they counselled me very well and encouraged me and I gained hope and I saw that if I persisted on the programme, my life will go on and the programme will keep me healthy" (Mother retained in care, Mukono district)

> "Every time we come here at the health center and we are treated courteously, we go back home contented." (Mother retained in care, Wakiso district)

> "When I go to the health facility to get the drugs and the health workers do not treat me badly, it gives me the strength to see that am still on treatment" (Mother retained in care, Luwero District)

On the other hand, poor provider attitudes were reported as reason why some mothers drop out of care:

> "After giving birth, I went back to the hospital and the health worker I found there was so abusive. When I tried to ask her some questions, she said I was stupid because she had told me everything and I did not need to ask her again. I had heard from a friend who is also HIV+ that when you are breastfeeding and feel discomfort in the breast, you should stop breastfeeding and go hospital. But for me, when I returned to hospital, i was told to breast feed until the child is one year old, yet I thought I was supposed to stop at 6 months. The nurse became so abusive and told me to follow my own knowledge" (Mother who dropped out of care, Mpigi district).

Poor treatment of mothers at the health facilities was also acknowledged by peer mothers:

> "There are some health workers who don't care about peoples' health, they are just there to make money. A mother may come and begs for assistance as if she doesn't deserve to be assisted. Some health workers don't have a humanitarian hearts" (FGD with peer mothers, Mityana district)

> "Some health workers have a bad approach. When mothers reach the health center and told to sit and wait, some mothers are given services first, even when they came late. This discourages the mothers. It should be first come, first serve. (FGD with peer mothers, Luweero district)

Stock out of ARV drugs

Another concern expressed by the peer mothers and the village health team members that contributed to low retention in care were stock outs of drugs in some facilities:

> "What contributes to these mothers to getting lost is drugs…….. at times a mother comes and finds there are no drugs and when she comes back on another day and finds that the drugs are still missing, she gets tired and gives up" (FGD with VHT members, Luweero district).

> "We have a challenge of drugs. The stock usually runs out for over a month before they have restocked. If you call the neighboring facility for assistance, they just give a few drugs which cannot serve all the mothers" (FGD with peer mothers, Masaka district)

5.0 DISCUSSION

This evaluation found that the proportion of HIV exposed infants who became infected based on the 1st PCR was 4.6%, which is below the national target of 5%. Poor adherence to ARV drugs by mothers and failure to provide infants with ARV prophylaxis were associated with a greater risk of transmission. Retention of mothers at 18 months post enrolment was moderate (62.0%). Results of qualitative data indicated that retention was influenced by several interrelated factors including the individual and interpersonal relationships, and institutional and community-based issues. These findings have important policy and programmatic implications for informing the design and implementation of the Option B+ strategy at national and district level.

5.1 MTCT of HIV

The low rate of MTCT of HIV in this evaluation needs to be interpreted consciously. It is important to note that only 58% infants could be linked to their mothers and less than a third of infants had a final HIV antibody test. It is possible that those infants could be at higher risk of becoming infected due to poor ART adherence on the part of the mother or failure to receive infant ARV prophylaxis. In addition, use of the 1st PCR test as a measure of the success of the Option B+ program does not provide information on transmission during the entire postpartum period.

The reasons for the inability to link infants to mothers are multiple, and their individual contributions are not clear. The research team witnessed poor filing and storage systems in many facilities in which infant files were kept separately from the mothers' files, making them difficult to locate. In addition, some infant records were not filled to completion to allow meaningful data abstraction. Nonetheless, the infection rate in this evaluation is comparable to that reported by PEPFAR-Uganda in 2014 which was 5.3% [26]. It is important to note that this evaluation was conducted among women enrolled on Option B+ at the very beginning of the program. At that time, the 'mother-baby care points' had not yet been institutionalized. Facilities that are now scheduling same-day mother-infant clinic visits should be able to demonstrate improved record keeping.

Suboptimal adherence to ART and failure to provide infant ARV prophylaxis could undermine the success of the Option B+ strategy. However, the majority of women who were retained were reported to have good adherence; in contrast, 17% of infants received no prophylaxis, and 5% received regimens that were not recommended. The number who received appropriate prophylaxis may be even lower, since the forms on which health care workers record ARV prophylaxis, do not account for infants enrolled well after birth.

Stock-outs of ARV drugs, particularly for paediatric medications have been reported in many parts of the country; ARV drug stock-outs have been shown to vary across districts [33]. This

may help explain why retention and MTCT rates also varied by district. During qualitative interviews and discussions, mothers and VHT members indicated that persistent lack of drug availability caused many women to drop out of care. Logistical challenges in providing adequate HIV services will continue to increase, as the CD4 threshold for adult ART initiation changes, and with expansion in the number of facilities providing Option B+. Improved forecasting and supply chain management are needed to ensure that the Option B+ strategy can be maximally effective.

5.2 Retention in care

This evaluation found that retention in care at 18 months post-ART initiation among mothers was moderate. This retention level is below the recent PEPFAR and UNAIDS targets of ensuring that more than 90% of those on treatment are retained throughout life [26]. However, similar retention levels have been reported among adult patients in south western Uganda [13] and in other sub Saharan African countries [16]. In this evaluation, retention in care varied widely across districts and facility levels; women being seen at lower level sites, such as HC IIIs, had the lowest levels of retention. This is in contrast to some other studies in Uganda [13] as well as in Malawi [34], and South Africa [35], in which retention was higher among lower level facilities compared to larger hospital-based sites. The lower retention among women seeking care at the lower level facilities could be attributed to the fact these women were more likely to be in rural areas with fewer economic resources and less able to pay for transport as some studies highlight [13].

Retention in this study could only be evaluated based on records available at the facility at which mothers and infants initially enrolled. It is possible that clients transferred care to other sites, but we were unable to link them. Therefore, retention in care may have been higher than reported here. Such estimates of retention defined by continued presence at a facility tantamount to retention in the facility rather than retention in care [13]. In a study of adult ART patients conducted in the southwestern region of the country, 60% to 80% of the patients lost in one facility were found to be alive and in care elsewhere [18]. Implementation of robust tracking systems for patients who may drop out or transfer to other facilities need to be strengthened.

5.3 Mean change in CD4 count

A significant increase in mean CD4 cell count among mothers enrolled and retained on treatment was observed over an 18 month follow-up period. In other studies, risk factors for immunological non-response were found to include young age, low baseline CD4 counts, high baseline viral loads, poor adherence to therapy and antiretroviral drug resistance [36]. In this evaluation, we did not find any of these factors to be associated with a reduction in CD4 cells count. Majority of the mothers had a high baseline CD4 cell count of more than 500 cells/µl, were initiated on the recommended first line ART regimen (TDF/3TC/EFV) and were reported

as being adherent. It is worth mentioning that in 22% of mothers, follow-up CD4 count fell below the pre-therapy count while 5.3% of mothers did not register an increase in CD4 cell count. The reduction in CD4 cell count at follow-up should not be interpreted to mean treatment failure because immunological criteria do not accurately predict virological failure, resulting in significant misclassification of therapeutic responses [36]. In this study, data on viral load could not be obtained because viral load testing is not routinely done within the PMTCT settings in Uganda.

The Ugandan national integrated guidelines on ART and PMTCT recommend bi-annual immunological monitoring of HIV-infected mothers enrolled on life-long ART using CD4 cell counts [6]. Although access to CD4 testing services in some parts of the country has greatly increased [33], less than 60% of the mothers in the study area had a CD4 test at the time of ART initiation, and among those, less than 70% had a follow-up test. Both baseline and follow-up CD4 cell monitoring was much poorer at lower level health facilities, and may be a result of poorer infrastructure and resources, including the ability to send samples for testing. Thus, reinforcement of good clinical decision-making seems to be the most practical approach for monitoring mothers on ART particularly in the peripheral health facilities.

5.4 Reasons for dropping out of care

The findings from the qualitative component of this evaluation suggest that factors underpinning low retention in care included: i) fear of ART side-effects, ii) concerns about disclosure, stigma and domestic violence, iii) inadequate facilitation of village health team members and peer educators iv) beliefs in divine healing, v) barriers to transportation to the facilities and, vi) barriers at the health facilities themselves.

Fear of side-effects of ARV drugs

The widespread concern about the side-effects of ARV drugs as a reason for disengagement from care needs to be acknowledged. Concerns about the side-effects of ARV drugs generated anxiety about taking ART that prevented mothers from coming to clinic, and/or adhering to medication. The primary side-effects reported included abnormal body swellings, headache, dizziness, drowsiness and abnormal dreams. Similar side-effects have been reported in other countries [37, 38]. Lack of food with which to take the drugs was an additional reason for non-adherence. The lack of food as barrier to ART adherence and retention in care has been reported in other countries [39, 40]. In Uganda, an estimated 20% of the population lives below the poverty line [41]. Many mothers, particularly in the rural areas, may not be able to afford adequate food to take with their medication. The mechanisms through which food insecurity contribute to disengagement from care and non-adherence have been evaluated elsewhere in Uganda and include: ARV drugs increase one’s appetite, exacerbation of side-effects of ARV drugs when taken without food, and long work days during which women forget to take their medication [42].

ART programs that provide nutritional support have registered substantially lower rates of loss to follow-up and higher ART adherence compared with programs that do not [43]. Thus, focusing on the logistic aspects of drug delivery does not guarantee success of the Option B+ program. Incorporating food supplementation could be an essential component of ART programs. The larger issue is a chronic lack of sustainable food production strategies.

Disclosure, stigma and domestic violence

In the study, many mothers expressed fear about disclosing their positive HIV status to their spouses or families because they believed that they would not be supported, and could be threatened with divorce and/or losing their children. In addition, women feared that their families would not keep their status secret, resulting in stigma and discrimination within the community.

It has been shown in other studies that social support can improve retention and adherence, and that stigma plays a role in disengaging from care [13]. The possibility of domestic violence also prevents women from revealing their status. Fear of disclosure means that women do not want to be seen attending frequent clinic appointments or taking medication. On the other hand, many women who were retained reported that support from their spouses was critical, and in some instances their husbands were also HIV infected, but had not yet told their wives; knowing that they were in the same situation was a relief. Encouraging and providing couple counseling by trained facilitators, including in the homes, needs to become a greater part of regular care for women testing seropositive in ANC.

Inadequate facilitation of village health team members and peer mothers

Although village health teams and peer mothers are envisaged as critical for strengthening the Ugandan health care system at the community level, it is important to acknowledge some of the limitations of these structures. Within the PMTCT program, these community volunteers are expected to provide health education about treatment and side-effects and emphasize the importance of adherence to ART, mobilize HIV-infected women to seek care and track those who have dropped out. However, in this evaluation, the VHTs and peer mothers reported that their tasks were extremely challenging because they do not receive adequate support to carry them out, including, lack funds for transportation, financial incentives or remuneration; poor treatment by health care workers; lack of training; and inadequate number of staff for the job. Currently, the national VHT training coverage is estimated at 55% [44]. Provision of transport allowances and in-kind gifts such as T-shirts or gumboots would enhance the ability of these community volunteers to do their job more effectively.

Belief in divine healing

In this evaluation, some mothers disengaged from care because they believed in, or were told to believe in spiritual healing rather than in modern medication to help them with HIV disease. Similar findings have been reported in other parts of the country [22]. Although religion may

be important to many people living with HIV, spiritual beliefs can have both positive and negative effects on adherence to ART among different groups of people. While some women use prayer in conjunction with their treatment, others may commit themselves solely to spiritual development and stop treatment [45]. Thus, discussions of spirituality and beliefs should be included in HIV and ART adherence counseling. In addition, HIV care programs should interface with local religious leaders to educate them about the importance of continuing with drug therapy.

Transportation to the facilities

Long distances and high transport costs to the health facilities were reported as major barriers to retention in care. This finding is consistent with other studies conducted both in Uganda and in other similar settings [18]. In a randomized trial conducted in south western Uganda to investigate the effect of a cash transfer program for transportation on retention in care, fewer patients were lost to follow-up if they received support for travel [46]. Among poor families, work and child care responsibilities compete with the cost of transportation and/or long travel times, preventing many women from attending clinics [38]. Innovative methods to overcoming transportation barriers, such as, conducting outreach services that can provide medications, check on adherence and monitor side-effects need to be implemented.

Health facility barriers

Inadequate health staff, poor provider attitudes and stock outs of ARV drugs were reported as some of the impediments to retention in care. Similar issues have been reported to impact follow-up in other studies [47]. Health facility barriers may be more amenable to intervention compared to patient socio-structural barriers such as distance and transportation, stigma and fear of disclosure. However, the proportion of the Government budget allocated to the health sector is approximately 8% [44], which is below the national target of 10% and far below the Abuja target of 15% [48]. Currently, more than 30% of approved posts at lower level health facilities, particularly HC IIIs are vacant [44]. Unless more funds are allocated to relieve the shortage of staff, clients will continue to experience long wait times, and stressed and impatient health care workers. However, discriminatory attitudes of health care staff towards patients and community volunteers could be remedied without much funding, by better training and support supervision. Stock-outs of drugs are also less a problem of financing, than poor logistics chain management.

5.5 Methodological considerations

Generalizability and transferability

This evaluation was conducted in only one region of Uganda, which has relatively better geographic and economic access to health services compared to other regions [49]. The central region has been ranked as the best in the country in terms of health service delivery and this may be interpreted as meaning that health services in the region might be better than in other

regions of Uganda with poor access to health services. Although the evaluation was conducted in only one region, most of the findings such as, low MTCT rates, moderate retention levels and the reasons for dropping out of care are similar to those reported in other parts of the country as discussed earlier. Moreover, the standard of HIV care is expected to be similar across the other regions of the country. Thus, the findings of this evaluation have a high chance of being generalizable and or transferable to other regions of the country.

Retrospective records review

This evaluation relied on a retrospective record review of mothers and infants; this type of methodology is much less expensive and time consuming than a longitudinal cohort study [50]. However, the information obtained is limited by data already recorded and the quality of records. Further still, the records abstracted belonged to women and infants who were enrolled at the very start of the Option B+ program, and may not reflect progress that has occurred over time. The low linkage of infant to maternal records and incomplete documentation reduces the accurate estimation of HIV transmission. Routine monitoring of the PMTCT program needs to occur in all regions of the country to better assess its impact.

6.0 CONCLUSIONS

- ✓ The rate of MTCT of HIV among infants born to HIV-infected mothers on Option B+ in this evaluation was found to be less than 5% and indicates that the country is on the right track towards virtual elimination of MTCT.

- ✓ Poor adherence to ART by the mothers and lack of ARVs for infants were associated with increased risk of MTCT of HIV.

- ✓ Retention in care among mothers over 18 months is moderate and could be explained by several interrelated influences including the individual, interpersonal, institutional and community factors.

- ✓ The Option B+ program resulted in overall improved immunological outcomes among women retained in care.

- ✓ The loss to follow-up among mothers could be attributed to the fear of ART side-effects, problems with disclosure and stigma, belief in divine healing, inadequate facilitation of the village health team members and peer mothers, problems with costs of transportation and distance to health facilities, drug stock-outs and poor attitudes of health care workers towards clients.

7.0 RECOMMENDATIONS

- ✓ Emphasis on the importance of having infants tested beyond a 1st PCR and after cessation of breastfeeding will be critical for accurately determining the impact of Option B+

- ✓ Measures to improve adherence to the program including better education about side-effects, provision of food supplementation to those who need it and enhanced patient tracking systems should be considered for integration into the Option B+ program

- ✓ Addressing stock outs of ARV drugs by strengthening logistics and supply chain management system continues to be an important issue and will improve retention in care.

- ✓ Financial support and improved training of the village health team members and peer mothers are needed for them to engage communities and support mothers.

- ✓ Strengthening the health management information systems at the health facilities through training of health workers to capture complete patient information, improve record keeping and tracking patients between facilities will result in more accurate estimates of patient outcomes.

- ✓ Reinforcing good clinical and client-centered practices through training, mentorship and support supervision is an important practical approach for improving care and retaining mothers.

- ✓ There is need to focus resources on intensified HIV/AIDS awareness campaigns aimed at sensitizing communities about stigma and discrimination, and dispelling inaccurate religious beliefs, myths and misconceptions about the Option B+ program. This will require close collaboration between HIV care programs and religious, cultural and political leaders

- ✓ Establishing outreach services at health facility level with functional home-based care services provided by trained community health workers will improve retention.

- ✓ Periodic design and evaluation of innovative strategies for patient retention are required for the long term success of the Option B+ strategy

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9.0 APPENDICES: List of institutions and individuals involved in the study

Institutions

Institution	Summary of key roles
Centers for Disease Control & Prevention.	Funding and contributing to protocol review
Ministry of Health of Uganda	Advocacy for the evaluation, contributions to protocol development, participation in supervision of protocol implementation, assistance with dissemination of findings to facilitate translation of findings into policy
Makerere University School of Public Health and University of California, San Francisco	Protocol development, field implementation of the evaluation, training of field teams, oversight of data collection, data management and analysis, report writing and dissemination of findings.

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Mpango Jonathan	Supervisor	Ayesiga carl	Research assistant
Muhanguzi Eva	Supervisor	Wabwire Freda	Research assistant
Muhumuza Simon	Supervisor	Kiconco Carol	Research assistant
Mulekya B Francis	Supervisor	Kyomukama Evelyn	Research assistant
Mukose Aggrey	Supervisor	Gashangwa Paul	Research assistant
Namagala Elizabeth	Supervisor	Naddamba Juliet	Research assistant
Ocaya Stephen	Supervisor	Opok Maureen	Research assistant
Rachel King	Supervisor	Nkoola Peter	Research assistant
Sebuliba Isaac	Supervisor	Kabatongore Doreen	Research assistant
Sendiwala Julius	Supervisor	Ampurira Mackline	Research assistant
Agaba Sheila	Supervisor	Ngalulirwe Isabella	Research assistant
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Tukahiirwa Anne	Team lead	Lule Gloria	Research assistant
Birungi Patience	Team lead	Bisirikirwa Brenda	Research assistant
Mwase Denis	Team lead	Muyambi Daniel	Research assistant
Odwengeni Margaret	Team lead	Mbabazi Grace M.	Research assistant

Name	Responsibility	Name	Responsibility
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Kasozi William	Team lead	Kanyiginya Annabel	Research assistant
Lule Geofrey	Team lead	Wanduru Phillip	Research assistant
Nziramwoyo Pelagia	Team lead	Kamatenesi Jovan	Research assistant
Belinda Rhona	Team lead	Karongo Moses	Research assistant
Nalwanga Angella	Team lead	Tusiime Ronald	Research assistant
Nalugya Josephine	Team lead	Nsubuga Baylone	Research assistant
Kibirige Leonard	Team lead	Nakaddu Margaret	Research assistant
Twinomujuni Cyprian	Team lead	Ndoboli Milly	Research assistant
Pacutto Andrew	Team lead	Nasasira Anitah	Research assistant
Nahabwe Alice	Team lead	Kyarimpa Jennifer	Research assistant
Birungi Diana	Research assistant	Ayebale Ivan	Research assistant
Okello Alfred	Research assistant	Kizza Bernard	Research assistant
Tuheebwe Doreen	Research assistant	Lubwama Hassan	Research assistant
Kiyingi Reginald	Research assistant	Mugisha Dorothy	Research assistant
Gumananye Jean	Research assistant	Tayebwa Andrew	Research assistant
Okuli Tolbert William	Research assistant	Bithire Jane	Research assistant
Muhanguzi Kenneth	Research assistant	Masika Florence	Research assistant
Nagasha Shakira	Research assistant	Naggawa Winnie	Research assistant
Namudde Harriet	Research assistant	Nayiga Grace	Research assistant
Namulondo Eunice	Research assistant	Nanyunja Flavia	Research assistant
Rwebuga Marjorie	Research assistant	Nyangoma Doreen	Research assistant
Ameny Andrew	Research assistant	Were Peter	Data entrant
Ndamwesiga Flavia	Research assistant	Abasa Anitah	Data entrant
Kiwuwa Harriet	Data entrant	Kansiime Edwin	Data entrant
Mubiru Benedict	Data entrant	Kanyike Bernard	Data entrant
Nalumansi Martha	Data entrant	Katushabe Glorious	Data entrant
Nuwagira Anthony	Data entrant	Katusiime Rita	Data entrant