CHANGES IN ADHERENCE AND PROGRAM RETENTION AND ASSOCIATED FACTORS AMONG HIV-INFECTED WOMEN RECEIVING OPTION B+ FOR PREVENTING MOTHER-TO-CHILD TRANSMISSION OF HIV IN KAMPALA, UGANDA: A MIXED METHODS APPROACH

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ABSTRACT

Background: Mother-to-child transmission of HIV continues to be the leading cause of pediatric HIV infections. Prevention of mother-to-child transmission (PMTCT) care and treatment strategies have been shown to drastically reduce rates of vertical transmission but attrition along the PMTCT cascade is a persisting issue. One barrier for PMTCT is inconsistent medication adherence and program retention. Option B+ is the current strategy recommended by the World Health Organization (WHO) for PMTCT and includes the provision of combination antiretroviral therapy (ART) to all pregnant and postpartum HIV-infected women, regardless of CD4 cell count or clinical stage, to be continued for life from the time of treatment initiation.

Study goal and specific aims: The overall goal of this dissertation was to further the current understanding of medication adherence and program retention of HIV-infected pregnant and postpartum women receiving Option B+ for PMTCT and how medication adherence and program retention may change over time. A mixed methods approach was used to address this goal. Manuscript one aims to summarize the existing Option B+ adherence and program retention literature. Manuscript two aims to measure rates of medication adherence and clinic visit attendance in pregnancy and the postpartum period as well as the effects of various factors on these outcomes for a cohort of HIV-infected pregnant women presenting for care and initiating treatment at Mulago National Referral Hospital. Manuscript three aims to explore the changing experiences of HIV-infected pregnant women and mothers with the Option B+ program at Mulago National Referral Hospital from pregnancy through six weeks postpartum as well as the changes in potential barriers and facilitators to adherence and program retention that may occur over time.

Methods: First, a systematic review of the current Option B+ adherence and program retention literature was performed by searching the PubMed, Embase, Global Health and Scopus databases for relevant peer-reviewed studies. Second, routinely collected PMTCT program data were used for a longitudinal analysis of adherence and clinic visit attendance from pregnancy through six months postpartum for a cohort of first-time initiators of Option B+ at Mulgo National Referral Hospital in 2014. Third, a series of longitudinal in-depth interviews during pregnancy and at six weeks postpartum were conducted with a subgroup of HIV-infected pregnant women participating in the "Friends for Life Circles" randomized controlled trial and assigned to receive the standard of care at Mulago National Referral Hospital.

Results: The systematic review found that loss to follow-up (LTFU), patient self-report and pill counts were the most commonly used measures of program retention and medication adherence and that these outcomes varied greatly across studies and program implementation settings. The longitudinal data analysis found that a relatively low proportion of HIV-infected women were adherent in pregnancy and that the proportion of adherent women decreased at six months postpartum. A number of factors were found to predict adherence in pregnancy and six months postpartum, but only status disclosure was associated with sustained adherence at both time points. This study also found that postpartum clinic visit attendance remained consistent and that previous PMTCT experience, previous HIV diagnosis, time spent on ART during pregnancy and male partner counseling and testing in antenatal care were predictors of sustained clinic visit attendance at six weeks and six months postpartum. The in-depth interviews found medication adherence and clinic visit attendance to be consistently high among participants, but also identified a number of themes surrounding experiences with ART adherence and the Option B+ program in pregnancy and at six weeks postpartum. Effective messaging and counseling at the time of HIV testing and treatment initiation, support from health workers between clinic visits,

HIV status disclosure during pregnancy and a desire for a healthy baby and a healthy life were the biggest motivators for good medication adherence and clinic visit attendance, while concerns with unwanted HIV status exposure, modifying daily routines to prioritize ART adherence and health, concerns with the Option B+ approach and health facility limitations came through as potential barriers to good adherence and clinic visit attendance.

Conclusions: The results of this dissertation may be useful as PMTCT clinical care and research teams continue to strive toward the goal of eliminating vertical HIV transmission. First, this work confirms the limitations that exist with pill count adherence measures and should encourage continued efforts to improve and standardize adherence measurements in the future. Second, this work underscores the need for continued monitoring and evaluation of maternal medication adherence and program retention as well as interventions aimed at improving these outcomes. Focusing on strategies for improving ART adherence during pregnancy might be effective for improving and sustaining good adherence and program retention over time. More specifically, increasing effective status disclosure, supporting health workers to provide appropriate guidance during HIV testing and ART initiation as well as throughout pregnancy and addressing the specific needs of HIV-infected pregnant women who work outside the home or desire to work outside the home may be appropriate for improving adherence and program retention in pregnancy and the postpartum period.

Thesis committee: Dr. Andrea Ruff, M.D. (primary adviser), Dr. Julie A. Denison, Ph.D. and Dr. Lawrence H. Moulton, Ph.D.

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willing to participate in this work and share their stories; I am inspired and humbled by their strength and resilience.

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This dissertation is dedicated to the memory of my grandparents:

Saba Ben, Safta Suzi, Saba Efraim and Safta Miriam

The bravest of pioneers, the most beautiful of souls.

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LIST OF ACRONYMS

3TC	Lamivudine
AACTG	Adult AIDS Clinical Trial Group
AIDS	Acquired immunodeficiency syndrome
ANC	Antenatal care
ART	Antiretroviral therapy
ARV	Antiretroviral
AZT or ZDF	Zidovudine
BAN	Breastfeeding, Antiretroviral Therapy and Nutrition Study
cART	Combination antiretroviral therapy
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
EFV	Efavirenz
EGPAF	Elizabeth Glaser Pediatric AIDS Foundation
EPHPP	Effective Public Health Practice Project
HAART	Highly active antiretroviral therapy
HIV	Human immunodeficiency virus
LPV	Lopinavir
LTFU	Loss to follow-up
MEMS	Medication event monitoring systems
MESH	Medical subject heading
MJAP ISS	Makerere University Joint AIDS Program Immune Suppression Syndrome Clinic
MoH	Ministry of health
MTCT	Maternal-to-child transmission
MU-JHU	Makerere University- Johns Hopkins University
NIH	National Institutes of Health
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
PAM	Pharmacy based adherence measure
PCR	Polymerase chain reaction
PEPFAR	President's Emergency Fund for AIDS Relief
PEPI	Post-Exposure Prophylaxis for Infants Study
PI	Protease inhibitor
PLWH	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PSS	Psychosocial support
RCT	Randomized controlled trial
RTV	Ritonavir
SDs	Standard deviations
SEM	Social Ecological Model
sd-NVP	Single dose nevirapine
STI	Sexually transmitted infection
SWEN	Six-Week Extended Nevirapine Studies
TFR	Total fertility rate

LIST OF ACRONYMS (CONTINUED)

TFV	Tenofovir
UNAIDS	Joint United Nations Program on HIV/AIDS
USAID	United States Agency for International Development
USPHS	United States Public Health Service
VAS	Visual analog scale
WHO	World Health Organization

BACKGROUND

Burden of HIV for women and children

Over the last 15 years, the number of people living with HIV (PLWH) has increased from 30.0 million[1] to 36.9 million.[2] Sub-Saharan Africa bears approximately 70% of the global HIV burden, and of the 25.8 million PWLH in this region, nearly 60% are estimated to be women.[3] Data show that HIV/AIDS has had an increasingly disproportionate impact on the women of sub-Saharan Africa. In 1985 the number of men and women living with HIV/AIDS in this region was approximately equal, but today women ages 15-24 are more than three times as likely to become infected with HIV as men of the same age group.[4]

Though most of the HIV epidemics across sub-Saharan African countries are generalized, national adult HIV prevalence varies substantially from 0.5% in Senegal to 27.7% in Swaziland.[5] Thus, in addition to looking at regional trends among women, it is important to note the country-specific variations in female HIV prevalence. Table 1 is adapted from a 2013 United States Agency for International Development (USAID) report estimating HIV prevalence patterns by age and sex, and demonstrates the difference in HIV prevalence between women and men ages 15-49, by country.[6] These data show the heterogeneous nature of the HIV epidemic in sub-Saharan Africa while supporting the notion that the HIV epidemic is largely driven by the increased prevalence among younger women of this region.

Table 1: HIV prevalence among women and men ages 15-49, by country[6]

	Age group													
	15-19		20-24		25-29		30-34		35-39		40-44		45-49	
	F*	M*	F	M	F	M	F	M	F	M	F	M	F	M
Southern Africa														
Lesotho 2009	4.1	2.9	24.1	5.9	35.4	18.4	40.7	40.2	42.3	35.4	36.1	39.3	29.5	32.1
Zambia 2007	5.7	3.6	11.8	5.2	19.9	11.4	26.0	17.1	24.9	22.4	18.3	24.1	12.2	18.6
Zimbabwe 2011	4.2	3.4	10.6	3.9	20.1	10.3	29.0	17.4	29.1	25.1	25.7	26.2	22.6	29.9
East Africa														
Ethiopia 2011	0.2	0.0	0.9	0.2	3.0	0.9	3.7	1.0	3.0	3.0	1.9	2.1	1.8	1.4
Kenya 2009	2.7	0.7	6.4	1.5	10.4	6.5	11.0	6.8	8.8	10.4	14.3	5.7	6.4	4.3
Malawi 2010	4.2	1.3	6.4	2.8	13.5	6.9	20.8	10.7	23.8	18.2	20.4	20.8	16.1	15.0
West Africa														
Burkina Faso 2010	0.2	0.4	0.4	0.5	1.2	0.5	2.4	1.1	1.7	1.2	2.0	1.4	1.7	1.1
Guinea 2005	0.9	0.5	1.6	0.7	1.8	1.2	3.0	0.7	2.1	0.9	1.4	2.8	3.3	0.6
Mali 2006	0.6	0.7	1.3	0.8	2.0	0.6	2.2	2.2	2.2	0.6	2.0	1.9	1.2	0.8

*F=female; M=Male

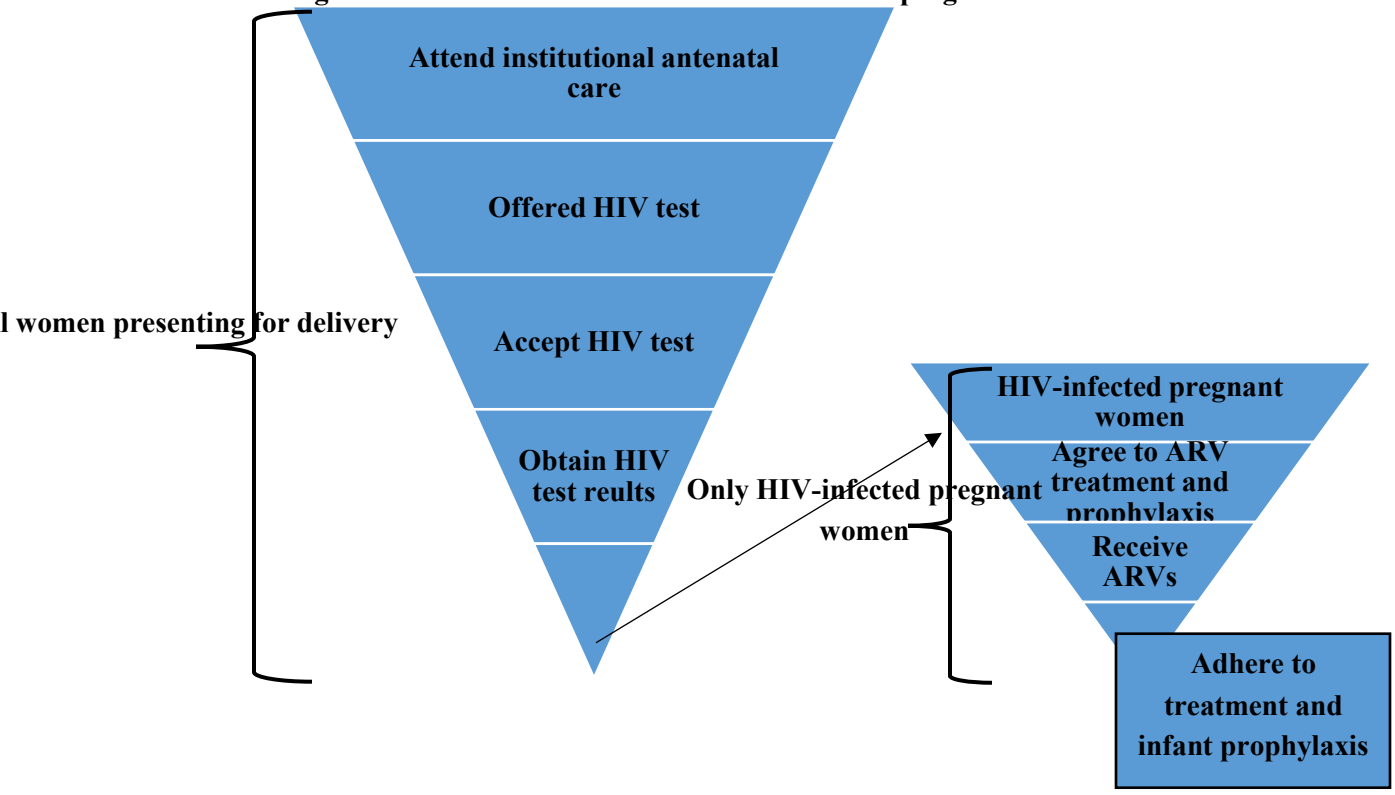
According to the Joint United Nations Program on HIV/AIDS (UNAIDS), there are approximately 1.5 million HIV-infected pregnant women around the world, 92% of whom reside in sub-Saharan Africa.[7] HIV is a leading cause of death during pregnancy and the postpartum period in countries with high HIV prevalence and it contributes to maternal mortality and morbidity, especially in sub-Saharan Africa where 91% of all maternal deaths due to HIV take place.[8] The World Health Organization (WHO) reports that approximately 1.8 million children under the age of 15 are currently living with HIV and 240,000 children were newly infected in 2015.[9] Without treatment, one in every three children living with HIV will die before his or her first year of life and one half of children living with HIV will die before reaching two years of age.[10] Unfortunately, the provision of HIV treatment to children has consistently lagged behind and in 2014, only one third of HIV-infected children received the proper treatment.[11]

Mother-to-child transmission of HIV

Mother-to-child transmission (MTCT) has been responsible for the majority of pediatric HIV-1 infections.[12] MTCT can happen in-utero, at delivery or during the breastfeeding period, with risks of transmission ranging from 5-10%, 10-20% and 5-20%, respectively, resulting in an overall transmission rate of between 15-45% without intervention.[13] Studies have shown that maternal HIV infection, factors associated with delivery, other maternal infections, breastfeeding practices, genetics and characteristics of the maternal virus may be associated with rates of MTCT, but the key maternal factors affecting rates of vertical HIV transmission are maternal viral load and use of antiretroviral therapy (ART).[14] Successful prevention of mother-to-child transmission (PMTCT) can reduce rates of transmission to less than 5%,[15] but implementation of PMTCT strategies continues to be difficult, especially in resource-limited settings such as sub-Saharan Africa. Experts in the field of HIV and PMTCT often refer to the "PMTCT cascade" as a way of addressing key areas along the HIV care and treatment continuum where challenges to PMTCT are most likely to occur. Figure 1 depicts a version of the PMTCT cascade similar to one put forth by the WHO. Attrition along the cascade is most commonly seen in resource-limited settings such that only a small proportion of all HIV-infected mothers present for care and successfully receive and adhere to the antiretroviral (ARV) prophylaxis regimens necessary for PMTCT. While developed countries are close to achieving elimination of vertical HIV transmission, it was estimated as recently as 2011 that only 15-30% of eligible women in resource-limited settings successfully completed the PMTCT cascade.[16] In an effort to improve PMTCT outcomes and consequently improve maternal and child health, experts from various research communities in collaboration with the WHO and community and government partners

from countries with high HIV burden have continued to evaluate ways to improve the uptake of and adherence to PMTCT care and treatment services.

Figure 1: The PMTCT cascade for HIV-infected pregnant women[17]



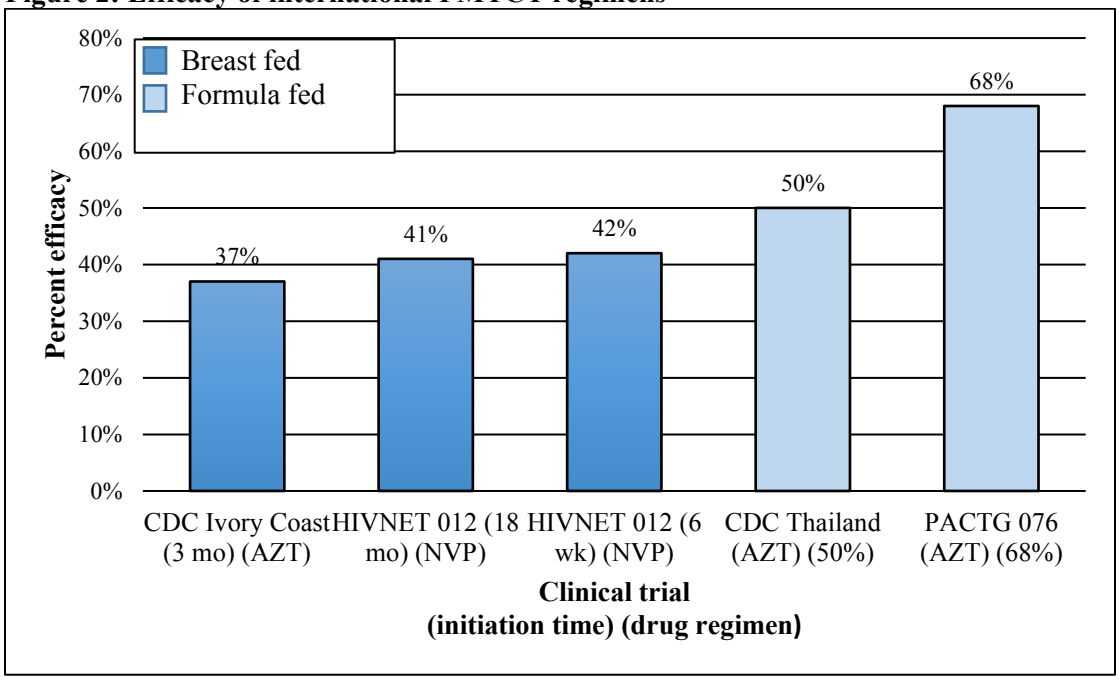
PMTCT literature review

Over two decades of research have shown that the use of ARVs can reduce the risk of MTCT by decreasing replication of the HIV virus and acting as HIV prophylaxis for the fetus and infant during and after virus exposure. The first clinical trial to show that an ARV regimen given to mothers and their infants could greatly reduce rates of MTCT of HIV was the ACTG 076 trial published in 1994.[18] ACTG 076 was a randomized, double-blind clinical trial that enrolled HIV-infected pregnant women and assessed the efficacy of zidovudine (AZT) for reducing the risk of vertical HIV transmission. Women with CD4+ cell counts greater than 200 cells/mm³ received

either AZT or placebo at 14 weeks gestation and through labor and delivery. HIV-exposed infants also received the same regimen for the first six weeks of life. The initial results demonstrated that AZT reduced MTCT by approximately two thirds with only minimal short-term toxic effects. During follow-up of the mother-infant pairs, the study found that only 7.6% of infants in the treatment group were infected with HIV at 18 months, compared to 22.6% of infants in the placebo group. Following the results of this trial, the United States Public Health Service (USPHS) published guidelines recommending the use of AZT for perinatal PMTCT along with HIV counseling and voluntary testing for pregnant women.

After the ACTG 076 trial, clinical trials between 1997 and 2002 continued to demonstrate reduced rates of MTCT in the United States and Europe, with vertical transmission rates decreasing to as low as 1.5%.[19] PMTCT regimens were also tested for their efficacy internationally by varying the regimens, timing of treatment initiation and infant feeding practices. Specifically, the Centers for Disease Control and Prevention (CDC) trials in Thailand and Côte d'Ivoire as well as the HIVNET 012 trial were instrumental in establishing feasible short-term PMTCT regimens in resource-limited settings (figure 2).

Figure 2: Efficacy of international PMTCT regimens



The CDC trial in Thailand was a randomized, placebo-controlled trial conducted with non-breastfeeding HIV-infected women evaluating a regimen of maternal AZT initiated at 36 weeks gestation and continuing through labor and delivery.[20] The study showed that short-course AZT was 50% efficacious, as well as safe and well-tolerated by the study population. It was concluded from this study that short-course AZT should be considered as an option for PMTCT in resource-limited settings unable to implement the 076 treatment regimen. A similar CDC study in the Côte d'Ivoire among HIV-infected breastfeeding mothers was stopped early when results from Thailand became available, but results from infants reaching 3 months of age in Côte d'Ivoire showed efficacy levels of 37%.[21] Similarly, the Ditrame Study Group evaluated the same maternal antepartum and intrapartum regimen with the addition of AZT for seven days postpartum among breastfeeding women in Burkina Faso and the Côte d'Ivoire and found a relative efficacy of 38% at 6 months.[22]

The HIVNET 012 study in Uganda was originally designed as a randomized, double-blind, triple-arm, placebo-controlled trial to determine the efficacy of short-course nevirapine

(NVP) and AZT for PMTCT in resource-limited settings, but once the efficacy of short-course AZT was demonstrated the placebo arm was dropped and mother-infant pairs were randomized to receive either single-dose nevirapine (sdNVP) for the mother and infant or AZT for the mother during the intrapartum period with 7 days of infant prophylaxis.[23] The study found a statistically significant difference in the estimated risk of HIV transmission at 14-16 weeks of 13.1% in the NVP group versus 25.1% in the AZT group. A subsequent intent-to-treat analysis found similar results that remained statistically significant.

While these early studies demonstrated the efficacy of ARV regimens for decreasing in-utero and intrapartum transmission, much of that efficacy was lost in the postpartum period due to transmission through breastfeeding. For instance, the Ditrame-Plus Study Group found that cumulative risks of vertical transmission for breastfeeding women receiving either zidovudine (ZDF) and sdNVP or ZDF and lamivudine (3TC) with sdNVP with early cessation within the first four months were higher than those receiving the same regimens but opting to formula feed.[24]

Though replacement feeding was shown to remove the risk of HIV transmission through breastfeeding, a number of studies showed that replacement feeding was likely to increase the risk of infant malnutrition and death due to other infections. These studies also indicated that compared to mixed feeding practices, exclusive breastfeeding was associated with lower rates of transmission, and that early weaning and replacement feeding decreased HIV exposure but did not necessarily result in improved infant survival. One of the first studies to indicate that exclusive breastfeeding was protective against MTCT was conducted by the South African Vitamin A Study Group and followed a cohort of mother-infant pairs and showed that exclusive breastfeeding carried a significantly lower risk of HIV transmission than mixed feeding and a similar risk as no breastfeeding.[25] The Mashi Trial also looked at differences in HIV infection rates between infants randomized to receive formula with one month of AZT and infants randomized to be breastfed with six months of AZT and found no significant difference in HIV-

free survival between the two study arms.[26] Similarly, a cohort study in Uganda examined infant survival by feeding practice and found excess mortality rates in the formula fed group when compared to the exclusively breastfed group.[27] These results led to a number of subsequent studies exploring ways to decrease the risk of MTCT during the breastfeeding period through extended antiretroviral (ARV) regimens for infants and/or their mothers.

Early studies examining infant prophylaxis for PMTCT included: a) the Six-Week Extended Nevirapine Studies (SWEN), evaluating six weeks of NVP infant prophylaxis[28]; b) the Post Exposure Prophylaxis for Infants Study (PEPI), evaluating 14 weeks of infant prophylaxis with NVP or NVP+AZT[29] and c) the Breastfeeding Antiretrovirals and Nutrition Study (BAN), which included an infant prophylaxis study arm of six months of NVP.[30] These studies demonstrated that infant prophylaxis with NVP greatly reduces vertical HIV transmission. These results along with the HPTN 046 study designed to evaluate the incremental benefit of a six-month regimen versus a six-week regimen and showing lower transmission rates at six months as compared to six weeks,[31] suggested that a longer duration of infant prophylaxis is more efficacious than a short-course regimen for PMTCT.

Some key studies examining the safety and efficacy of maternal prophylaxis during the breastfeeding period for the purposes of PMTCT included: a) the Kesho Bora study, comparing the safety and efficacy of triple ARVs to AZT+sdNVP prophylaxis in pregnant women with WHO stage 1,2 or 3 infection or CD4 cell counts between 200 and 500 cells/mm³ and showing that vertical transmission during breastfeeding was significantly lower in the triple ARV group;[32] b) the Mma Bana study, comparing the administration of prophylaxis through a combination of nucleoside reverse transcriptase inhibitors (NRTIs) to the administration of protease inhibitor (PI) lopinavir/ritonavir (LPV/R) with AZT+3TC among HIV-infected women with CD4 cell counts greater than 200 cells/mm³ and resulting in an overall vertical transmission rate of 1.1% (though not powered to compare the two regimens)[33] and c) the BAN study, comparing the efficacy of

maternal triple ARV prophylaxis for women with CD4 cell counts less than or equal to 250 cells/mm³ to extended infant prophylaxis with NVP as a way to reduce postnatal vertical transmission of HIV and showing that when compared to the control group, both infant and maternal prophylaxis during the breastfeeding period resulted in a significantly lower risk of vertical transmission.[30] These maternal ARV studies showed that prophylaxis for HIV-infected mothers can significantly reduce MTCT during breastfeeding and have informed WHO guidelines for PMTCT, leading to what is now referred to as Option B.

WHO PMTCT recommendations and Option B+

Since 2000 when the WHO first put forth guidelines for PMTCT and infant feeding strategies for HIV-infected mothers, the international health community has continued to regularly update recommendations for PMTCT and infant feeding to reflect the most recent findings from the biomedical, public health and social science fields. The WHO guidelines influence the direction of international and bilateral funding agencies and are aimed at managers and healthcare providers in resource-limited countries responsible for establishing national policies, implementing PMTCT services and ensuring that high quality services are provided to those in need.

The first version of the WHO PMTCT recommendations in 2000 supported the use of sdNVP for the mother at least two hours before delivery, oral sdNVP for the infant within the first 72 hours of life and avoidance of all breastfeeding when replacement feeding was acceptable, feasible, affordable, sustainable and safe, with the option of exclusive breastfeeding for the first months of life in settings where replacement feeding was not appropriate.[34] Since then recommendations have changed with the presentation of new evidence for best PMTCT practices. For instance, over time additional ARVs were recommended for the postpartum period when research found that administering sdNVP to the mother and infant, while efficacious and

affordable, resulted in a high incidence of viral resistance in women and children.[35] Tables 1 and 2a, b and c in Appendix A summarize the PMTCT and infant feeding recommendations revised by the WHO between 2004 and 2006. It is important to note that these recommendations did not address means of decreasing MTCT in the postpartum period except through modified breastfeeding practices.

In 2010 the WHO differentiated between women requiring lifelong ART for their own health and those not qualifying for treatment. Tables 3a, b and c in Appendix A are from the 2010 WHO document and outline the 2010 recommendations in detail. In summary, pregnant women qualified for treatment based on their CD4 cell counts and WHO disease stages and women who did not qualify for treatment for their own health could receive either Option A or Option B as PMTCT prophylaxis. Option A included a shorter prophylaxis regimen for the mother comprised of AZT as early as 14 weeks gestation and sdNVP at labor with daily AZT and 3TC from labor until seven days postpartum and a longer prophylaxis regimen for the infant comprised of daily NVP from birth through one week beyond complete cessation of breastfeeding (or through four- to six weeks of age if the mother was not breastfeeding). On the other hand, Option B included a longer prophylaxis regimen for the mother comprised of triple ARVs starting as early as 14 weeks gestation and continued through the intrapartum period and childbirth if not breastfeeding or until one week after cessation of all breastfeeding, and a shorter prophylaxis regimen for the infant comprised of daily NVP or AZT from birth through four to six weeks of age regardless of infant feeding method. Option A and Option B were thought to be programmatically different but equally efficacious for reducing the risk of vertical HIV transmission for mothers ineligible for treatment, and countries were encouraged to evaluate each option and determine the best strategy for a national program.[36]

Since 2010 the WHO has moved toward promotion of a third PMTCT option known as Option B+. This approach has been described as a single, universal strategy for both the treatment

of HIV-infected pregnant women and for PMTCT prophylaxis.[37] Option B+ includes the provision of triple ART for HIV-infected pregnant women at the antenatal clinic regardless of clinical stage or CD4 cell count, to be continued for life. Table 2 is adapted from the April 2012 WHO programmatic update and summarizes the differences between Option A, Option B and Option B+.

With the deadline set by the Global Plan for 2015 for achieving elimination of MTCT on the horizon[38] and growing concern that the global health community was not on track to meet this goal, the WHO asserted that switching to Option B+ could likely help overcome the operational and programmatic complexities that countries had been experiencing with the implementation of Option A, without increasing cost.[39]

Between 2010 and 2012 key findings serving as rationale for the 2012 update included: 1) new evidence from the HPTN052 study supporting ARV treatment as prevention for individuals with higher CD4 cell counts[40]; 2) reassuring data on the safety of efavirenz (EFV) as a first-line drug during pregnancy and approval of the tenofovir (TDF)/3TC/EFV fixed dose combination[41]; 3) improved prevention of sexual transmission of HIV to serodiscordant partners[42]; 4) increased risks to maternal health associated with stopping and starting triple ART in settings of high fertility and improved maternal health outcomes associated with earlier initiation of treatment[37] and 5) the decreasing cost of ARVs.[43]

Table 2: WHO recommended options for PMTCT[37]

	Mother		Infant
	Treatment (CD4 count <350 cells/mm³	**Prophylaxis (CD4 count ≥350 cells/mm³)**	
Option A	Triple ARVs starting as soon as diagnosed, *continued for life*	*Antepartum:* AZT starting as early as 14 weeks gestation *Intrapartum:* at onset of labor, sdNVP and first dose of AZT/3TC *Postpartum:* daily AZT/3TC through 7 days postpartum	Daily NVP from birth through 1 week beyond complete cessation of breastfeeding; or if not breastfeeding or if mother is no treatment, through age 4-6 weeks
Option B	Triple ARVs starting as soon as diagnosed, *continued for life*	Triple ARVs starting as early as 14 weeks gestation and *continued intrpartum and through childbirth if not breastfeeding or until 1 week after cessation of all breastfeeding*	Daily NVP or AZT from birth through age 4-6 weeks regardless of infant feeding method
Option B+	Regardless of CD4 count, triple ARVs starting as soon as diagnosed, *continued for life* (Same for treatment and prophylaxis)		Daily NVP or AZT from birth through age 4-6 weeks regardless of infant feeding method.

Malawi and Option B+

In 2011 the Malawian Ministry of Health (MoH) decided to implement Option B+ as the national PMTCT approach. This decision was based on the high incidence of infant HIV infections occurring in Malawi at that time and the notion that a major barrier for PMTCT in Malawi was the limited capacity of laboratories to perform CD4 cell counts necessary to implement either Option A or Option B.[44] The implementation of Option B+ required the integration and decentralization of ART to all antenatal care (ANC) settings, re-training healthcare workers to familiarize them with the new strategy, changing the adult first-line ART regimen to include EFV and policy changes relating to task-shifting that allowed for clinical officers, medical assistants and nurses to start women on ART.

Evaluations of Option B+ implementation in Malawi showed the program to be successful in some respects, but there were challenges that must also be addressed. The Malawi MoH reported an increase from 303 ART sites in June 2011 to 641 integrated PMTCT/ART sites

in September 2012[45] and a 2014 report from the WHO summarizing the Malawi experience with Option B+ stated that 80% of mothers testing positive were initiating ART.[45] Currently it appears that Option B+ has led to increased availability, accessibility and utilization of PMTCT services in Malawi, but a 2015 study found that women who initiated Option B+ in Malawi exhibited greater withdrawal from services, greater loss to follow-up and decreased ART retention at 6 months postpartum when compared to women enrolled in the PMTCT program before Option B+.[46]

While promoting Option B+ as the way forward for PMTCT, the WHO also cautioned that limitations to the program might include: 1) insufficient health infrastructure for accommodating the increased clientele, 2) inadequate linking of maternal and pediatric care and a lack of mechanism for tracking losses to follow-up, leading to confusion about the follow-up schedule, suboptimal coverage of testing, diagnosing and treating HIV-exposed infants and a high potential for poor long-term program adherence, 3) limited data management capacity at the lower levels of the healthcare system, 4) stock-outs of HIV test kits and poor estimations of necessary medicine quantities, 5) negative reception from healthcare providers and clients to the same-day testing, counselling and ART initiation practices, 6) problematic quality of HIV testing (in 2012, 20% of HIV-infected pregnant women were falsely identified as HIV-negative and 4% of HIV-negative pregnant women were falsely identified as HIV-positive), 7) a feeling that the Option B+ program does not actively promote male partner involvement, 8) a loss of HIV-infected pregnant women and mothers to neighboring countries where Option B+ is not being implemented and 9) a lack of human resources and a shortage of health workers needed to successfully implement Option B+.[47]

To date, evaluation of the Option B+ program in Malawi has yielded mixed results. A CDC-funded national evaluation of Malawi's PMTCT program evaluating vertical HIV transmission across 54 randomly selected health facilities in 10 districts found that among the

1,851 HIV-infected mothers with infants between four and 12 weeks of age, the overall MTCT rate was 3.9% while the transmission rate among women who had initiated ART during pregnancy was 2.8%.[47] The same evaluation also noted that MTCT varied by timing of ART initiation, from 1.4% among women who initiated ART prior to the current pregnancy to 21.3% among women who had never initiated ART. However, a different evaluation of the Malawi Option B+ program found that close to one fifth of women initiating Option B+ in Malawi had become lost to follow-up by six months on treatment and that compared to women initiating ART due to low CD4 cell count or advanced clinical disease staging, women who initiated ART during pregnancy were five times more likely to never return for a follow-up visit after ART initiation.[48]

The introduction of Option B+ in Malawi removed the need for a CD4 cell count and decentralized ART to all ANC sites, allowing for improved access and initiation of treatment for PMTCT. It is also possible that the Option B+ program could lower vertical rates of HIV transmission. However, ongoing monitoring and evaluation is necessary to further examine the challenges facing long-term Option B+ adherence and program retention after initial infant HIV test results are received. In addition, data from other countries currently implementing Option B+ must continue to be gathered and analyzed to see if the initial success experienced in Malawi is being replicated in other resource-limited settings and whether or not these countries are experiencing or will experience similar challenges with long-term implementation of Option B+.

PMTCT and Option B+ in Uganda

Uganda is one of the countries in sub-Saharan Africa that has transitioned from Option A to Option B+. The WHO has classified Uganda as one of the top ten high burden countries for PMTCT[49] and thus, addressing PMTCT in Uganda is essential to achieving the goal of eliminating vertical HIV transmission. This categorization is due in combination to the number of HIV-infected pregnant women reaching approximately 120,000,[50] the high maternal mortality

ratio of 343 per 100,000 live births[51] and an infant mortality rate of approximately 62 per 1000 live births.[52]

The diversity of the Ugandan population, specifically of its women, is reflected in the variations in total fertility rates (TFRs) and percentages of women delivering at a facility by region and residence. The overall TFR in Uganda is 6.2 and 57.4% of all pregnant women deliver in a health facility, [53] but the differences in the regional TFRs and percentages of women delivering at facilities are presented in table 3 below.

Table 3: Regional and residence-specific TFRs and health facility delivery coverage in Uganda[54]

Region	Total fertility rate	Percent of women delivering at a facility (%)
Kampala	3.3	92.9
Central 1	5.6	61.7
Central 2	6.3	69.1
East Central	6.9	67.1
Eastern	7.5	51.2
Karamoja	6.4	27.1
North	6.3	51.9
West Nile	6.8	58.7
Western	6.4	55.9
Southwest	6.2	40.3
Urban	3.8	89.5
Rural	6.8	52.0
Total	**6.2**	**57.4**

According to the Uganda HIV and AIDS Country Progress Report put forth in 2014, the AIDS Indicator Survey showed an estimated HIV prevalence of 7.4% in the general population.[54] The report states that while adult HIV prevalence is 2% higher in women as compared to men ages 15-49 (8.2% vs. 6.1%), young women ages 15-29 are at least twice as likely to be infected with HIV as men of the same age. The report also showed variations in HIV prevalence by region, with the highest HIV prevalence observed in the Central 1 region including Kampala (10.1%) and the lowest HIV prevalence observed in the Mid-eastern region (4.1%). Figures 3 and 4 below, adapted from the Country Progress Report, display HIV prevalence in Uganda according to age, sex and region and support the notion that the epidemic is generalized yet heterogeneous.

The same report demonstrates attrition along the PMTCT cascade. In 2014, approximately 93% of pregnant women in Uganda presented for at least one ANC visit. Of these women, approximately 94% received and HIV test and results, meaning in actuality only 87% of all pregnant women in Uganda received an HIV test and results. Of the 8% found to be HIV-infected, 84% received ARTs, including women on ART prior to their current pregnancy and those initiating Option B+ for PMTCT. However, only 51% of HIV-exposed infants received an HIV test in the first two months of life, only 25% of HIV-exposed infants received ARVs for PMTCT and the proportion of women exhibiting good adherence throughout pregnancy, delivery and the postpartum period was not stated in this report. The gaps in the Uganda PMTCT cascade have resulted in a MTCT rate of somewhere between 5 and 8% across the country.[55]

Figure 3: HIV prevalence in Uganda by age and gender[55]

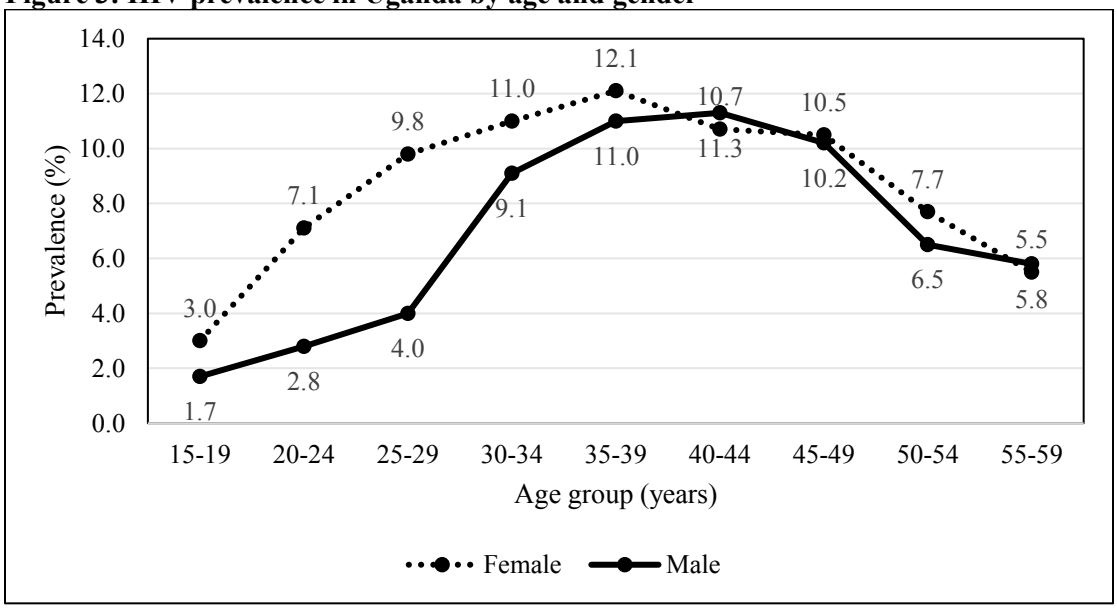
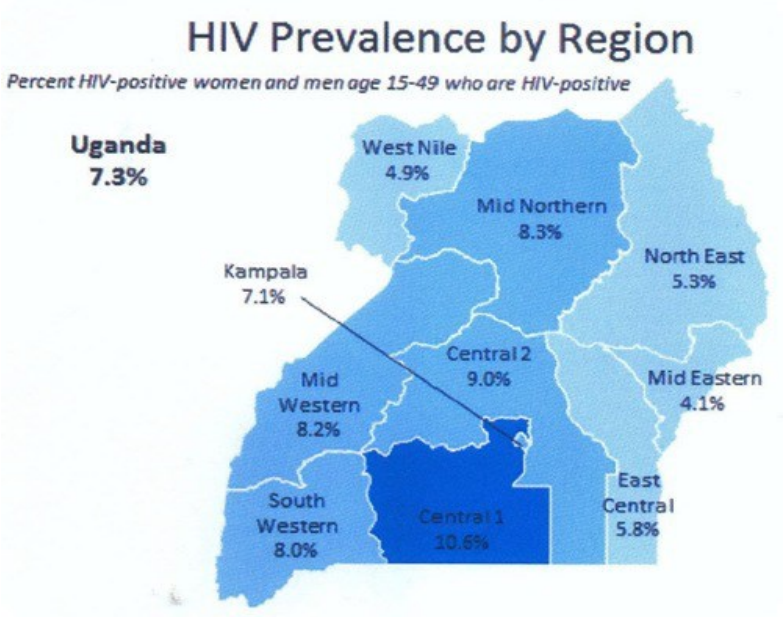


Figure 4: HIV prevalence in Uganda by region (2011)[56]



In 2011, the MoH reported that a modes of transmission analysis in Uganda found vertical HIV transmission accounted for 18% of all new HIV infections and was the leading cause of HIV infection in children under 5.[57] This data, coupled with the launch of the Global Plan, an ambitious initiative by the President's Emergency Plan for AIDS Relief (PEPFAR) aimed toward elimination of childhood HIV infections by 2015, [58] led to the development of a country-specific vision for an HIV/AIDS-free generation by 2015. This MoH plan included the goal of virtual elimination of vertical HIV transmission and the reduction of mortality and morbidity among women living with HIV and among HIV-exposed and infected infants through four objectives aimed at providing: 1) reproductive health, HIV and sexually transmitted infection (STI) prevention and treatment services to 80% of women of reproductive age; 2) family planning

services to 80% of all women living with HIV; 3) the recommended package for PMTCT to 80% of HIV-infected women and their infants and 4) family-centered HIV care and treatment to 80% of HIV-infected pregnant and lactating women and their children, if infected with HIV.[59] Initially, the MoH instructed that these objectives would be achieved through implementation of the WHO-recommended Option A until further communication to transfer to Option B.

However, following the rapid scale-up of Option B+ in Malawi, the government of Uganda decided to launch a similar program in September, 2012. The policy shift was welcomed with the understanding that under Option B+, pregnant women would receive the most effective care and treatment, HIV-exposed infants would receive the most effective prophylaxis regimen throughout pregnancy, birth and delivery, discordant male partners would be protected from infection and the implementation of this program would be easier on clinical staff and the Uganda health system.[60] It was decided that due to financial challenges, health infrastructure limitations and an on-going shortage of public health human resources, Option B+ would be rolled out in a phased approach beginning with districts reporting the highest HIV prevalence.[61]

Option B+ roll-out was completed in Uganda in 2013. According to the PEPFAR 2015 Uganda Country Operational Plan, implementation focused on the introduction of facility-level mother-baby care points, decentralization of services and strengthening of monitoring and evaluation techniques to improve adherence and retention in care along the PMTCT cascade.[61] The same report pointed to successful outcomes such as an increase in the number of health facilities offering PMTCT services from 1,596 in 2012 to 3,248 in 2015 and maternal ART coverage increasing from 65% in 2012 to 87% in 2014. Despite these significant improvements, the effect of Option B+ on PMTCT program adherence and retention in Uganda remain largely unknown and the influence of Option B+ on the documented barriers to PMTCT program adherence and retention are unclear.

Measures of Adherence and Retention in Care

Adherence is commonly thought of as the extent to which a patient takes medication or utilizes health services in the way intended by the healthcare provider.[62] Accurate and reliable measures of adherence are difficult to obtain, especially in resource-limited settings and specifically for PMTCT treatment and care services. Though the WHO recommends adherence assessments for every patient initiating ART[63] there is no gold standard for this measurement.[64] A number of studies have established that adherence is highly correlated with virologic suppression and therefore biological markers such as plasma concentrations of ART and HIV plasma viral load are considered the most objective measures of adherence.[65] However, in resource-limited settings these indicators are generally not routinely collected and other strategies must be used to evaluate HIV medication adherence and program retention. Common strategies for measuring adherence are described in this section below.

Patient self-report

In resource-limited settings where regular blood tests are not feasible due to limitations associated with costs and infrastructure, patient self-report is often used as an indicator of medication adherence. Self-report does not require sophisticated lab techniques or highly trained personnel but may lead to an overestimation of adherence.[66] Techniques for measuring self-report have not been standardized, making it difficult to compare estimates across studies. Nevertheless, patient self-report remains a popular tool for measuring adherence, especially as studies such as one conducted in Tanzania validate this method by showing a high correlation between results obtained from blood samples and patient self-report.[67] A variety of self-report measures have been used to measure adherence, with recall periods varying from one to 30 days and studies differing in conclusions about which method and timeframe is most accurate.[68] Some common strategies of self-report include: 1) visual analog scales (VAS) in which participants are asked to

indicate their degree of adherence along a straight horizontal line ranging from 0% to 100% adherence; 2) qualitative single item measures in which participants are asked to grade their ability to take all of their medications over a specific timeframe; 3) Adult AIDS Clinical Trial Group four-day recall (AACTG) in which participants are asked to report their number of missed doses over the past four days and 4) a seven-day qualitative measure in which participants are asked how many days they correctly took all doses of their medication in the past week. [69]

Pharmacy-based measures

Compared to patient self-report, these measures of adherence are more routinely available, objective and less affected by recall or social desirability bias.[70] According to a review of the ART adherence literature, pharmacy-based adherence measures (PAMs) do not include pill counts performed independently from routine clinic visits or monitoring with electronic devices.[71] The same review identified three categories of PAMs: 1) medication or drug possession ratio; 2) pill count and 3) pill pickup. Table 4 below is adapted from this literature review and summarizes these measures. The review found that PAMs consistently predicted patient outcomes but concluded that additional research was necessary to determine the most predictive measures of adherence. Table 5 below is adapted from a recent USAID report on adult adherence to treatment and retention in care and highlights the advantages and disadvantages of the adherence measures described above.

Table 4: Pharmacy-based adherence measures (PAM)[71]

PAM category	Definition	Formula(e)
Medication or drug possession ratio	Amount of time an individual is in possession of ≥1 ARV or prescriptions for ARVs as a proportion of the time between 2 ARV pick-ups or prescriptions.	# of days ARV prescribed or dispensed/# of days in the interval
Pill count	Quantity of ARV pills an individual has used between 2 ARV pickups as a proportion of the number of pills dispensed or as a proportion of time between pick-ups.	(# of ARV pills dispensed-# of ARV pills returned)/#of ARV pills dispensed (#of days ARV pills dispensed-#of days ARV pills returned)/# of days in the interval
Pill pickup	Whether an individual picks up all or a majority of their prescribed ARVs and expresses the adherence estimate in dichotomous fashion.	"Adherent"=(ARV refills picked up/ARV refills prescribed)> predefined cutoff value "Adherent" = (ARV refills picked up prior to previous refill finishing/ARV refills prescribed)> predefined cutoff value

Table 5: Advantages, disadvantages and potential bias of adherence measurements[72]

Method	Advantages	Disadvantages	Direction of bias	Comparative accuracy
Patient self-report	Simple, cheap	Subjective; accuracy affected by patient recall	Overestimates adherence	Weak yet significant association with viral load
Pill counts	Simple, objective	Accuracy affected by inability to confirm who took pills, timing of doses and possibility of throwing away pills prior to count	Overestimates adherence	Moderate associations with viral load and CD4 counts with unannounced pill counts appearing more predictive of viral load than self-report
Pharmacy data	Simple, cheap, objective	Requires patients to bring back pill bottles which may not be standard of care; inability to confirm who took pills and timing of doses	Overestimates adherence	Moderate to strong associations with viral load, CD4 counts and AIDS-related mortality
Viral load testing	Objective	Expensive; technically difficult; invasive; uncommon in resource-limited settings	Overestimates or underestimates adherence	May vary based on viral resistance, prior treatment failure or poor absorption of drug

Medication event monitoring system (MEMS)

The medication event monitoring system (MEMS) for measuring adherence is performed by electronically recording the opening and closing dates of bottles and is thought to be less susceptible to overestimation in comparison to patient self-report or pill counts.[73] The rate of adherence is calculated as the number of times the drug bottle is opened divided by the number of prescribed doses and multiplied by 100%. While MEMS may be considered a more objective measure of adherence, it is also subject to limitations, namely that opening a bottle does not necessarily mean medication has been consumed. MEMS is also a more difficult measure of adherence to execute in resource-limited settings and limited data exists regarding the feasibility of this method in these environments.[74]

Service utilization indicators and measures of program retention

In addition to measuring ART adherence, other measures of service utilization can be collected to monitor and assess PMTCT adherence and program retention. Some indicators commonly found in the literature evaluating PMTCT programs include: 1) number of ANC and/or PMTCT visits attended; 2) whether or not a pregnant woman receives HIV counseling and testing services; 3) whether or not a pregnant woman receives her HIV test results; 4) whether or not an HIV-infected pregnant woman receives ART at the time of labor and delivery; 5) whether or not the HIV-exposed infant receives an HIV test and 6) whether or not an HIV-infected pregnant woman receives counseling on appropriate infant feeding practices.

Adherence and Option B+

Adherence research prior to 2005 concluded that for successful long-term virologic suppression to be achieved 95% of the prescribed combination ART (cART) doses must be consumed.[75] Since then, studies of ritonavir (RTV)-enhanced PIs or regimens based on

nonnucleoside reverse transcriptase inhibitors (NNRTIs) such as EFV have shown that successful virological suppression may be achieved at lower adherence levels of between 70-80%[76] due to the higher potency and longer half-lives of these newer ART regimens.[77] Regardless of ART regimen, a linear dose response relationship exists between higher adherence and improved virologic outcomes.[78] To date, there are limited data on ART adherence during pregnancy and in the postpartum period under Option B+. A meta-analysis of existing adherence data from low-, middle- and high-income countries in the pre-Option B+ era found that ART adherence dropped from 73.5% during pregnancy to 53% in the postpartum period.[79] More recently, an evaluation of virologic and immunologic failure in the first 24 months postpartum among HIV-infected women who initiated ART for life as part of the Mitra plus Study in Tanzania found that the proportion of women with viral loads greater than or equal to 400 copies/mL decreased significantly from 97% at enrollment to 16% at three months postpartum, but increased to 86% at 24 months postpartum.[80] This trend is worrisome for the long-term effectiveness of Option B+ which by definition requires equally high levels of triple ART adherence during pregnancy and the postpartum period and does not necessarily address barriers to long-term adherence or program retention.

The preliminary data from Malawi indicated that transitioning to Option B+ may increase the number of pregnant women who attend ANC, receive an HIV test, become aware of their positive status and subsequently begin ART for PMTCT, but it remains to be seen if long-term adherence can be achieved under this PMTCT approach or if these results can be replicated in other settings. A recent implementation science study of the lessons learned from the early application of Option B+ put forth by the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) reported varying levels of success for improving the percent of HIV-infected pregnant women accessing ART under Option B+, with results ranging from as high as 97% in Lesotho to as low

as 35% in the Democratic Republic of Congo and only four of the 11 countries reporting data for Option B+ program retention. [81]

Despite support for Option B+ from the WHO and many other international agencies and organizations, there are a number of issues that must be considered and studied relating to the long-term effectiveness of Option B+. As a recent Lancet editorial suggests, it is critically important to assess the feasibility of maintaining lifelong maternal ART adherence in resource-limited settings constrained by unstable health infrastructure and challenging social norms.[82] Inconsistent adherence is a serious barrier for the elimination of HIV/AIDS and specifically for PMTCT and maternal and child health since it is associated with an increased risk for opportunistic infections,[83] HIV disease progression[84] and viral resistance to ART.[85] Thus, it must be decided if the PMTCT benefits that could be achieved under Option B+ outweigh the potential negative effects on maternal and child health that could occur if appropriate levels of adherence cannot be maintained.

As countries such as Uganda continue to carry out Option B+, country-specific implementation and program evaluation research is necessary to understand if adequate levels of adherence to this PMTCT program are being achieved. In addition to studying levels of adherence, it is equally important to describe the factors affecting adherence for HIV-infected pregnant women and so that appropriate interventions can be proposed for reducing the risk of suboptimal adherence and program retention that can negatively affect maternal health, child health and PMTCT.

Factors affecting PMTCT adherence

While research focusing on PMTCT-specific barriers to adherence in the Option B+ era is on-going, studies looking at barriers to adherence, both in the context of PMTCT and adult HIV treatment and prevention, do exist. It is believed that these factors can affect more than one

stage of the care and treatment cascade and may interact or reinforce each other at different times, leading to decreased levels of program retention and adherence.[86] The most commonly identified barriers to PMTCT and HIV program adherence appearing in the literature are briefly described below.

Health status

Studies show that poor physical or mental health can negatively affect care-seeking practices. For example, depression has been linked to lower ARV adherence.[87] A recent case-control study of HIV-infected adults in Uganda showed that HIV-positive adults with lifetime depressive disorders had an increased risk of non-adherence when compared to those without lifetime depressive disorders and that the association was stronger for females versus males.[88] Additionally, individual state of health is a commonly cited risk factor associated with missing scheduled appointments.[89]

Previous HIV diagnosis

Whether a pregnant woman is finding out her HIV status for the first time during the current pregnancy or was diagnosed prior to the current pregnancy may also affect adherence. A systematic review of factors affecting the uptake of ART for PMTCT in sub-Saharan Africa found that psychological issues following HIV diagnosis were a key barrier to ART uptake.[90] It can be hypothesized that a woman who is aware of her HIV status prior to her current pregnancy may have already had the opportunity to confront some of the psychological issues following initial HIV diagnosis, such as denial, shock and fear, and is therefore more likely to adhere to the PMTCT program during her current pregnancy than a pregnant woman who has been newly diagnosed with HIV. Similarly, a study looking at the timing of maternal HIV testing and uptake of PMTCT interventions in South African found that women diagnosed with HIV before their

current pregnancy were more likely to attend ANC before 20 weeks gestation and were more likely to receive maternal and infant prophylaxis as compared to women diagnosed with HIV during or after the current pregnancy.[91]

Maternal CD4 cell count at ART initiation

There is some evidence that maternal CD4 cell count at the time of ART initiation may affect PMTCT program retention. For instance, the same cohort study conducted in Kenya that is described above found that a higher CD4 count at the time of ART initiation was associated with an increased odds of disengagement from PMTCT treatment.[93] A systematic review of barriers and facilitators to uptake of ARTs for PMTCT in sub-Saharan Africa claimed that maternal CD4 cell count was not significantly associated with NVP adherence[90] but this could be largely due to the fact that many of the included studies looked at women initiating ART under older WHO recommendations excluding those with higher CD4 counts from initiating treatment.

Previous PMTCT experience

Although this is difficult to measure and the strength of association varies by study, some research indicates that previous PMTCT experience could be associated with adherence. For example, a cohort study of adherence and virologic suppression during the first 24 weeks of ART among women in South Africa showed that women who were previously enrolled in a PMTCT program and had received sdNVP in a prior pregnancy were less likely to demonstrate incomplete adherence, defined as returning greater than 5% of medications as estimated by pill counts at scheduled visits, than women who had not received sdNVP for PMTCT.[92] Currently, there is a lack of data comparing the rates of adherence to PMTCT programs between HIV-infected pregnant mothers who have had previous PMTCT program experience and those that are experiencing a PMTCT program for the first time.

Gestational age

Gestational age appears to be associated with PMTCT program retention. A recent cohort study conducted in South Africa looking at the disengagement of HIV-infected pregnant and postpartum women from ART services found that later gestational age at ART initiation was a significant predictor of disengagement from care, defined as no clinic attendance within 56 days of a scheduled visit.[93] On the other hand, a different cohort study of HIV-infected, ART-naïve, pregnant women initiating ART for PMTCT in Kenya showed that the odds of disengagement from care, defined as an interval of greater than 30 days between visits or before delivery, decreased with increased gestational age.[94]

The postpartum period

Research indicates that HIV-infected pregnant women and mothers are less likely to have good adherence in the postpartum period as compared to the antepartum period. For example, a meta-analysis of ART adherence in low-, middle- and high-income countries during and after pregnancy reported pooled estimates of adherence that were significantly higher in the antepartum period than in the postpartum period.[80] Similarly, the same cohort study from South Africa cited above showed disengagement from care among pregnant women initiating ART was twice as likely in the postpartum period as compared to the antenatal period.[92]

Perceived risk

Today knowledge about HIV transmission and treatment is much improved, but just as a woman in a monogamous marriage may not consider herself at high risk for acquiring HIV and therefore resist an HIV test,[95] an HIV-infected woman believing that she is healthy may feel that she has a low risk of vertically transmitting HIV and may therefore exhibit sub-optimal PMTCT adherence or program retention. Similarly, an HIV-infected mother receiving negative HIV test

results for her infant at 6 weeks postpartum may believe her child is no longer at risk of acquiring HIV and become less vigilant about adhering to medication or clinic visits for PMTCT in the breastfeeding period.

Self-efficacy

Self-efficacy can be defined as the belief one has in one's own ability to complete a task or reach a goal.[96] Although many pregnant women are concerned about their HIV status and preventing transmission to their infants, they may lack the self-efficacy to adhere to the PMTCT regimen. A recent cross-sectional analysis in Vietnam found that increased perceived self-efficacy, defined in the study as participant confidence that he or she can comply with ART regimens, was associated with optimal adherence.[97] Likewise, it was found that improved adherence-related self-efficacy was significantly associated with decreased viral load among minority women in the United States.[98] For HIV-infected pregnant women in resource-limited settings, lacking the confidence that they can overcome barriers to PMTCT care and treatment may negatively affect their feelings of self-efficacy and result in suboptimal program adherence.

Dynamics in the home

Family relationships are another factor associated with adherence to PMTCT services. A study in Malawi showed that inequality in the house restricts women from accessing necessary resources for care and are therefore reliant upon others to decide if and when to initiate and continue PMTCT services.[99] The relationship of women with certain family members such as mothers-in-law[100] is also a factor that may be associated with PMTCT program adherence.

Male partner involvement

Many studies have shown that male partner involvement plays a significant role in the uptake and adherence to PMTCT services. For instance, some women refused HIV counseling or testing because they feared the reaction from their partners.[101] Studies have also shown that HIV-infected women are at an increased risk for intimate partner violence.[102] Alternatively, women are often more likely to start ARV prophylaxis, [103] deliver in a facility[104] and adhere to follow-up care[105] when male partners are involved in the care of their partners. Studies have also shown that HIV-infected mothers with higher male partner involvement exhibited improved adherence to maternal and infant prophylaxis.[106]

HIV-associated stigma

Stigma has been an on-going obstacle for all HIV-infected individuals and especially for ART adherence. For example, a cross-country analysis of HIV-infected individuals in five African countries found that perceived stigma had a highly significant association with neglecting to take all prescribed medications.[107] In 2012, a policy paper sponsored by the USAID, PEPFAR and the Healthy Policy Project reviewed existing academic and programmatic evidence of the effects of stigma and discrimination on PMTCT and found that HIV-related stigma and discrimination negatively impacted service uptake and adherence for women and infants along each step of the PMTCT cascade.[108] The same report also presented a mathematical model hypothesizing that an estimated 44% of all vertical HIV transmission could be avoided with a significant reduction in stigma and discrimination.

Disclosure of HIV status

It has been found that status disclosure by HIV-infected pregnant women to their partners is associated with an increased utilization of PMTCT services and that HIV-infected pregnant

women who have disclosed their status to their partners find it easier to store and take their ART than those women who have not disclosed their HIV status to their partners.[109] A cross-sectional study in Ethiopia found that disclosure was more likely at later disease stages and when partners lived the same house, discussions about HIV testing had already taken place and the partner's HIV status was known. [110]

Social networks and support

Research has shown that social support is important for HIV program retention and has been linked to improved drug adherence.[111] Qualitative studies looking at adherence in Botswana[112] and Tanzania[113] found that patients who reported not having strong social networks within the community lost motivation for treatment adherence. On the other hand, motivational groups for HIV-infected women in Nigeria have been associated with significantly higher levels of ART adherence when compared to a control group.[114] Similarly, a pilot study in South Africa[115] found that HIV-infected pregnant women receiving support from the mothers2mothers peer mentoring program showed an improved ability to establish social support and reduce depression scores as compared to HIV-infected pregnant women in the control group receiving standard services. The same study showed that compared to women in the control group, women participating in the intervention had improved attendance at follow-up medical visits, a common measure of PMTCT program adherence. Recently, a cross-sectional study in Rwanda[116] found that HIV-infected individuals participating in an association for PLWHA and/or receiving care at sites which regularly conducted home visits exhibited lower odds of ART non-adherence when compared to controls receiving standard services.

Place of delivery

Studies show that place of delivery may affect the adherence and program retention of HIV-infected pregnant women and mothers. For instance, a cohort study in Zambia looking at predictors of non-adherence to sdNVP found an increased odds of both maternal non-adherence and infant non-adherence, defined as no maternal NVP consumption and no infant NVP consumption respectively, for women delivering at home as compared to women delivering in clinics.[81] Similarly, a recent literature review looking at medication adherence for PMTCT in sub-Saharan Africa found that giving birth at home was associated with low adherence to ARV prophylaxis.[117]

Transportation and economic concerns

The time and distance it takes to travel to facilities as well as the cost of transportation have been shown to affect behaviors associated with HIV testing, receipt of results and service utilization.[118] A qualitative study of HIV-infected women attending ANC in Malawi found that economic concerns such as transport costs represented the greatest barrier to accessing treatment.[119] Along the same lines, a case-control study of determinants of non-adherence to sdNVP for PMTCT in Rwanda found that women attending two or less ANC visits were more likely to be non-adherent than those attending more than two visits.[120] Regular ANC attendance is directly associated with utilization of ANC services and the underlying cause of irregular ANC attendance may be the cost of travel to and from the clinic.

Political and health system environment and functionality

Studies have shown that social welfare and insurance policies can affect HIV service use and health outcomes.[121] Health system functionality also affects PMTCT adherence behaviors. For instance, a qualitative study from Uganda found that health service factors such as long

waiting times at the clinic and negative interactions with staff were barriers for adherence to highly active antiretroviral therapy (HAART) for HIV-infected mothers.[122] Similarly, a cross-sectional analysis of mostly African American males from the Johns Hopkins HIV Cohort Study[123] as well as a cross-sectional pilot study of HIV-infected pregnant women in South Africa[124] found that a close patient-provider relationship (i.e. the patient perceiving that he or she is "known as a person") was significantly associated with receiving and adhering to HAART. In resource-limited settings, ensuring an adequate supply of ART drugs is also a significant barrier to adherence.[125]

Conceptual framework

Evolution of the Social Ecological Model

The factors described above can be thought of as determinants of PMTCT medication adherence and program retention. Some of these factors are individual characteristics while others are structural and environmental factors that influence and are influenced by the characteristics of the individual HIV-infected pregnant woman. This notion of reciprocal causation between the individual and the environment, as well as the theory that health behaviors simultaneously shape and are shaped by multiple levels of social influence, are features of the Social Ecological Model (SEM) for health promotion put forth by McLeroy et al. in 1988. The underlying assumption of the model is that changes to a specific social environment may produce the desired changes in health behavior of the individual, and that support of the individual within the population is key to realizing this environmental change.[126] McLeroy et al. adapted the ecological model formalized by Bronfenbrenner in the 1970s and 1980s[127] to describe five levels at which the health outcome of interest (i.e. health behavior) is determined: 1) intrapersonal factors (characteristics of the individual); 2) interpersonal processes and primary groups (formal and informal social networks and social support systems); 3) institutional factors (social institutions

with organizational characteristics and rules and regulations for operation); 4) community factors (relationships among organizations, institutions and informal networks within defined boundaries) and 5) public policies (local, state and national laws and policies).[103]

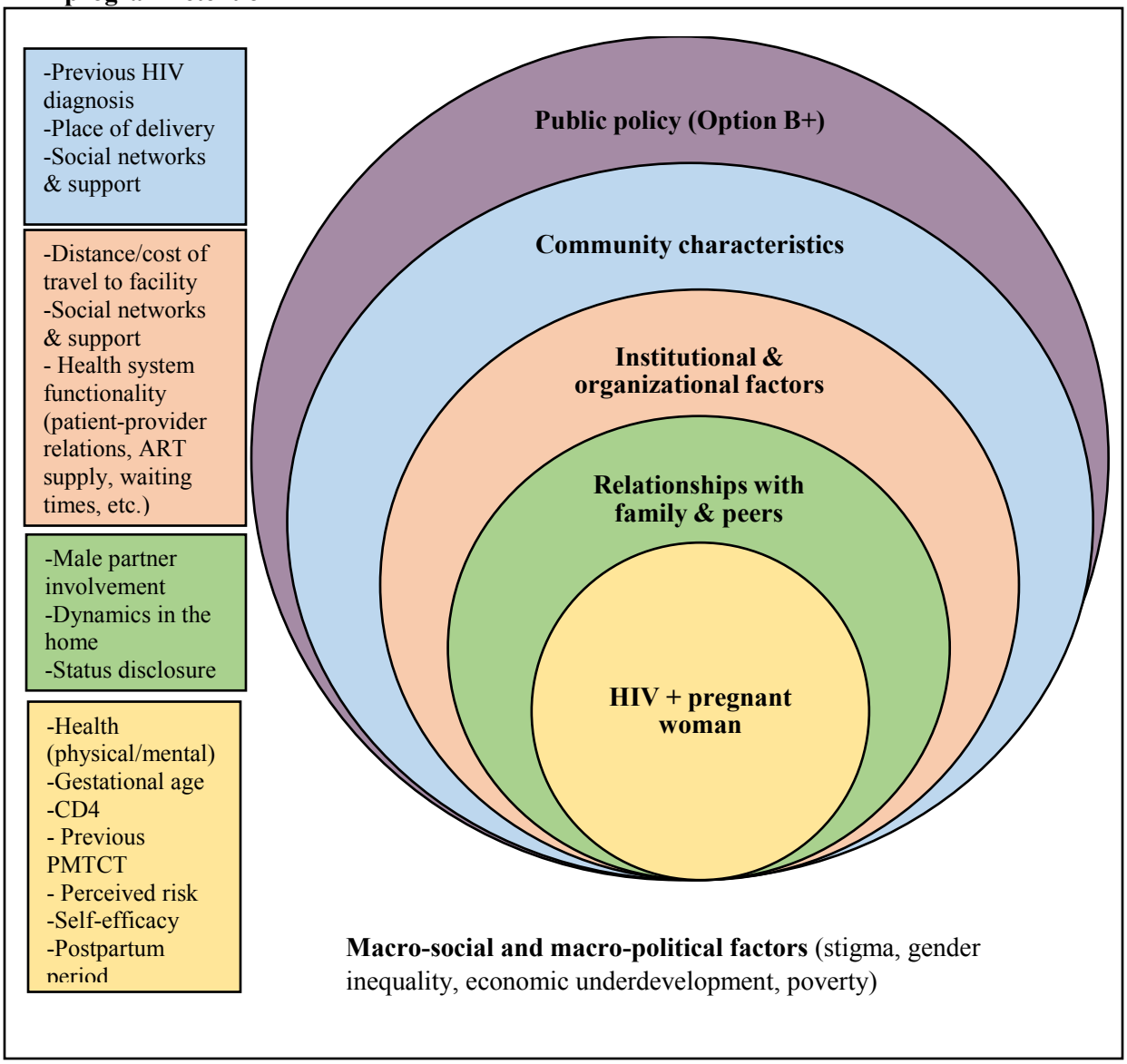
The McLeroy SEM addressed the importance of moving away from an individual behavior change model and toward interventions directed at changing structural and environmental factors that negatively affect health behaviors. However, this SEM did not account for the role that contextual factors such as culture, social class, racism, gender or economics may play in individual health behaviors.[128] These factors are especially important for explaining and intervening on HIV/AIDS-related behaviors such as adherence and program retention, especially since HIV is now more commonly recognized as a social disease driven largely by discrepancies in resources and power, such that disadvantaged individuals are less likely to adhere to HIV medication and stay in care. To examine structural and environmental interventions for reducing the risk of HIV in developing countries, Sweat and Denison developed an ecological theory of levels of causation of HIV incidence that comprised four levels of causation, including a superstructural level absent from the SEM made up of macrosocial and political arrangements, resources and power differences resulting in unequal advantages such as economic underdevelopment, poverty and sexism.[129] The three levels nested within the superstructural level were the structural level (laws, policies and standard operating procedures similar to the SEM level of public policy), the environmental level (individual living conditions, resources and opportunities as well as recognition of individual, structural and superstructural factors) and the individual level (the way the environment is experienced and acted upon by the individual).[106]

Conceptual framework for PMTCT adherence and program retention

The theoretical approach of Sweat and Denison and the SEM proposed by McLeroy et al. informed the conceptual framework developed for this dissertation. The factors affecting PMTCT

medication adherence and program retention described above have been grouped together by the level of social influence at which they act. These levels include: 1) the individual HIV-infected pregnant woman; 2) relationships with family and peers; 3) institutional and organizational factors; 4) community characteristics; 5) public policy and 6) macro-social and macro-political factors. The double sided arrows represent the potential for bi-directional influence at each level. For example, the Option B+ policy has the potential to affect the PMTCT adherence behaviors and program retention of the individual HIV-infected pregnant woman both directly and indirectly through the nested levels of social influence, but changes to the Option B+ policy may also occur as a result of factors associated with the individual HIV-infected pregnant woman and the additional nested levels of social influence. Similarly, macro-social and macro-political factors such as HIV-associated stigma, gender inequality, economic underdevelopment and poverty undoubtedly affect the implementation of Option B+ as well as other factors associated with PMTCT adherence and program retention at the different levels of social influence, but at the same time, altering these macro-level influences may be dependent on changes happening at the lower levels of social influence. The conceptual framework depicted in figure 5 below was used to inform the goal, specific aims and methods of this study.

Figure 5: Conceptual framework for determinants of PMTCT medication adherence and program retention



PURPOSE

Study goal

The overall goal of this project was to improve the current understanding of changes to medication adherence and program retention over time for HIV-infected pregnant women and mothers enrolled in the Option B+ program for PMTCT of HIV and how various factors may affect these outcomes in pregnancy and the postpartum period. A mixed methods approach was used to accomplish this study goal.

Specific aims

Specific aim 1:

To summarize the most current medication adherence and program retention findings in the antenatal and postnatal periods for HIV-infected pregnant women and mothers receiving Option B+ for PMTCT in different implementation settings through a systematic review of the current Option B+ adherence and program retention literature.

Specific aim 2:

To measure changes to Option B+ adherence and program retention from pregnancy to six months postpartum for a representative sample of HIV-infected pregnant women and mothers at Mulago National Referral Hospital who are newly initiating Option B+ for their current pregnancies and to assess the impact of the following factors on Option B+ adherence and program retention over time: 1) Previous HIV diagnosis; 2) Previous PMTCT program experience; 3) Status disclosure; 4) Baseline CD4 cell count; 5) Time since ART initiation during pregnancy; 6) Male partner counseling and testing for HIV and 7) Psychosocial support group meeting attendance.

Specific aim 3:

To qualitatively explore the experiences of HIV-infected pregnant women with adherence and the Option B+ program under the standard of care at Mulago National Referral Hospital and to understand how these experiences, as well as factors affecting these experiences, may change from pregnancy to the early postpartum period.

METHODS

Specific aim 1: Systematic review of the Option B+ adherence and program retention literature

The systematic review of Option B+ adherence and program retention literature included all peer-reviewed articles assessing Option B+ maternal medication adherence and program retention in countries that had adopted or were beginning to adopt this approach as the national strategy. Studies measuring the medication adherence and program retention of HIV-infected pregnant women and mothers seeking care and treatment during pregnancy and in the postpartum period in the countries implementing Option B+ as the national strategy for PMTCT were included in the systematic review.

The following databases were searched for this review: PubMed (last searched on December 29, 2016), Embase (last searched on December 30, 2016), Global Health (last searched on December 30, 2016) and Scopus (last searched on December 30, 2016). The databases were searched using key words and medical subject headings (MESH) for HIV, Option B+ countries, pregnancy, the postpartum period, and vertical transmission. To account for the start of Option B+ implementation, the search strategy was limited to studies published since January 1, 2010 and taking place in countries known to be piloting, rolling out or fully implementing the Option B+ guidelines. Titles and abstracts were imported into EndNote X7.7 and duplicates were identified and removed. Reference lists of included articles were also searched for additional relevant publications.

Titles and abstracts were independently screened by one researcher using criteria established prior to the study selection process and then full-text versions of potentially relevant articles were assessed for eligibility. Given the outcomes of interest for this review, all quantitative and mixed-methods study designs were eligible, but qualitative studies were excluded. Further inclusion criteria included: 1) Option B+ as the PMTCT approach, 2) pregnant or postpartum women living with HIV as the study population, 3) reporting of medication adherence or program retention and 4) presentation of primary data and the eligibility criteria were applied to each study in that order. To ensure quality of data through the peer review publication process, conference and presentation abstracts were excluded. Commentaries, editorials and reviews were also excluded from the study, but references were searched for potential sources of primary data.

Data extraction was performed independently and the paper authors, journal, year of publication, study period, country, year of national Option B+ implementation, study setting, study population, study design, sample size, ART regimen, adherence or program retention indicator(s) and study findings were obtained from each study. Results of statistical tests for measures of association were included when relevant to the study. Additional information provided in the study about the PMTCT program, such as recommended number of clinic visits before delivery or counseling and testing procedures, was also noted for context.

Study quality was independently assessed with guidance from the Effective Public Health Practice Project criteria (EPHPP). Studies were rated as strong, moderate or weak in terms of selection bias, study design, confounders, methods for data collection and appropriateness of data analysis.

Specific aim 2: Measuring changes in Option B+ adherence and clinic visit attendance over time

Changes in Option B+ ART adherence and clinic visit attendance over time were measured through the utilization of routine PMTCT program data collected and entered into an electronic database by Makerere University-Johns Hopkins University (MU-JHU) Research Collaboration staff at Mulago National Referral Hospital for the purposes of routine program evaluation. Longitudinal data from HIV-infected pregnant women attending Mulago Hospital and enrolling in the PMTCT program during pregnancy in 2014 were analyzed in this study. Mulago Hospital was chosen as the study site due to the high volume of HIV-infected pregnant women presenting for care and the richness of the existing PMTCT databases as well as the partnership that exists between Johns Hopkins University and Makerere University though the MU-JHU research collaboration.

Mulago National Referral Hospital is located in the northern part of Kampala City and is one of two national referral hospitals in the country. It is the largest hospital in Uganda and the teaching hospital for the Makerere University College of Health Sciences. The PMTCT program at Mulago National Referral Hospital began in April, 2000 with funding from EGPAF and included voluntary counseling and testing for pregnant women and sd-NVP at onset of labor with sd-NVP for the infant at birth. In 2005 the PMTCT guidelines were updated to include routine counseling and HIV testing and AZT or AZT/3TC from 28 weeks gestation and sd-NVP at the onset of labor for HIV-infected pregnant women with a CD4 count of less than or equal to 200 cells/mm.[3] The routine counseling and testing approach resulted in a large increase in the number of identified HIV-infected pregnant women attending Mulago for ANC and as a result, the follow-up clinic was created in February, 2006. The purpose of the follow-up clinic was to retain HIV-infected pregnant women and mothers in care for the first 18 months postpartum before they were referred to the Makerere University Joint AIDS Program Immune Suppression Syndrome (MJAP ISS) clinic or a different clinic of choice for ongoing HIV care and treatment. The follow-

up clinic dispensed ART, provided treatment for opportunistic infections and offered sexual and reproductive health services such as family planning and cervical cancer screening. In 2010, Mulago adopted the WHO-recommended Option A approach PMTCT. Option A included a prophylaxis regimen of AZT from 14 weeks gestation and NVP syrup for infants for the first six weeks of life. In 2012, Mulago transitioned from Option A to Option B+ to reflect the most current WHO guidelines for PMTCT.

Today, the Option B+ program includes provider initiated HIV counseling and testing in ANC and same-day ART initiation with a TFV/3TC/EFV triple combination regimen as the first-line therapy, irrespective of CD4 cell count. All HIV-infected pregnant women are also expected to receive Co-trimoxazole prophylaxis. The timing and frequency of ANC clinic visits varies by a number of factors including gestational age at presentation to ANC, psychosocial (PSS) evaluation and disease severity, but HIV-infected pregnant women enrolled in care are generally scheduled to return to clinic two weeks after ART initiation and then monthly until delivery. HIV-infected women delivering at Mulago are expected to initiate exclusive breastfeeding within an hour of delivery and HIV-exposed infants are expected to receive NVP syrup at birth. Follow-up of HIV-exposed infants and mothers takes place at the postnatal clinic and includes DNA polymerase chain reaction (PCR) testing of HIV-exposed infants, distribution of infant prophylaxis, immunization and growth monitoring. The first infant HIV test is expected to be done by six weeks postpartum and results are expected to be received one week later or at the next clinic visit. As previously stated, maternal health services and ART are provided at the follow-up clinic.

This longitudinal cohort study included HIV-infected pregnant women presenting for ANC at Mulago National Referral Hospital from January 1, 2014 to December 31, 2014. All HIV-infected pregnant adult women of reproductive age (18-49 years old) who presented to Mulago National Referral Hospital in 2014, had attended at least two ANC visits and were new

initiators of Option B+ for their current pregnancies were included in this study. HIV-infected pregnant women included in the study were either ART-naïve or had initiated a previous form of ART prophylaxis for past pregnancies under old PMTCT guidelines but were new initiators of Option B+. Women were excluded from the study if they were younger than 18 years old at the time of Option B+ initiation, had initiated a PMTCT regimen other than the one indicated by Option B+, were not new initiators of Option B+ for PMTCT or initiated Option B+ after the ANC period. Women were also excluded if the pregnancy did not result in a live birth. A longitudinal cohort study design was used to account for changes in Option B+ ART adherence and program retention over time from ANC through six months postpartum.

Data abstracted for this study took place from May 4, 2016 to August 1, 2016. Routinely collected indicators regularly entered into the Mulago PMTCT program electronic database were extracted for this study. In addition, data abstraction was performed from patient medical charts and the PMTCT clinic log books to obtain ART adherence and program retention information for the first ANC visit post-ART initiation and again at six weeks postpartum and six months postpartum. As described above, data was collected for all HIV-infected pregnant women who enrolled in the Option B+ PMTCT program beginning on January 1, 2014. A local research assistant was trained to assist the first author of this study with data abstraction and her work was validated by the first author of this study. Data from the PMTCT database and medical chart/log book abstraction were merged to create the longitudinal dataset necessary for this analysis to take place.

The primary outcomes for this study were maternal ART adherence and clinic visit attendance at the first ANC visit after enrollment into the PMTCT program and again at six weeks and six months postpartum. At Mulago, medication adherence is measured and recorded by PMTCT clinic counselors trained to perform ART pill counts. Patients are instructed to return to each clinic appointment with the ART pill box and counselors count the number of pills

remaining at the current clinic visit. The number of pills remaining are subtracted from the number of pills dispensed at the last clinic visit to determine the number of pills swallowed between visits. The number of pills wasted, as self-reported by the patient, are also subtracted from the number of pills last dispensed and ART adherence is then calculated by dividing the number of pills actually swallowed by the number of pills expected to have been swallowed based on the date ART was last dispensed and the number of pills left over at the last visit. Patients were categorized as adherent or non-adherent based on a 95% and an 80% pill count adherence cutoff. The 95% cutoff was utilized to remain consistent with the definitions of optimal and suboptimal adherence used by the PMTCT clinic at Mulago. The 80% cutoff was included to reflect the minimum level of adherence necessary for successful viral suppression described in the literature.[76] If adherence at any time point could not be ascertained, it was recorded as "unknown." An unknown adherence outcome was the result of either patients failing to return with the pill box or not being able to determine the number of pills last dispensed at the previous visit due to incomplete information in the medical charts or clinic log books. In addition to the medication adherence definition described above, a broader definition of non-adherence was also utilized in a separate analysis to capture patients who were either non-adherent to ART or had either failed to return with the pill box or did not return for the scheduled clinic visit.

The six-week and six-month postpartum visits were identified for each patient by estimating the scheduled clinic visit dates using the infant date of birth found in the PMTCT database for each patient. Due to variations in scheduling of clinic visit appointments, visits occurring between five and eight weeks postpartum and five and seven months postpartum were considered valid time points for data collection for the six-week and six-month postpartum visits, respectively. If visits occurred both before and after the estimated visit date but within the indicated window, the visit determined to be closest to the estimated visit date was used for the purposes of this study.

Information routinely entered into the PMTCT database and the clinic log books were used to obtain demographic and clinic characteristics and to measure the effects of the following factors on changes in ART adherence and clinic visit attendance: 1) Previous HIV diagnosis was determined using the PMTCT screening form and recorded as "Yes" if the patient had been diagnosed before the current pregnancy or "No" if the patient had been newly diagnosed with HIV during the current pregnancy; 2) Previous PMTCT experience was determined using the PMTCT enrollment form and recorded as "Yes" if the patient had initiated ART for PMTCT during a previous pregnancy or "No" if the patient had never initiated ART for PMTCT prior to the current pregnancy; 3) Status disclosure by the first visit post-ART initiation was obtained from the PMTCT psychosocial form and recorded as "Yes" if HIV status had been disclosed or "No" if the patient had not disclosed her status at that time. The relationship of the disclosed to the participant (e.g. husband, mother, friend, etc.) was also recorded when available; 4) Baseline CD4 count at program enrollment was collected from the PMTCT registration and lab forms and categorized as greater than 350 cells/mm^3 or less than or equal to 350 cells/mm^3 in accordance with the previous WHO CD4 cutoff for treatment vs. prophylaxis for HIV-infected pregnant and postpartum women; 5) Time since ART initiation during pregnancy was calculated using the date of ART initiation and the date of delivery and categorized as more than 30 days on ART before delivery or less than or equal to 30 days on ART before delivery; 6) Partner counseling and testing by the first ANC visit post-ART initiation was determined using the PMTCT screening form and recorded as "Yes" if the partner had been tested for and counseled about HIV or "No" if the partner had not been tested for or counseled about HIV at this time; 7) Psychosocial support group meeting attendance was determined using the clinic log books and recorded as "Yes" if the patient had attended at least one psychosocial support group meeting or "No" if the patient had not attended any psychosocial support group meetings during pregnancy or by six weeks and six months postpartum.

Statistical analyses were performed using Stata software version 12 (StataCorp, College Station, TX). Baseline characteristics and demographics were summarized categorically and with means and standard deviations (SDs) when relevant.

The proportions of adherent patients and patients attending scheduled clinic visits were calculated for each visit and McNemar's Chi Squared statistic for paired data was used to detect differences in the proportion of adherent patients and patients attending scheduled clinic visits between each time point of interest. Unadjusted and adjusted odds ratios with 95% confidence intervals (CIs) were obtained using univariate and multivariate logistic regression to estimate the associations between medication adherence or clinic visit attendance and each factor of interest. Multivariate logistic regression included all factors tested in the univariate analyses and then backward selection was used to select the final models predicting medication adherence and clinic visit attendance at each time point. P-values less than or equal to 0.05 were considered statistically significant in the univariate and multivariate analyses. A "p-to-remove" value of p=0.20 was used in the model selection process such that predictors were removed one at a time beginning with the predictor with the highest p-value until the p-values of all predictors left in the model were less than or equal to 0.20.

Specific aim 3: Understanding experiences with adherence and the Option B+ program

The experiences of HIV-infected pregnant women and mothers with ART adherence and the Option B+ program were also explored at Mulago National Referral Hospital. A subset of HIV-infected pregnant women who had been randomized to the control arm of a randomized controlled trial (RCT) entitled, "Using Enhanced Peer Group Strategies to Support Option B+ in Uganda." This RCT aims to measure the effectiveness of a community-based peer support group intervention at improving long-term ART adherence under Option B+. The RCT, commonly referred to as the "Friends for Life Circles" study, began enrollment in May, 2015 and participant

enrollment is ongoing. The study aims to randomize a combined total of 540 HIV-infected pregnant women at Mulago Hospital in Kampala and Mityana Hospital the Mityhana District, approximately 74 kilometers (48 miles) northwest of Kampala. A 1:1 randomization is taking place such that 270 participants will receive the community-based peer support group intervention and 270 participants will receive the MoH standard of care under the Option B+ Program.

To be eligible for inclusion into the RCT, women must be 1)18 years or older; 2) pregnant, as confirmed through a clinical assessment or pregnancy test; 3) HIV-positive, as confirmed through a HIV-positive sero-status at the time of screening; 4) accepting of Option B+ for PMTCT; 5) able and willing to provide written informed consent to participant in the randomized trial; 6) agreeing to attend the study clinic for scheduled appointments and 7) accepting of home visits as needed, to ensure follow up throughout the study period. When enrolling participants, distance from the study clinic and intentions to move out of the catchment area within the next two years is also being taken into account. To be included in the subset of control arm participants enrolled in this study, HIV-infected pregnant women were required to meet the study eligibility criteria described above. In addition, only HIV-infected pregnant women presenting for care in the last trimester of pregnancy at Mulago Hospital were included in this study.

Longitudinal in-depth interviews with HIV-infected pregnant women were conducted prospectively to gain a better understanding of the experiences of HIV-infected pregnant women and mothers with adherence and the Option B+ program over time. In this study, a subset of the first 16 participants in the last trimester of pregnancy who were enrolled in the "Friends for Life Circles" study and randomized to receive standard of care at Mulago Hospital were purposively selected to be interviewed once during pregnancy at the one month post-ART initiation study visit and again at six weeks postpartum. The "Friends for Life Circles" RCT began enrollment on May

16, 2016 and the final in-depth interview participant was enrolled into the study on January 27, 2017.

All interviews were conducted by a local co-investigator or one of two local study counselors with the aid of semi-structured field guides. The co-investigator conducting interviews had a master's degree in nursing, extensive experience in HIV counseling and some prior experience with qualitative research. This was the first qualitative research experience for the two study counselors conducting the interviews. One counselor had a bachelor's degree in nursing and the other had a bachelor's degree in social work. Both counselors had HIV counseling experience prior to study initiation. The interview team received multiple trainings on proper interview techniques, use of the semi-structured field guides and the goals of each interview prior to study initiation.

The semi-structured field guides were created prior to study initiation and included suggested interview questions and probes relevant to the activities and experiences surrounding each study visit. The ANC interview aimed to focus on the experiences of the HIV-infected pregnant women with HIV testing, treatment initiation, status disclosure, male partner involvement, stigma and social networks and how these experiences may have influenced the ART adherence and clinic attendance. The six-week postpartum interview aimed to focus on the experiences of the HIV-infected mothers with infant HIV testing, infant HIV prophylaxis, maternal ART adherence, clinic visit attendance and changes in status disclosure, male partner involvement, stigma and/or social networks. Interviews lasted between 30 minutes to one hour and took place upon completion of all other "Friends for Life Circles" study activities. The in-depth interview team consisting of the study coordinator, the co-investigator and two study counselors met weekly with the first author prior to and during the initial data collection period and then monthly as data collection progressed, to practice interviewing techniques, discuss arising themes and refine the interview guides for a more iterative research process.

All interviews were conducted in Luganda and digitally recorded after obtaining verbal approval from each participant. Interviews were then directly transcribed and translated into English for analysis by a trained qualitative analysis consulting team with experience in previous National Institutes of Health (NIH) or PEPFAR-supported qualitative research studies. No identifying information was linked to any audio files or transcripts. To protect privacy and maintain confidentiality, interviews were held in a private location within the health facility. Participants were offered light refreshments and reimbursed for transportation to and from the clinic.

Transcripts were reviewed and read over multiple times as they were received, and analytic memos were written to reflect on developing patterns, categories, themes and concepts in the data. The analytic memos were then coded and categorized according to their content. The coding and categorization process was based both on emergent themes from the data and a priori themes based on the interview guides. All transcripts were coded using the scheme developed from the analytic memos, with additional codes added as they appeared, if considered relevant to addressing the study goal. Transcripts from interviews at pregnancy and six-weeks postpartum were coded and analyzed separately, and another series of analytic memos and codes were developed to reflect the changes in experiences of participants over time from pregnancy to six-weeks postpartum. Coding was performed manually and tracked through the use of multiple Excel spreadsheets.

Ethical approval to conduct this research was obtained from the institutional review boards of the Johns Hopkins University School of Medicine, the University of California San Francisco, the Joint Clinical Research Centre and the Uganda National Council for Science and Technology.

ROLE OF THE AUTHOR

The author of this dissertation is responsible for the conception and design of this research project and served as the lead investigator for each of the specific aims. The author traveled to Kampala, Uganda from November 2015 to December 2016 and April 2016 to August 2016 to conduct and oversee fieldwork for this dissertation. For the systematic review, the author independently executed the database search strategy as well as the screening of abstracts and articles for inclusion into the final review. For the program evaluation of regularly collected PMTCT programmatic data, the author created the data collection tools, consulted with PMTCT clinic staff and trained and supervised two research assistants tasked with assisting in the abstraction of medical chart adherence data. The author also abstracted medical chart data alongside the research assistants and reviewed their work to ensure quality control. For the longitudinal in-depth interviews, the author created the semi-structured field guides and trained the entire randomized controlled study staff on the qualitative study goals, objectives and methods. The author collaborated with the study coordinator and investigators to ensure smooth integration of the qualitative study into the randomized controlled trial and trained a local team of three study counselors to conduct the in-depth interviews with the use of the semi-structured field guides. The trainings included information on qualitative research methods and ethics as well as mock interviews to practice probing and using the guides. Throughout the data collection period, the author read the translated and transcribed interview transcripts as they were received to provide feedback and conduct routine quality control. The author also led weekly debriefing meetings while in Kampala and has continued to initiate monthly Skype calls since returning to Baltimore to ensure regular communication with the study team. The author was responsible for all data analyses conducted as part of this dissertation.

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PART ONE:

Maternal ART adherence and program retention in pregnancy and the postpartum period for HIV-infected women receiving Option B+ for prevention of mother-to-child transmission of HIV: A systematic review

ABSTRACT

Mother-to-child transmission of HIV is responsible for the majority of pediatric HIV infections. Implementation strategies to prevent vertical HIV transmission have continued to evolve over time. Option B+ is the current World Health Organization recommendation for preventing mother-to-child transmission of HIV and consists of a single, universal strategy for both treatment of HIV-infected pregnant women and for infant prophylaxis. Option B+ includes the provision of triple ART for all HIV-infected pregnant women at the antenatal clinic regardless of clinical stage or CD4 cell count to be continued for life. Inconsistent adherence is a serious barrier for the elimination of HIV/AIDS and specifically for preventing vertical HIV transmission and maternal and child health. Previous research, including systematic reviews and meta-analyses, have shown that medication adherence and program retention of HIV-infected pregnant women and mothers decreases over time, but this research was mostly published before countries adopted the current WHO recommendation for PMTCT.

The goal of this systematic review was to summarize the maternal medication adherence and program retention literature since implementation of the Option B+ program began in Malawi in 2010. The PubMed, Embase, Global Health and Scopus databases were searched for relevant data and study quality was rated based on bias, study design, confounders, methods for data collection and appropriateness of the data analysis.

Out of the 4,712 records screened, 19 studies were included in this review. All of the studies were from sub-Saharan Africa. The most common measures of program retention and medication adherence were loss to follow-up, self-report and pill count adherence. Program retention and adherence varied greatly across studies. Overall, more evidence is necessary to improve the current understanding of Option B+ maternal medication adherence and program retention over time and the factors that may affect these outcomes in pregnancy and the postpartum period.

INTRODUCTION

Mother-to-child transmission (MTCT) is responsible for the majority of pediatric HIV-1 infections.[1] MTCT can happen in-utero, at delivery or during the breastfeeding period, with risks of transmission ranging from 5-10%, 10-20% and 5-20%, respectively, resulting in an overall vertical transmission rate of between 15-45% without intervention.[2] Successful prevention of mother-to-child transmission of HIV (PMTCT) can reduce rates of transmission to less than 5%,[3] but implementation of PMTCT strategies continues to be difficult, especially in resource-limited settings such as sub-Saharan Africa. Experts in the field of HIV and PMTCT often refer to the "PMTCT cascade" as a way of addressing key areas along the HIV care and treatment continuum where challenges to PMTCT are most likely to occur. Attrition along the cascade is most commonly seen in resource-limited settings such that only a small proportion of all HIV-infected mothers present for care and successfully receive and adhere to the antiretroviral (ARV) prophylaxis regimens necessary for PMTCT[4]. While developed countries are close to achieving elimination of vertical HIV transmission, it has been estimated that only 15-30% of eligible women in resource-limited settings successfully completed the PMTCT cascade.[4] In an effort to improve PMTCT outcomes and consequently improve maternal and child health, experts from various research communities in collaboration with the World Health Organization (WHO) and community and government partners from countries with high HIV burden have continued to evaluate ways to improve the uptake and adherence to PMTCT care and treatment services.

Inconsistent adherence is a serious barrier for the elimination of HIV/AIDS and specifically for PMTCT and maternal and child health since it is associated with an increased risk for opportunistic infections,[5] HIV disease progression[6] and viral resistance to ART.[7] Previous research, including a meta-analysis of adherence to antiretroviral therapy during pregnancy and after pregnancy in low-, middle- and high-income countries, has shown that medication adherence tends to decrease between the antenatal and postnatal periods.[8] Similarly, a review

looking at linkage and retention of HIV-positive pregnant women in care and treatment services found high attrition between HIV testing and accessing long-term services.[9] However, these reviews were based mostly on research evaluating programs implementing past WHO recommendations, before Option B+ became the recommended PMTCT strategy for resource-limited countries.

Option B+ is the current WHO recommendation for PMTCT. This approach has been described as a single, universal strategy for both the treatment of HIV-infected pregnant women and for PMTCT prophylaxis.[10] Option B+ includes the provision of triple ART for HIV-infected pregnant women at the antenatal clinic regardless of clinical stage or CD4 cell count, to be continued for life as soon as HIV status is ascertained. Option B+ implementation began in Malawi in 2010 as a response to the high incidence of infant HIV infection and limited capacity of laboratories to perform CD4 cell counts necessary to implement the previous WHO recommendations.[11] As implementation of Option B+ programs continues in different settings, more information is being uncovered about maternal ART adherence and program retention. The scope of this systematic review focuses specifically on maternal ART adherence and retention in care after ART initiation in order to gain a more current and comprehensive understanding of the feasibility of consistent long-term maternal ART adherence and program retention under the Option B+ approach for PMTCT in different HIV care and treatment settings.

METHODS

Search strategy

A review of the Option B+ adherence and program retention literature was conducted by searching for data published in the following databases: PubMed (last searched on December 29, 2016), Embase (last searched on December 30, 2016), Global Health (last searched on December 30, 2016) and Scopus (last searched on December 30, 2016). The databases were searched using

key words and medical subject headings (MESH) for HIV, Option B+ countries, pregnancy, the postpartum period, and vertical transmission. As a reference, the detailed electronic search strategy for the PubMed search can be found in Appendix B. To account for the start of Option B+ implementation, the search strategy was limited to studies published since January 1, 2010 and taking place in countries known to be piloting, rolling out or fully implementing the Option B+ guidelines. Titles and abstracts were imported into EndNote X7.7 and duplicates were identified and removed. Reference lists of included articles were also searched for additional relevant publications.

Study selection

Titles and abstracts were independently screened by one researcher using criteria established prior to the study selection process and then full-text versions of potentially relevant articles were assessed for eligibility. Given the outcomes of interest for this review, all quantitative and mixed-methods study designs were eligible, but qualitative studies were excluded. Further inclusion criteria included: 1) Option B+ as the PMTCT approach, 2) pregnant or postpartum women living with HIV as the study population, 3) reporting of medication adherence or program retention and 4) presentation of primary data and the eligibility criteria were applied to each study in that order. To ensure that published data had gone through a comprehensive peer review process, conference and presentation abstracts were excluded. Commentaries, editorials and reviews were also excluded from the study, but references were searched for potential sources of primary data.

Data extraction and analysis

Data extraction was performed independently and the paper authors, journal, year of publication, study period, country, year of national Option B+ implementation, study setting,

study population, study design, sample size, ART regimen, adherence or program retention indicator(s) and study findings were obtained from each study. Results of statistical tests for measures of association were included when relevant to the study. Additional information provided in the study about the PMTCT program, such as recommended number of clinic visits before delivery or counseling and testing procedures, was also noted for context.

Assessment of bias and study quality

Study quality was independently assessed with guidance from the Effective Public Health Practice Project criteria.[12] Studies were rated as strong, moderate or weak in terms of selection bias, study design, confounders and methods for data collection.

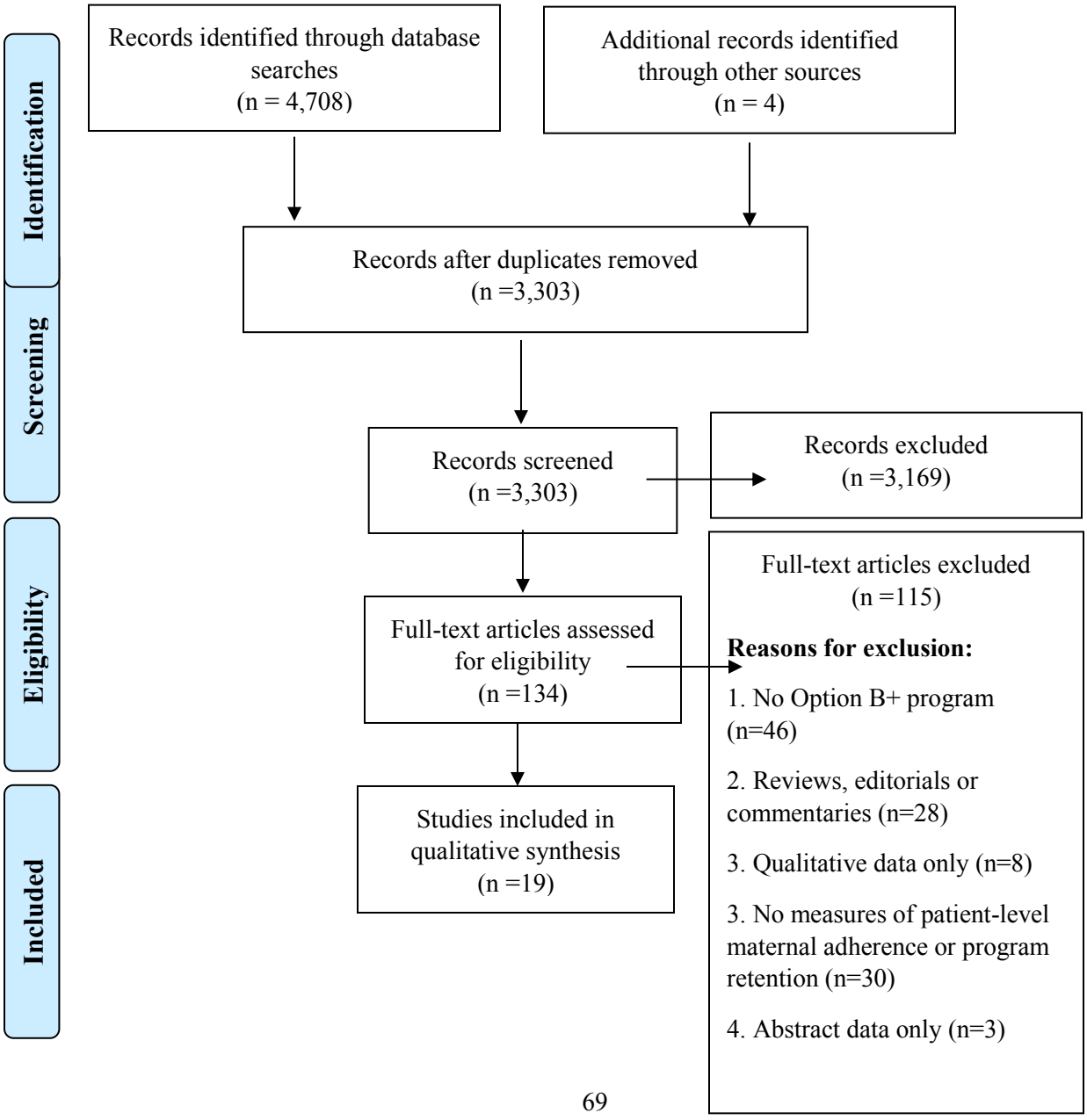
FINDINGS

Characteristics of included studies

The database searches yielded 4,708 records with an additional 4 records found through searching the reference lists of included articles and relevant reviews. After removing duplicates, screening abstracts and full-text reviews, 19 studies were identified that met the inclusion criteria for this review (Figure 1). Overall, the studies were conducted in seven different countries. The majority of studies were conducted in Malawi (n=7), three studies were conducted in Ethiopia, two studies each were conducted in Mozambique, South Africa, Uganda and Zimbabwe and one study was conducted in Rwanda. Six studies were conducted in urban settings, five in rural settings and five in both urban and rural settings. For three studies the study setting was not explicitly stated and therefore unclear. The majority of studies were conducted at a variety of health facilities (n=9). Four studies each were conducted exclusively in either hospitals or health centers and two studies did not specify the type of health facility. The studies included in this review were either prospective cohort studies (n=8), retrospective cohort studies (n=7) or cross-

sectional studies (n=3), and one study was described as a pre-post quasi-experimental study. Nine of the studies reported on retention in care, four studies reported on medication adherence and six studies provided information for both outcomes. For all studies, the Option B+ maternal ART regimen was a once-daily combination regimen comprised of tenofovir (TFV), lamivudine (3TC) and efavirenz (EFV).

Figure 1: Prisma flow diagram summarizing literature search



Program retention

The most frequently used indicator of Option B+ program retention was loss to follow-up (LTFU) from the time of ART initiation. However, the period of time used to define LTFU ranged from three weeks to six months. Some studies also differentiated between study participants being LTFU and having no follow up since the first ART initiation visit. Seven of the studies looked at program retention for pregnant women and six looked at program retention for pregnant and postpartum women. Two studies looked only at program retention in the postpartum period. The basic characteristics of studies evaluating retention in care are summarized in Table 1 of Appendix C.

Table 2 of Appendix C summarizes the program retention findings of each study. The median LTFU rate among all studies reporting this outcome was 17% (range: 11.2%, 48.5%). Studies that were able to compare program retention under Option B+ to program retention under the previous Option A recommendation consistently reported an increased risk of LTFU associated with the Option B+ program.[29,31] For example, one study comparing Option B+ LTFU to Option A LTFU in a historical cohort in Mozambique found that women in the Option B+ program were nearly twice as likely to be lost to follow-up at one year since ART initiation and over three times more likely to stop care after the ART initiation visit.[29] Similarly, all studies looking at day of ART initiation found that initiating ART on the same day as HIV diagnosis was associated with an increased risk of LTFU when compared to initiating treatment at least one day after HIV diagnosis.[26,34] Risk of LTFU was also found to be significantly greater for younger women as compared to older women across most studies.[27,28, 34, 38, 39] While some studies found pregnant women significantly more likely to be LTFU than postpartum women,[33, 39]others found this association to be nonsignificant.[28] Type of health facility and CD4 cell count and/or WHO clinical stage at ART initiation were sometimes found to be significantly associated with LTFU, however the direction of association was inconsistent across studies.

Maternal ART adherence

Of the 10 studies reporting maternal ART adherence under the Option B+ program, six utilized self-report, two utilized pill counts, one utilized prescription pick-up and one utilized treatment discontinuation as the adherence indicator. In studies using self-report, participants were asked to assess the number of missed doses in either the last three days or the last month. The number of missed doses were reported and zero missed doses was commonly used as the definition of good adherence. In studies using pill counts as the measure of adherence, 95% adherence was the cutoff for adequate or good adherence. The study population consisted of pregnant women, pregnant and postpartum women or only postpartum women for seven, two and one study, respectively. The basic characteristics of studies evaluating Option B+ medication adherence are summarized in Table 3 of Appendix C.

Table 4 of Appendix C reports the medication adherence findings of each study. The time at which adherence was evaluated varied, with some studies measuring adherence at three, six or 12 months after ART initiation while others assessing it specifically at the time of the study visit. Only one study measured adherence during pregnancy and in the postpartum period, but reported only an overall measure of adherence over time.[42] The median percent of adherent participants across studies was 87.9% (range: 51.3%, 97.8%). The one study comparing ART adherence in the post-Option B+ and the pre- Option B+ eras in one year since ART initiation found adherence to be slightly higher in the pre-Option B+ era, but the difference was not statistically significant.[30] Only one studied assessed differences in adherence between pregnant and postpartum women, but no significant difference was found.[33] One study in Ethiopia looking at ART adherence during pregnancy found that receiving counseling on side effects and HIV status disclosure were significantly associated with improved medication adherence,[40] while a different study in Ethiopia looking at adherence in pregnancy and the postpartum period found that women were less likely to be adherent if they received care at a hospital vs. a health facility, resided in a rural

residence vs. urban residence or faced challenges with initiating ART on the same day as HIV testing.[43] One study in South Africa looking specifically at the effects of ART side effects on adherence found that frequency and severity of side effects were both associated with an increased risk of missed doses.[42]

Quality assessment

The results of the Effective Public Health Practice Project (EPHPP) quality assessment are summarized in Appendix D. In this review, the "intervention" being evaluated was the implementation of the Option B+ program. Since the majority of the studies included in this review were evaluations of existing Option B+ programs using programmatic data, there were no randomized controlled trials and risk of bias was largely due to lack of blinding and/or study design. Similarly, it was difficult to assess intervention integrity since the consistency with which the Option B+ program was being implemented was not explicitly reported in most studies.

DISCUSSION

This study aimed to systematically review measures of program retention and medication adherence for HIV-infected pregnant women and mothers receiving Option B+ for PMTCT. In a WHO meeting to address retention in HIV programs, program retention was defined as, "continuous engagement from diagnosis in a package of prevention, treatment, support and care services."[13] The same meeting also identified important challenges and inconsistencies with regards to defining interruptions in program retention along the HIV care and treatment continuum as well as distinguishing between "loss to follow-up," defined as patients with unknown outcomes and reflecting gaps in knowledge and information systems versus "disengagement from care," which implies known reasons for ceasing to access care and reflects the need for a service delivery response.[13] Nevertheless, this review found that LTFU was the

most commonly used indicator of Option B+ program retention. The length of time since ART initiation at which LTFU was assessed varied between studies and rates of LTFU also varied across studies and ranged from 11.2% to 48.5%, indicating that differences in specific program settings as well as the length of time for which LTFU is evaluated may have significant effects on the program retention outcome. In the studies that were able to compare program retention between the Option B+ and the Option A approaches, LTFU was significantly higher under with the Option B+ program. With Option A, only women with CD4 cell counts of less than or equal to 350 cells/mm^3 were started on triple ART, while women with higher CD4 counts received short-course AZT prophylaxis through seven days postpartum.[10] It is therefore possible that the difference observed in program retention between the two approaches could be due to the fact that women with lower CD4 cell counts who are in need of HIV treatment for their own health are more likely than women with higher CD4 cell counts who feel otherwise healthy to be retained in care. In addition, initiating ART on the same day as HIV testing was found to be significantly associated with an increased risk of LTFU across studies. This finding was consistent with qualitative research findings that reported same-day initiation of treatment as a health facility challenge to the provision of Option B+.[14] Both of these findings suggest that challenges with transitioning to Option B+ from Option A may have existed during study implementation and underscore the importance of providing adequate support and counseling on the day of HIV testing and treatment initiation to ensure program retention. Alternatively, re-considering the test-and-treat approach as part of the Option B+ recommendation may be appropriate and evaluating an intervention focused on delaying treatment initiation could be useful. It may also be the case that as Option B+ becomes more familiar to clinic staff and patients, the barriers associated with the test-and-treat approach may subside. For instance, one study included in this review found that program retention improved in later years of program implementation.[39] It is also important to note that clinic visit attendance was not a primary

outcome in any of the studies included in this review. While it is important to measure rates of LTFU it is equally important to assess whether or not HIV-infected pregnant women and mothers are adhering to their scheduled visits since it has been shown that HIV-infected patients who missed clinic visits in the first six months of treatment but were retained in care were at an increased risk of death and LTFU and may have poorer immunological and virologic outcomes.[15] Furthermore, additional research is needed to specifically track HIV-infected pregnant women and mothers who have been reported as LTFU by facilities to understand firstly if these women have been truly lost, and secondly to understand the reasons for LTFU or changes in location of care. For example, one study in western Kenya looking at outcomes of HIV patients defined as LTFU who were enrolled in the Academic Model Providing Access to Healthcare (AMPATH) program found that 12.8% of those originally classified as lost were not truly LTFU and that of these, 14% were receiving care at a different clinic from the one where treatment was initiated and 51.5% had transferred to a different program.[16] Understanding what happens to HIV-infected pregnant women and mothers defined as LTFU under Option B+ is crucial for not only improving PMTCT care and treatment services, but for improving the methods used to trace and follow women who choose to continue care somewhere different from where care was initiated.

Patient self-report and pill count adherence were the indicators most commonly utilized by studies included in this review to measure maternal medication adherence and the proportion of adherent participants in each study varied greatly from 51.3% to 97.8%, signifying the potential effects of different implementation settings as well as the limitations associated with these measures of medication adherence. While pill counting is a low-cost approach, it requires additional time from already overburdened health workers as well as effective training, monitoring and evaluation of the pill count calculation and recording process.[17] Patient self-report is also a simple and inexpensive method for measuring adherence but may be affected by social desirability bias, recall bias or confusion surrounding the way self-report questions are interpreted

by patients.[18] Viral load testing is considered the most objective indicator of medication adherence, but is still considered too expensive to implement regularly for the purposes of adherence monitoring in most resource-limited settings.[19] As a result, more work needs to be done to evaluate adherence screening tools that are cheap and easy to implement across various settings but have high sensitivity and good reliability. In one example, a recent study evaluating a self-report adherence measure using a simple three-item scale to screen for elevated viral load among pregnant and postpartum women on ART in South Africa concluded that having an increased viral load was consistently associated with lower median adherence scores.[20] The study investigators concluded that using this tool may be a good first-stage screening procedure for adherence but that the routine use of this specific adherence scale in different settings must be further evaluated and that more attention should be given to maternal ART adherence monitoring in low resource settings.[20]

Among the studies included in this review, good adherence was commonly defined as either missing zero doses by self-report or achieving 95% adherence by pill count. These adherence definitions are consistent with earlier ART effectiveness research that found 95% pill consumption was necessary for successful long-term virologic suppression.[21] However, more recent studies evaluating nonnucleoside reverse transcriptase inhibitors (NNRTIs) such as EFV have shown that successful virus suppression may be achieved at levels of adherence between 70% and 80%[22] due to the higher potency and longer half-lives of these ART regimens.[23] It could be useful to conduct additional maternal ART adherence studies to evaluate if viral load suppression can be obtained or if rates of vertical HIV transmission and maternal and child health outcomes are negatively affected at these lower rates of medication adherence under the Option B+ approach.

Maternal ART adherence was not significantly affected by the switch to Option B+ in the one study comparing adherence in the pre- and post- Option B+ era, but selection bias may have

affected this outcome since the review showed LTFU was greater in the post-Option B+ era but adherence measures were not available for study participants who had been LTFU. Only one study looked at the difference in Option B+ medication adherence between pregnant and postpartum women and the association was not significant. The PMTCT adherence literature prior to Option B+ implementation consistently found adherence to be greater in pregnancy as compared to the postpartum period,[8] so more studies aimed at assessing differences in adherence between the antenatal and postnatal periods under the current WHO recommendation for PMTCT are needed. One study included in this review found that frequency, type and severity of side effects were associated with maternal medication adherence while a different study found that being counseled on potential side effects was associated with a significantly increased odds of adherence in pregnancy. These findings are consistent with qualitative research conducted in Malawi that reported side effects to be one of the most commonly cited reasons for stopping ART among women enrolled in the Option B+ program in Lilongwe.[24] As a result, interventions targeting health workers and PMTCT counselors that are aimed specifically at effective techniques for counseling about potential ART side effects may prove useful for improving medication adherence among HIV-infected pregnant women and mothers across a variety of PMTCT care and treatment settings. Similarly, strategies to reduce the severity and frequency of side effects could also improve maternal ART adherence.

The narrow scope of this review may be considered one limitation of the study. This review only assessed ART adherence and program retention after ART had been initiated and did not look more broadly at gaps along the PMTCT cascade. As some of the studies included in this review suggest, the same-day test-and-treat approach to Option B+ implementation may negatively affect ART adherence and program retention and it would therefore be useful to study gaps between HIV testing and ART initiation in more detail. Similarly, this review does not assess infant prophylaxis adherence or program retention, which are key outcomes necessary for a

comprehensive understanding of the Option B+ program effect on PMTCT. Another limitation of the study is that this database search did not include viral load as a key search term for assessing adherence. Though viral suppression is considered the most objective indicator of ART adherence, it was not being regularly and routinely performed in many of the low-income settings implementing Option B+ at the time of concept search formulation for this review. There is also a distinction to be made between viral suppression and the act of medication adherence, which was the outcome of interest for this study. An additional limitation of this review is that the strength of evidence provided by each study is restricted by study design. There were no randomized controlled trials evaluating adherence or program retention at the time of the database search and only observational studies were included in the review. Although randomized controlled trials are considered the strongest study design with respect to limiting bias and determining a true association, it was most likely difficult to assign Option B+ as an intervention in a randomized controlled trial after it had already become the WHO recommendation for PMTCT. In the future, randomized controlled trials evaluating interventions aimed at improving Option B+ program retention and adherence may be utilized to acquire more information about these outcomes under various standards of care. A final limitation of this study is that differences in the stages of Option B+ program rollout and implementation as well as specific program implementation strategies across different settings are not reflected in this review. Some of the studies included do evaluate the associations between year of program implementation or health care delivery model on adherence and program retention, but this information was not systematically captured across studies.

This is the first study, to the knowledge of the author, to conduct a systematic review of maternal medication adherence and program retention for PMTCT in the context of Option B+. This review found a wide range of program retention and adherence outcomes across studies and did not identify any studies measuring changes in medication adherence and program retention

over time for the same cohort of women. Furthermore, the effects of different factors on program retention and medication adherence varied across studies and the limited number of studies evaluating these effects made it difficult to confidently draw conclusions about these associations. As a result, these findings support the need for long-term, longitudinal monitoring and evaluation of Option B+ program retention and medication adherence in different health care delivery settings as well as additional studies assessing the effects of various factors on these important outcomes.

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PART TWO:

Changes in adherence and clinic visit attendance for HIV-infected pregnant women and mothers receiving Option B+ for prevention of mother-to-child transmission of HIV: An evaluation of routinely collected program data

ABSTRACT

Option B+ is the current WHO-recommended approach for preventing vertical HIV transmission and includes the provision of combination antiretroviral therapy to all pregnant and postpartum HIV-infected women, regardless of CD4 cell count or clinical stage, to be continued for life form the time of treatment initiation. Program retention and long-term medication adherence continue to be of concern under this approach and little is currently known about changes to adherence or clinic visit attendance over time for HIV-infected pregnant women and mothers. This study aims to improve the understanding of changes to Option B+ adherence and clinic visit attendance over time from pregnancy through six months postpartum.

A program evaluation of adherence and clinic visit attendance from pregnancy to six months postpartum was performed in a cohort of first-time initiators of Option B+ at Mulago National Referral Hospital in 2014. Data from the PMTCT program database as well as medical charts and clinic log books were used to measure pill count adherence and clinic visit attendance as well as a variety of factors potentially associated with these outcomes. Univariate and multivariate logistic regression was used to estimate the associations between the outcomes and each factor of interest. Backward model selection was used to select the final models predicting medication adherence and clinic visit attendance at each time point.

480 HIV-infected women were included in the study. Of these, 52.1% and 44.8% were adherent during pregnancy and at six months postpartum, respectively, using a 95% adherence cutoff and 64.4% and 56.9% were adherent during pregnancy and at six months postpartum, respectively, using an 80% adherence cutoff. 71.9% and 73.8% attended clinic at six weeks and six months postpartum, respectively. A number of factors were found to predict adherence in pregnancy and at six months postpartum, but disclosure was the only factor associated with sustained adherence at both time points. Previous PMTCT experience, previous HIV diagnosis, time since ART initiation during pregnancy and male partner counseling and testing in antenatal

care were all predictors of sustained clinic visit attendance at six weeks and six months postpartum.

This study underscores the importance of continued monitoring and evaluation of adherence and clinic visit attendance from pregnancy throughout the postpartum period and the need for interventions aimed at improving adherence and clinic visit attendance under the Option B+ approach.

INTRODUCTION

The most recently issued World Health Organization (WHO) recommendation for preventing mother-to-child transmission of HIV (PMTCT) is called Option B+ and includes the provision of combination antiretroviral therapy (ART) to all pregnant and postpartum HIV-infected women, regardless of CD4 cell count or WHO clinical stage, to be continued for life from the time of treatment initiation.[1] It is believed that in addition to improving PMTCT in pregnancy and the breastfeeding period, successful implementation of the Option B+ approach may reduce the risk of sexual transmission and ensure improved maternal health outcomes due to uninterrupted HIV treatment.[2] However, improved PMTCT and maternal and child health outcomes can only be achieved with consistently high medication adherence since a linear dose response relationship exists between adherence and improved virologic outcomes.[3] PMTCT program retention also needs to be considered in the context of Option B+ since retention in care has been shown to directly affect adherence outcomes and viral suppression.[4]

Since its initial implementation in Malawi in 2011, the number of HIV-infected women initiating treatment during pregnancy has consistently and significantly improved in settings that have adopted the Option B+ approach.[5] Nevertheless, inconsistent retention in care and long-term medication adherence continue to be of concern. For example, only two thirds of women initiating ART during pregnancy in Malawi were retained in care after three years[6] and an evaluation of viral load (an outcome shown to be highly correlated with medication adherence[7]) in the first 24 months postpartum among HIV-infected women who initiated ART for life as part of the Mitra plus Study in Tanzania found that the proportion of women with viral loads greater than or equal to 400 copies/mL decreased significantly from 97% at enrollment to 16% at three months postpartum, but increased to 86% at 24 months postpartum.[8]

Uganda adopted Option B+ for PMTCT in 2012.[9] In 2016, Ministry of Health (MoH) facilities reported that over 95% of pregnant women had been tested for HIV and that the large

majority of the pregnant women testing positive were initiated on ART.[10] However, a recent study in Western Uganda found that only 51% of HIV-infected women who initiated Option B+ exhibited greater than or equal to 95% adherence during pregnancy and over 20% exhibited poor adherence, defined as a pill count adherence of less than 80%.[11] In addition, little is currently known about Option B+ adherence or program retention in the postpartum period in Uganda or other settings implementing Option B+ and a recent paper aimed at identifying gaps in the research literature with respect to uptake and barriers to postpartum HIV care found that few studies have focused on continued engagement of HIV-infected mothers beyond six weeks postpartum.[12] This study aims to improve the current understanding of changes to Option B+ medication adherence and program retention over time from pregnancy through six months postpartum for a cohort of HIV-infected women at Mulago National Referral Hospital who were first-time initiators of Option B+ for PMTCT.

METHODS

Mulago National Referral Hospital and the PMTCT program

Mulago National Referral Hospital is located in the northern part of Kampala City and is one of two national referral hospitals in the country. It is the largest hospital in Uganda and the teaching hospital for the Makerere University College of Health Sciences. The PMTCT program at Mulago National Referral Hospital began in April, 2000 with funding from the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) and included voluntary counseling and testing for pregnant women and single-dose Nevirapine (sd-NVP) at onset of labor with sd-NVP for the infant at birth. In 2005 the PMTCT guidelines were updated to include routine counseling and HIV testing and Zidovudine (AZT) or Zidovudine/Lamivudine (AZT/3TC) from 28 weeks gestation and sd-NVP at the onset of labor for HIV-infected pregnant women with a CD4 count of less than or equal to 200 cells/mm.[3] The routine counseling and testing approach resulted in a

large increase in the number of identified HIV-infected pregnant women attending Mulago for antenatal care (ANC) and as a result, the follow-up clinic was created in February, 2006. The purpose of the follow-up clinic was to retain HIV-infected pregnant women and mothers in care for the first 18 months postpartum before they were referred to the Makerere University Joint AIDS Program Immune Suppression Syndrome (MJAP ISS) clinic or a different clinic of choice for ongoing HIV care and treatment. The follow-up clinic dispensed ART, provided treatment for opportunistic infections and offered sexual and reproductive health services such as family planning and cervical cancer screening. In 2010, Mulago adopted the WHO-recommended Option A approach PMTCT and then transitioned to Option B+ to reflect the most current WHO guidelines for PMTCT.

Today, the Option B+ program includes provider initiated HIV counseling and testing in ANC and same-day ART initiation with the Tenofovir/Lamivudine/Efavirenz (TFV/3TC/EFV) triple combination regimen as the first-line therapy, irrespective of CD4 cell count. All HIV-infected pregnant women are also expected to receive Co-trimoxazole prophylaxis. Though the timing and frequency of ANC clinic visits vary by a number of factors including gestational age at presentation to ANC, psychosocial (PSS) evaluation and disease severity, HIV-infected pregnant women enrolled in care are generally scheduled to return to clinic two weeks after ART initiation and then monthly until delivery. HIV-infected women delivering at Mulago are expected to initiate exclusive breastfeeding within an hour of delivery and HIV-exposed infants are expected to receive Nevirapine (NVP) syrup at birth. Follow-up of HIV-exposed infants and mothers takes place at the postnatal clinic and includes DNA polymerase chain reaction (PCR) testing of HIV-exposed infants, distribution of infant prophylaxis, immunization and growth monitoring. The first infant HIV test is expected to be done by six weeks postpartum and results are expected to be received one week later or at the next clinic visit. As previously stated, maternal health services and ART are provided at the follow-up clinic.

Study design and population

Changes in Option B+ ART adherence and clinic visit attendance over time were measured through the utilization of routine PMTCT program data collected and entered into an electronic database by Makerere University-Johns Hopkins University (MU-JHU) Research Collaboration staff at Mulago Hospital for the purposes of routine program evaluation. Longitudinal data from HIV-infected pregnant women attending Mulago Hospital and enrolling in the PMTCT program during pregnancy from January 1, 2014 to December 31, 2014 were included in this study. All HIV-infected pregnant adult women of reproductive age (18-49 years old) who presented to Mulago National Referral Hospital in 2014, had attended at least two ANC visits and were new initiators of Option B+ for their current pregnancies were included in this study. HIV-infected pregnant women included in the study were either ART-naïve or had initiated a previous form of ART prophylaxis for past pregnancies under old PMTCT guidelines but were new initiators of Option B+. Women were excluded from the study if they were younger than 18 years old at the time of Option B+ initiation, had initiated a PMTCT regimen other than the one indicated by Option B+, were not new initiators of Option B+ for PMTCT or initiated Option B+ after the ANC period. Women were also excluded if the pregnancy did not result in a live birth. A longitudinal cohort study design was used to account for changes in Option B+ ART adherence and program retention over time from ANC through six months postpartum.

Data collection

Data collection for this study took place from May 4, 2016 to August 1, 2016. Routinely collected indicators regularly entered into the Mulago PMTCT program electronic database were extracted for this study. In addition, data abstraction was performed from patient medical charts and the PMTCT clinic log books to obtain ART adherence and program retention information for

the first ANC visit post-ART initiation and again at six weeks postpartum and six months postpartum. As described above, data was collected for all HIV-infected pregnant women who enrolled in the Option B+ PMTCT program beginning on January 1, 2014. A local research assistant was trained to assist the first author of this study with data abstraction and her work was validated by the first author of this study. Data from the PMTCT database and medical chart/log book abstraction were merged to create the longitudinal dataset necessary for this analysis to take place.

Study outcomes, exposures and definitions

The primary outcomes for this study were maternal ART adherence and clinic visit attendance at the first ANC visit after enrollment into the PMTCT program and again at six weeks and six months postpartum. At Mulago, medication adherence was measured and recorded by PMTCT clinic counselors trained to perform ART pill counts. Patients were instructed to return to each clinic appointment with the ART pill box and counselors counted the number of pills remaining at the current clinic visit. The number of pills remaining were subtracted from the number of pills dispensed at the last clinic visit to determine the number of pills swallowed between visits. The number of pills wasted, as self-reported by the patient, were also subtracted from the number of pills last dispensed and ART adherence was then calculated by dividing the number of pills actually swallowed by the number of pills expected to have been swallowed based on the date ART was last dispensed and the number of pills left over at the last visit. Patients were categorized as adherent or non-adherent based on a 95% and an 80% pill count adherence cutoff. The 95% cutoff was utilized to remain consistent with the definitions of optimal and suboptimal adherence used by the PMTCT clinic at Mulago. The 80% cutoff was included to reflect the minimum level of adherence necessary for successful viral suppression described in the literature.[13] If adherence at any time point could not be ascertained, it was recorded as

"unknown." An unknown adherence outcome was the result of either patients failing to return with the pill box or not being able to determine the number of pills last dispensed at the previous visit due to incomplete information in the medical charts or clinic log books. In addition to the medication adherence definition described above, a broader definition of non-adherence was also utilized in a separate analysis to capture patients who were either non-adherent to ART or had either failed to return with the pill box or did not return for the scheduled clinic visit.

The six-week and six-month postpartum visits were identified for each patient by estimating the scheduled clinic visit dates using the infant date of birth found in the PMTCT database for each patient. Due to variations in scheduling of clinic visit appointments, visits occurring between five and eight weeks postpartum and five and seven months postpartum were considered valid time points for data collection for the six-week and six-month postpartum visits, respectively. If visits occurred both before and after the estimated visit date but within the indicated window, the visit determined to be closest to the estimated visit date was used for the purposes of this study.

Information routinely entered into the PMTCT database and the clinic log books were used to obtain demographic and clinic characteristics and to measure the effects of the following factors on changes in ART adherence and clinic visit attendance: 1) Previous HIV diagnosis was determined using the PMTCT screening form and recorded as "Yes" if the patient had been diagnosed before the current pregnancy or "No" if the patient had been newly diagnosed with HIV during the current pregnancy; 2) Previous PMTCT experience was determined using the PMTCT enrollment form and recorded as "Yes" if the patient had initiated ART for PMTCT during a previous pregnancy or "No" if the patient had never initiated ART for PMTCT prior to the current pregnancy; 3) Disclosure status by the first visit post-ART initiation was obtained from the PMTCT psychosocial form and recorded as "Yes" if HIV status had been disclosed or "No" if the patient had not disclosed her status at that time. The relationship of the disclosed to

the participant (e.g. husband, mother, friend, etc.) was also recorded when available; 4) Baseline CD4 count at program enrollment was collected from the PMTCT registration and lab forms and categorized as greater than 350 cells/mm^3 or less than or equal to 350 cells/mm^3 in accordance with the previous WHO CD4 cutoff for treatment vs. prophylaxis for HIV-infected pregnant and postpartum women; 5) Time since ART initiation during pregnancy was calculated using the date of ART initiation and the date of delivery and categorized as more than 30 days on ART before delivery or less than or equal to 30 days on ART before delivery; 6) Partner counseling and testing by the first ANC visit post-ART initiation was determined using the PMTCT screening form and recorded as "Yes" if the partner had been tested for and counseled about HIV or "No" if the partner had not been tested for or counseled about HIV at this time; 7) Psychosocial support group meeting attendance was determined using the clinic log books and recorded as "Yes" if the patient had attended at least one psychosocial support group meeting or "No" if the patient had not attended any psychosocial support group meetings during pregnancy or by six weeks and six months postpartum.

Sample size considerations

The estimated sample size necessary to correctly reject the null hypothesis with 95% confidence and 80% power that there would be no difference in the proportion of adherent patients between pregnancy and six months postpartum was first calculated based on a recent longitudinal ART adherence study for PMTCT in Zambia since it was one of the only studies reporting medication adherence in a resource-limited setting for the same cohort of HIV-infected women in pregnancy and six months postpartum.[14] This study found a 12% drop in ART adherence between pregnancy (82.5%) and six months postpartum (70.5%). Utilizing the sample size calculation for paired data, it was estimated that a sample size of approximately 98 HIV-infected women would be necessary to detect a 12% change in the proportion of adherent women

between pregnancy and six months postpartum. Since longitudinal measures of adherence in the Option B+ era are largely unknown, a more conservative sample size estimate predicting a 5% change in the proportion of adherent patients from pregnancy to at six months postpartum was also calculated. Utilizing these parameters, it was estimated that a sample size of approximately 218 HIV-infected women would be needed to detect this change in adherence with 95% confidence and 80% power.

Data analysis

Statistical analyses were performed using Stata software version 12 (StataCorp, College Station, TX). Baseline characteristics and demographics were summarized categorically and with means and standard deviations (SDs) when relevant.

The proportions of adherent patients and patients attending scheduled clinic visits were calculated for each visit and McNemar's Chi Squared statistic for paired data was used to detect differences in the proportion of adherent patients and patients attending scheduled clinic visits between each time point of interest. Unadjusted and adjusted odds ratios with 95% confidence intervals (CIs) were obtained using univariate and multivariate logistic regression to estimate the associations between medication adherence or clinic visit attendance and each factor of interest. Multivariate logistic regression included all factors tested in the univariate analyses and then backward selection was used to select the final models predicting medication adherence and clinic visit attendance at each time point. P-values less than or equal to 0.05 were considered statistically significant in the univariate and multivariate analyses. A "p-to-remove" value of p=0.20 was used in the model selection process such that predictors were removed one at a time beginning with the predictor with the highest p-value until the p-values of all predictors left in the model were less than or equal to 0.20.

RESULTS

Study population characteristics

In 2014, 1,106 HIV-infected pregnant women presented to Mulago National Referral Hospital for ANC and required ART initiation. Of these women, 880 were newly enrolled into the Option B+ program and 599 attended at least two ANC visits. 102 patients were excluded from the analysis due to missing charts (72 active patients and 30 inactive patients at the time of data collection) and 17 were excluded due to a non-live birth pregnancy outcome (i.e. still birth, miscarriage or death soon after birth), resulting in a sample size of 480 for the study.

The socio-demographic and clinical characteristics of the patients included in this analysis are summarized in Table 1. The mean age of the study population was 25.9 (SD=4.8 years). 42.9% were between 18 and 24, 49.2% were between 25 and 34 and 6.0% were at least 35 years of age. 56.3% had at least a secondary level of education and 34.2% reported a primary education level or no education. Approximately 45% of the pregnant women included in the study reported being employed and 86.9% reported being married at the time of enrollment into the PMTCT program. 65.4% of pregnant women reported having given birth at least once before the current pregnancy while 31.3% were nulliparous. 64.6% of pregnancy women included in the study had a baseline CD4 cell count of greater than 350 cells/mm^3 and 34.4% had a baseline CD4 cell count of less than or equal to 350 cells/mm^3. Only 16.9% of pregnant women had previous experience with PMTCT and only 25.4% had been diagnosed with HIV prior to the current pregnancy. 35.4% of pregnant women had not disclosed their HIV status at the time of PMTCT program enrollment. Of the 58.3% who had disclosed, the majority had disclosed to a spouse (33.5%), a female relative (12.9%) or mother (6.5%).

Table 1: Socio-demographics and clinical characteristics at PMTCT program enrollment (N=480)

Characteristic	N (%)
Age (years)	
18-24	206 (42.9)
25-34	236 (49.2)
35-60	29 (6.0)
Missing	9 (1.9)
Mean (SD)	25.9 (4.8)
Education	
None/primary	164 (34.2)
Secondary/post-secondary	270 (56.3)
Missing	46 (9.6)
Employment status	
Housewife/not employed	218 (45.4)
Employed	216 (45.0)
Missing	46 (9.6)
Marital Status	
Married	417 (86.9)
Not married (single, widowed, divorced/separated)	26 (5.4)
Missing	37 (7.7)
Parity	
0	159 (31.3)
≥1	314 (65.4)
Missing	7 (1.5)
Baseline CD4 (cells/mm$^{3)}$	
≤350	165 (34.4)
>350	310 (64.6)
Missing	5 (1.0)
Mean (SD)	466.0 (241.7)
Previous PMTCT experience	
No	390 (81.3)
Yes	81 (16.9)
Missing	9 (1.9)
Previous HIV diagnosis	
No	356 (74.2)
Yes	122 (25.4)
Missing	2 (0.4)
Disclosure	
No	171 (35.4)
Yes	279 (58.3)
Missing	30 (6.3)

Trends in medication adherence

Table 2a summarizes the ART adherence profile of the study population at each visit. The proportion of adherent patients decreased over time between pregnancy and six months postpartum from 52.1% to 44.8% using the 95% adherence cutoff and 64.4% to 56.9% using the

80% adherence cutoff. 17.1% of pregnant women had an unknown adherence status at the first ANC visit post-ART initiation. At six months postpartum, 14.8% had an unknown adherence status and 18.3% did not return for the six months postpartum visit. At six weeks postpartum, more than half of the women (51.7%) had an unknown adherence status because the number of pills dispensed at the time of labor and delivery (i.e. the number of pills dispensed at the last clinic visit before six weeks postpartum) was not being routinely recorded in the patient medical charts or clinic log books at this time. Adherence information at six weeks postpartum was only available for women who had presented for an unscheduled or early clinic visit in the postpartum period before six weeks postpartum. Due to these findings, the six-week postpartum time point was excluded from the subsequent medication adherence analyses.

Table 2b summarizes the data utilized for McNemar's Chi Squared test for paired data to test the hypothesis that the proportion of adherent patients remained constant over time between the first ANC visit post-ART initiation and six months postpartum. Using the 95% cutoff and both definitions of non-adherence (less than 95% medication adherence only or less than 95% medication adherence, returned without the pill box or did not return for clinic visit), the differences in the proportions of women who were adherent at the first ANC visit post-ART initiation and adherent at the six-month postpartum visit were only marginally significantly different ($p=0.074$ and $p=0.055$, respectively). However, when the 80% adherence cutoff was applied to both definitions of non-adherence (less than 80% medication adherence only or less than 80% medication adherence, returned without pill box or did not return for clinic visit), the differences in the proportions of women who were adherent at ANC were significantly different than the proportions of women who were adherent at six months postpartum ($p<0.001$ and $p=0.037$, respectively).

Table 2a: Adherence at ANC, six weeks and six months postpartum, N=480

Adherence cutoff	Proportion adherent at ANC (%)	Proportion adherent at six weeks postpartum (%)	Proportion adherent at six months postpartum (%)
≥95%	52.1	9.6	44.8
<95%	27.5	12.3	16.9
Unknown*	17.1	51.7	14.8
Missing	3.3	5.0	5.2
Did not return**	0.0	21.5	18.3
≥ 80%	64.4	13.8	56.9
<80%	15.2	8.1	4.8
Unknown*	17.1	51.7	14.8
Missing	3.3	5.0	5.2
Did not return**	0.0	21.5	18.3

*Patients who returned without pill boxes or the number of pills last dispensed could not be determined from the information in the medical charts.
**Patients who did not return within the time window.

Table 2b: Proportion of adherent women at ANC and six months postpartum

95% adherence (nonadherence=<95%medication adherence)			
	Adherent at six months postpartum (%)	**Non-adherent at six months postpartum (%)**	**Total (%)**
Adherent in ANC (%)	130 (70.7)	37 (57.8)	167 (67.3)
Non-adherent in ANC (%)	54 (29.3)	27 (42.2)	81 (32.7)
Total (%)	184 (100.0)	64 (100.0)	248 (100.0)
95% adherence (nonadherence= <95% adherence or returned without pill box/did not return)			
	Adherent at six months postpartum (%)	**Non-adherent at six months postpartum (%)**	**Total (%)**
Adherent in ANC (%)	130 (62.2)	105 (45.5)	235 (53.4)
Non-adherent in ANC (%)	79 (37.8)	126 (54.5)	205 (46.6)
Total (%)	209 (100.0)	231 (100.0)	440(100.0)
80% adherence (nonadherence= <80% medication adherence)			
	Adherent at six months postpartum (%)	**Non-adherent at six months postpartum (%)**	**Total (%)**
Adherent in ANC (%)	195 (84.8)	12 (66.7)	207 (83.5)
Non-adherent in ANC (%)	35 (15.2)	6 (33.3)	41 (16.5)
Total (%)	230 (100.0)	18 (100.0)	248 (100.0)
80% adherence (nonadherence= <80% adherence or returned without pill box/did not return)			
	Adherent at six months postpartum (%)	**Non-adherent at six months postpartum (%)**	**Total (%)**
Adherent in ANC (%)	195 (73.6)	98 (56.0)	293 (66.6)
Non-adherent in ANC (%)	70 (26.4)	77 (44.0)	147 (33.4)
Total (%)	265 (100.0)	175 (100.0)	440 (100.0)

Adherence in antenatal care

Tables 1a and 1b in Appendix E summarize the results of the univariate and multivariate logistic regression models looking at the effects of different factors on achieving 95% adherence

in ANC. Using the nonadherence definition of medication adherence less than 95%, factors that affected medication adherence were education level, baseline CD4 cell count and whether or not a patient had received PMTCT treatment or prophylaxis for a previous pregnancy. In the univariate analyses, patients with at least a secondary education level were almost 50% more likely to be adherent than patients with no education or a primary education level (unadjusted OR=1.48, p=0.096) and women who had received PMTCT treatment or prophylaxis during a previous pregnancy were 39% less likely to be adherent at ANC than women who were first-time initiators of a PMTCT program (unadjusted OR=0.61, p=0.071). In the multivariate analysis, education and previous PMTCT program experience remained marginally significant with respect to medication adherence (adjusted OR=1.73, p=0.056 and adjusted OR=0.53, p=0.086, respectively) and additionally, HIV-infected pregnant women with higher CD4 cell counts were significantly more likely than women with lower CD4 cell counts at ART initiation to be non-adherent in ANC (adjusted OR=0.55, p=0.036).

In the analysis defining nonadherence as medication adherence less than 95% or not having returned to clinic with the ART pill box, the univariate analyses found similar trends for education level and baseline CD4 cell count as described above (unadjusted OR=1.69, p=0.010 and unadjusted OR=0.60, p=0.009, respectively). In addition, having been diagnosed with HIV prior to the current pregnancy and disclosure before the first ANC visit post-ART initiation were significantly associated with achieving at least 95% adherence at this clinic visit (unadjusted OR=1.61, p=0.028 and unadjusted OR=1.72, p=0.006, respectively). In the multivariate analysis, education level, baseline CD4 cell count, previous HIV diagnosis and disclosure remained significantly associated with 95% adherence at the first ANC visit post-ART initiation (adjusted OR=2.00, p=0.005, adjusted OR=0.53, p=0.010, adjusted OR=1.52, p=0.112 and adjusted OR=1.84, p=0.011, respectively).

Tables 1c and 1d in Appendix E summarize the results of the univariate and multivariate logistic regression models looking at the effects of different factors on achieving 80% adherence in ANC. Using the nonadherence definition of medication adherence less than 80%, HIV-infected pregnant women who reported being married were 2.34 times as likely to be adherent at the first ANC visit post-ART initiation (p=0.062), but this association become non-significant in the multivariate analysis (adjusted OR=2.48, p=0.107). HIV-infected pregnant women with higher baseline CD4 cell counts remained less likely to be adherent in ANC in both the univariate and multivariate logistic regressions and this association became marginally significant in the adjusted model (unadjusted OR=0.67, p=0.156 and adjusted OR=0.52, p=0.070).

In the analysis defining nonadherence as medication adherence less than 80% or returning to clinic without the ART pill box, lower baseline CD4 cell count continued be associated with adherence in the univariate and multivariate analyses (unadjusted OR=0.54, p=0.005 and adjusted OR=0.55, p=0.022). In addition, HIV-infected pregnant women who had disclosed their status were approximately two times as likely to be adherent (unadjusted OR=183, p=0.004 and adjusted OR=2.07, p=0.003).

Predictive models for adherence in antenatal care

Table 3 lists the factors included in the predictive models obtained from the backwards selection process for each definition of adherence. For all the predictive models, in model 1 a 95% adherence cutoff was used and nonadherence was defined as a pill count adherence of less than 95%. In model 2, a 95% adherence cutoff was used and nonadherence was defined as a pill count adherence of less than 95%, having returned to ANC without the pill box, or not having returned to clinic. In model 3, an 80% adherence cutoff was used and nonadherence was defined as a pill count adherence of less than 80%. In model 4, an 80% adherence cutoff was used and

nonadherence was defined as a pill count adherence of less than 80%, having returned to ANC without the pill box, or not having returned to clinic.

CD4 cell count at baseline and disclosure by the first ANC visit post-ART initiation were included in all four models. In all four cases, HIV-infected pregnant women with CD4 cell counts greater than 350 cells/mm^3 were approximately 50% less likely to be adherent at the first ANC visit post-ART initiation than women with CD4 cell counts less than or equal to 350 cells/mm^3. HIV-infected pregnant women who had disclosed their HIV status by the time of the first ANC visit post-ART initiation were more likely to be adherent than women who had not disclosed, with the odds of good adherence ranging from 49% in model 1 to 96% in model 4. Higher education level and having been diagnosed with HIV prior to the current pregnancy were predictors of good adherence in all the models except model 3. Women with at least a secondary education level were between 50% (model 1) and 90% (model 2) more likely to be adherent than women with a primary education level or no education, and women who had been diagnosed with HIV prior to the current pregnancy were between 47% (model 4) and 66% (model 2) more likely to be adherent than women who were newly diagnosed with HIV during the current pregnancy. Previous experience with PMTCT was associated with an approximately 40% decreased odds of adherence in model 1 and model 2 and being employed was as associated with a 48% decreased odds of adherence in morel 3 and a 31% decreased odds of adherence in model 4. Parity was only predictive of adherence in model 2, with multiparous women expected to be 41% more likely than nulliparous women to be adherent in ANC. Marital status was only predictive of adherence in model 3, with married women expected to be more than two times as likely as unmarried women to be adherent in ANC.

Table 3: Predictive models for adherence in antenatal care*

Model 1: 95% adherence (nonadherence=<95%medication adherence)		
Factor	**Adjusted OR (95% CI)**	**p-value**
Education	1.50 (0.92, 2.45)	0.107
Baseline CD4	0.55 (0.33, 0.91)	0.021
Previous PMTCT	0.60 (0.33, 1.09)	0.093
Previous HIV diagnosis	1.62 (0.92, 2.85)	0.094
Disclosure	1.49 (0.91, 2.43)	0.113
Model 2: 95% adherence (nonadherence=<95% adherence or returned without pill box/did not return)		
Education	1.90 (1.22, 2.96)	0.004
Parity	1.41 (0.89, 2.24)	0.143
Baseline CD4	0.52 (0.33, 0.81)	0.004
Previous PMTCT	0.64 (0.37, 1.09)	0.102
Previous HIV diagnosis	1.66 (1.01, 2.72)	0.044
Disclosure	1.80 (1.17, 2.76)	0.008
Model 3: 80% adherence (nonadherence= <80% medication adherence)		
Employment	0.52 (0.28, 0.98)	0.043
Marital status	2.12 (0.74, 6.07)	0.160
Baseline CD4	0.51 (0.26 (1.00)	0.051
Disclosure	1.69 (0.91, 3.13)	0.094
Model 4: 80% adherence (nonadherence= <80% adherence or returned without pill box/did not return)		
Education	1.51 (0.95, 2.40)	0.078
Employment	0.69 (0.44, 1.08)	0.107
Baseline CD4	0.52 (0.32, 0.83)	0.007
Previous HIV diagnosis	1.47 (0.87, 2.48)	0.152
Disclosure	1.96 (1.26, 3.04)	0.003

*Reference groups: 1) Education: none/primary; 2) Baseline CD4: ≤350 cells/mm$^{3;}$ 3) Previous PMTCT: No; 4) Previous HIV diagnosis: No; 5) Disclosure: No; 6) Parity: 0; 7) Employment: housewife/not employed; 8) Marital status: Not married

Adherence at six months postpartum

Tables 2a and 2b in Appendix E summarize the results of the univariate and multivariate logistic regression models looking at the effects of different factors on achieving 95% adherence at six months postpartum. Using the nonadherence definition of medication adherence less than 95%, education, parity, baseline CD4 cell count and adherence status in ANC were found to be associated with adherence at six months postpartum in the univariate analyses. HIV-infected mothers with at least a secondary level of education were nearly 80% more likely to be adherent than mothers with a primary level of education or no education (unadjusted OR=1.79, p=0.039). Mothers who had given birth at least once before the current pregnancy were 50% less likely to be adherent at six months postpartum than nulliparous mothers (unadjusted OR=0.50, p=0.022) and mothers with a CD4 cell count of greater than 350 cells/mm^3 were also approximately 50%

less likely to be adherent at six months postpartum than mothers with baseline CD4 cell count of less than or equal to 350 cells/mm^3 (unadjusted OR=0.52, p=0.020). Under this definition of adherence, having been adherent at the ANC visit was associated with a 76% increased odds of adherence at six months postpartum (unadjusted OR=1.76, p=0.061). In the multivariate analysis, only the association between parity and adherence remained significant (adjusted OR=0.39, p=0.043)

In the analysis defining nonadherence as medication adherence less than 95%, returning to clinic without the ART pill box or not returning to clinic for the six-month postpartum visit, baseline CD4 cell count and adherence status in ANC followed the same trends as described above (unadjusted OR=0.57, p=0.005 and unadjusted OR=1.97, p<0.001, respectively). In addition, length of time spent on ART during pregnancy as well as having attended at least one psychosocial support group meeting between ART initiation and six months postpartum and having attended the six-week postpartum clinic visit were significantly associated with an odds of adherence at six months postpartum. HIV-infected pregnant women who had initiated ART more than 30 days prior to delivery were 42% less likely to be adherent at six months postpartum compared to women who had initiated ART 30 days or less prior to delivery (unadjusted OR=0.58, p=0.004). On the other hand, having attended at least one psychosocial support group meeting between ART initiation and six months postpartum as well as having attended the six-week postpartum clinic visit were associated with an approximately two (unadjusted OR=1.97, p=0.009) and three (unadjusted OR=3.12, p<0.001) times increased odds of adherence at six months postpartum, respectively. However, the multivariate analysis results showed that only adherence status at the first ANC visit post-ART initiation and clinic visit attendance at six weeks postpartum were associated with an increased odds of adherence at six months postpartum (adjusted OR=2.00, p=0.006 and adjusted OR=2.78, p=0.001, respectively).

Tables 2c and 2d in Appendix E summarize the results of the univariate and multivariate logistic regression models looking at the effects of different factors on achieving 80% adherence at six months postpartum. Using the nonadherence definition of medication adherence less than 80%, adherence status at ANC was the only factor found to be associated with adherence at six months postpartum in the univariate analyses and women who were adherent in ANC were nearly three times as likely to be adherent at six months postpartum (unadjusted OR=2.79, p=0.054). Having been diagnosed with HIV prior to the current pregnancy was also marginally associated with a decreased odds of adherence at six months postpartum (unadjusted OR=0.44, p=0.071). In the multivariate analysis, adherence at the first ANC visit post-ART initiation remained significantly associated with adherence at six months postpartum (adjusted OR=3.12, p=0.012) and the association between previous HIV diagnosis and adherence also became significant (adjusted OR=0.10, p=0.003).

In the analysis defining nonadherence as medication adherence less than 80%, returning to clinic without the ART pill box or not returning to clinic for the scheduled visit, older age, baseline CD4 cell count, psychosocial group meeting attendance, clinic attendance at six weeks postpartum and adherence at the first ANC visit post-ART initiation were associated with adherence at six months postpartum in the univariate analyses. HIV-infected women ages 35-60 were over four times as likely to be adherent at six months postpartum than women ages 18-24 (unadjusted OR=4.64, p=0.006). HIV-infected pregnant women with a baseline CD4 cell count of greater than 350 remained less likely to be adherent at six months postpartum than women with a baseline CD4 cell count of less than or equal to 350 cells/mm^3 (unadjusted OR=0.70, p=0.077) and having attended at least one psychosocial support group meeting between ART initiation and six months postpartum as well as having attended the six week postpartum clinic visit were associated with an increased odds of adherence at six months postpartum (unadjusted OR=2.23, p=0.004 and unadjusted OR=3.73, p=<0.001, respectively). HIV-infected pregnant women who

were defined as adherent in ANC under this definition of adherence were more than two times as likely to be adherent as at six months postpartum as compared to women who were not adherent in ANC (unadjusted OR=2.19, p<0.001). In the multivariate analysis, the associations between maternal age, CD4 at baseline and psychosocial support group attendance with adherence at six months postpartum became non-significant (adjusted OR=2.61, p=0.166, adjusted OR=0.82, p=0.492 and adjusted OR=1.31, p=0.446, respectively) while the associations between adherence at the first-ANC visit post-ART initiation and clinic attendance at six weeks postpartum with adherence at six months postpartum remained strong (adjusted OR=2.00, p=0.014 and adjusted OR=2.81, p=0.001), respectively). In addition, women who had been previously diagnosed with HIV were 46% less likely than women who were newly diagnosed with HIV during the current pregnancy to be adherent at six months postpartum in the multivariate analysis (adjusted OR=0.54, p=0.043).

Predictive models for adherence at six months postpartum

Table 4 lists the factors included in the predictive models obtained from the backwards selection process for each definition of adherence. The only factor found to be predictive of adherence at six months postpartum in all four models was adherence at the first ANC visit post-ART initiation. HIV-infected pregnant women found to be adherent in ANC were predicted to be between two (model 1) and 3.65 (model 3) times as likely as women who were not adherent in ANC to be adherent at six months postpartum. Parity was predictive of adherence at six months postpartum in model 1 and model 2, but contrary to adherence in ANC, women who were multiparous were between 35% (model 2) and 58% (model 1) less likely than nulliparous women to be adherent at six months postpartum. Baseline CD4 count was also predictive of adherence at six months postpartum in model 1 and model 2, and women with higher CD4 cell counts continued to be approximately 50% less likely to be adherent than women with lower CD4 cell

counts in these two prediction models. Previous HIV diagnosis was predictive of adherence at six months postpartum in model 3 and model 4, but having been previously diagnosed with HIV was associated with between a 30% (model 4) and 76% decreased odds of adherence at six months postpartum in comparison to being newly diagnosed with HIV during the current pregnancy. Having a partner who was counseled and tested for HIV in ANC as well as having attended at least one psychosocial support group meeting between ART initiation and six months postpartum were predictive of good adherence in model 2 and model 4. Women with partners who had been counseled and tested for HIV were approximately 60% more likely than women with partners who had not been counseled and tested for HIV to be adherent at six months postpartum and women who had attended at least one psychosocial support group meeting were more than twice as likely as women who had attended no psychosocial support group meetings to be adherent at six months postpartum.

Table 4: Predictive models for adherence at six months postpartum*

Model 1: 95% adherence (nonadherence=<95%medication adherence)		
Factor	**Adjusted OR (95% CI)**	**p-value**
Parity	0.42 (0.21, 0.85)	0.015
Baseline CD4	0.54 (0.29, 1.01)	0.054
Previous PMTCT	0.61 (0.31, 1.20)	0.151
Adherence in ANC	2.00 (1.07, 3.74)	0.000
Model 2: 95% adherence (nonadherence=<95% adherence or returned without pill box/did not return)		
Parity	0.65 (0.43, 0.99)	0.047
Baseline CD4	0.58 (0.38, 0.87)	0.009
Partner counseled/tested for HIV	1.63 (0.99, 2.68)	0.055
PSS group attendance	2.17 (1.28, 3.66)	0.004
Adherent in ANC	1.99 (1.34, 2.97)	0.001
Model 3: 80% adherence (nonadherence= <80% medication adherence)		
Previous HIV diagnosis	0.24 (0.09, 0.67)	0.006
Adherent in ANC	3.65 (1.21, 11.01)	0.022
Model 4: 80% adherence (nonadherence= <80% adherence or returned without pill box/did not return)		
Previous HIV diagnosis	0.70 (0.45, 1.11)	0.131
Partner counseled/tested for HIV	1.67 (0.99, 2.81)	0.053
PSS group attendance	2.29 (1.29. 4.06)	0.005
Adherent in ANC	2.28 (1.50, 3.45)	0.000

*Reference groups: 1) Parity: 0; 2) Baseline CD4: ≤350 cells/mm; 3) Previous PMTCT: No; 4) Adherence in ANC: No; 5) Partner counseled/tested: No; 6) PSS group attendance: No; 7) Previous HIV diagnosis: No

Adherence at ANC and six months postpartum

Tables 3a and 3b in Appendix E summarize the results of the univariate and multivariate logistic regression models looking at the effects of different factors on achieving 95% adherence at both the ANC visit and the six-month postpartum visit. Using the nonadherence definition of medication adherence less than 95%, the univariate analyses found that a higher education level, status disclosure and having a partner who was counseled and tested for HIV in ANC were associated with a 71%, 67% and 77% increased odds of adherence at both time points, but that these results were only marginally significant (unadjusted OR=1.71, p=0.055, unadjusted OR=1.67, p=0.064 and unadjusted OR=1.77, p=0.075, respectively). In the multivariate analysis, only higher education remained associated with adherence at both time points (adjusted OR=2.01, p=0.051). Employment also became associated with adherence at both time points in the multivariate analysis, and HIV-infected women who reported being employed were 47% less likely to be adherent at both time points than women who reported being unemployed or housewives (adjusted OR=0.53, p=0.060).

In the analysis defining nonadherence as medication adherence less than 95%, returning to clinic without the ART pill box or not returning to clinic for the six-month postpartum visit, the univariate analyses once again showed that a higher education level, disclosure and having a partner who was counseled and tested for HIV in ANC were associated with adherence at both clinic visits (unadjusted OR=1.37, p=0.047, unadjusted OR=1.75, p=0.016 and unadjusted OR=1.66, p=0.047, respectively). In addition, HIV-infected pregnant women and mothers with a CD4 cell count of greater than 350 cells/mm^3 were found to be 39% less likely to be adherent at both time points as HIV-infected pregnant women and mothers with a CD4 cell count of less than or equal to 350 cells/mm^3 (unadjusted OR=0.61, p=0.020). Having attended at least one psychosocial support group meeting between ART initiation and six months postpartum was also marginally associated with increased odds of adherence at both time points in the univariate

analysis (unadjusted OR=1.57, p=0.087). In the multivariate analysis, education and disclosure continued to remain associated with adherence at both time points (adjusted OR=1.79, p=0.043 and adjusted OR=1.84, p=0.028, respectively). In addition, women who had spent more than 30 days on ART during pregnancy were 41% less likely than women who had spent 30 days or less on ART during pregnancy to be adherent at both time points in the multivariate analysis (adjusted OR=0.59, p=0.039).

Tables 3c and 3d in Appendix E summarize the results of the univariate and multivariate logistic regression models looking at the effects of different factors on achieving 80% adherence at both the ANC visit and the six-month postpartum visit. Using the nonadherence definition of medication adherence less than 80%, the univariate analyses found that HIV-infected pregnant women and mothers who were employed at the time of ART initiation were 44% less likely than HIV-infected pregnant women and mothers who were not employed at the time of ART initiation to be adherent at both time points, but the association was only marginally significant (unadjusted OR=0.56, p=0.083). The univariate analyses also found that married women were over five times as likely as unmarried women to be adherent at both time points and that women who had disclosed their HIV status were nearly two times as likely as women who had not disclosed their HIV status to be adherent at both time points (unadjusted OR=5.07, p=0.003 and unadjusted OR=1.97, p=0.036, respectively). In the multivariate analysis, education, marital status and disclosure continued to be associated with adherence at both time points (adjusted OR=0.46, p=0.061, adjusted OR=3.93, p=0.045 and adjusted OR=2.08, p=0.072, respectively).

In the analysis defining nonadherence as medication adherence less than 80%, returning to clinic without the ART pill box or not returning to clinic for the six-month postpartum visit, baseline CD4 cell count, disclosure and time spent on ART during pregnancy were significantly associated with adherence at both time points in the univariate analyses. Women who had baseline CD4 cell counts greater than 350 cells/mm^3 were 37% less likely than women who had

baseline CD4 cell counts less than or equal to 350 cells/mm^3 to be adherent at both time points (unadjusted OR=0.63, p=0.024). HIV status disclosure was associated with a 31% increased odds of adherence at both time points while having spent more than 30 days on ART during pregnancy was associated with a 42% decreased odds of adherence at both time points (unadjusted OR=1.69, p=0.011 and unadjusted OR=0.58, p=0.006, respectively). In the multivariate analysis, the association between baseline CD4 cell count and adherence at both time points became nonsignificant (adjusted OR=0.76, p=0.260) but the associations between disclosure and adherence and time spent on ART during pregnancy and adherence remained strong (adjusted OR=1.91, p=0.009 and adjusted OR=0.54, p=0.007, respectively).

Predictive models for adherence in antenatal care and six months postpartum

Table 5 lists the factors included in the predictive models obtained from the backwards selection process for each definition of adherence. The only factor found to be predictive of adherence at both time points was disclosure. Women who had disclosed their HIV status by the first ANC visit post-ART initiation were between 1.56 (model 4) and 2.03 (model 3) times more likely to be remain adherent at both time points than women who had not disclosed their HIV status by the first ANC visit post-ART initiation. Education was predictive of sustained adherence in model 1 and model 2, with women reporting at least a secondary level of education being between 14% (model 1) and 47% (model 2) more likely than women reporting a primary level of education or no education to maintain adherence at both time points. Employment was predictive of adherence in model 1 and model 3, with women who were employed being between 39% (model 1) and 51% (model 3) less likely than women who were not employed to maintain adherence at both time points. Marital status was predictive of adherence in model 3 and model 4, with women who were married being between approximately two (model 4) and three and a half

(model 3) times more likely than women who were not married to maintain adherence at both time points.

Table 5: Predictive models for adherence at ANC and six months postpartum*

Model 1: 95% adherence (nonadherence=<95%medication adherence)		
Factor	**Adjusted OR (95% CI)**	**p-value**
Education	1.86 (1.00, 3.46)	0.050
Employment	0.61 (0.34, 1.11)	0.109
Disclosure	1.65 (0.92, 2.97)	0.093
Model 2: 95% adherence (nonadherence=<95% adherence or returned without pill box/did not return)		
Education	1.53 (0.95, 2.46)	0.084
Baseline CD4	0.65 (0.41, 1.03)	0.064
Disclosure	1.91 (1.18, 3.10)	0.008
Model 3: 80% adherence (nonadherence= <80% medication adherence)		
Employment	0.49 (0.23, 1.03)	0.059
Marital status	3.50 (1.02, 12.06)	0.047
Disclosure	2.03 (0.98, 4.31)	0.055
Model 4: 80% adherence (nonadherence= <80% adherence or returned without pill box/did not return)		
Marital status	1.91 (0.75, 4.91)	0.178
Disclosure	1.56 (1.00, 2.44)	0.051
Time on ART in pregnancy	1.44 (0.83, 2.52)	0.196

*Reference groups: 1) Education: none/primary; 2) Employment: housewife/not employed; 3) Disclosure: No; 4) Baseline CD4: ≤350 cells/mm^3; 5) Marital status: not married; 6) Time on ART in pregnancy: ≤30 days

Clinic visit attendance in the postpartum period

Tables 6a and 6b summarizes the clinic visit attendance profile of the study population at six weeks and six months postpartum. 21.9% of HIV-infected mothers did not return within the designated window for the six-week postpartum visit and 19.0% did not return within the designated window for the six-month postpartum visit. McNemar's Chi Squared test for paired data found that the proportion of HIV-infected mothers who attended the clinic at six weeks postpartum was not significantly different from the proportion of HIV-infected mothers who attended the clinic at six months postpartum (p=0.178).

Table 6a: Clinic visit attendance at six weeks and six months postpartum, N=480

	Yes (%)	No (%)	Missing/Unknown (%)
Attended at six weeks postpartum	345 (71.9)	105 (21.9)	30 (6.25)
Attended at six months postpartum	354 (73.8)	91 (19.0)	35 (7.2)

Table 6b: Proportion of HIV-infected mothers attending clinic visits at six weeks and six months postpartum

	Attended at six months postpartum		
Attended at six weeks postpartum	**Yes (%)**	**No (%)**	**Total (%)**
Yes (%)	298 (84.9)	40 (45.5)	**338 (77.0)**
No (%)	53 (15.1)	48 (54.6)	**101 (23.0)**
Total (%)	351 (100.0)	88 (100.0)	**439 (100.0)**

Clinic visit attendance at six weeks postpartum

Table 4 in Appendix D summarizes the results of the univariate and multivariate logistic regression models looking at the effects of different factors on clinic attendance at six weeks postpartum. In the univariate analyses, previous PMTCT program experience was associated with 47% decreased odds of attending the clinic at six weeks postpartum and having been diagnosed with HIV prior to the current pregnancy was associated with a 95% increased odds of attending the clinic at six weeks postpartum (unadjusted OR=0.53, p=0.020 and unadjusted OR=1.95, p=0.022, respectively). Being classified as adherent at the first ANC visit post-ART initiation was also associated with an increased odds of attending the clinic at six weeks postpartum in the univariate analyses under both the 95% and 80% adherence cutoffs (unadjusted OR=1.96, p=0.003 and unadjusted OR=1.81, p=0.010, respectively). In the multivariate analyses, the effect of adherence in ANC was no longer significant (adjusted OR=1.58, p=0.117 and adjusted OR=1.63, p=0.108 for 95% and 80% adherence cutoffs, respectively) and the effects of previous PMTCT program experience and previous HIV diagnosis became only marginally significant (adjusted OR=0.47, p=0.082 and adjusted OR=2.05, p=0.092, respectively).

Predictive models for clinic visit attendance at six weeks postpartum

Table 7 lists the factors included in the predictive models obtained from the backwards selection process for each definition of adherence. Having been previously diagnosed with HIV before the current pregnancy and good adherence in ANC were predictive of clinic visit attendance at six weeks postpartum in all four models. Women who had learned their HIV status before the current pregnancy were between 58% (model 1) and 91% (model 4) more likely than women who were newly diagnosed with HIV to attend the clinic at six weeks postpartum and women who were classified as having good adherence in ANC were between 61 % (model 3) and 71% (model 1) more likely than women who had poor adherence in ANC to attend the clinic at six weeks postpartum. Older age and previous PMTCT program experience were predictive of attendance at six weeks postpartum in all the models with the exception of model 1. Women between the ages of 25 and 60 were more likely to attend the clinic at six weeks postpartum than women between the ages of 18 and 24. On the other hand, Women who had been previously exposed to a PMTCT program were between 35% (model 3) and 49% (model 4) less likely than women who were new to the PMTCT program to attend the clinic at six weeks postpartum. Having a partner who was counseled and tested for HIV in ANC as well as having attended at least one psychosocial support group meeting between ART initiation and six weeks postpartum were predictive of good adherence in model 2 and model 4. Women with partners who had been counseled and tested for HIV were between 31% (model 4) and 38% (model 2) more likely than women with partners who had not been counseled and tested for HIV to attend the clinic at six weeks postpartum and women who had attended at least one psychosocial support group meeting were almost 70% more likely than women who had attended no psychosocial support group meetings to attend the clinic at six weeks postpartum.

Table 7: Predictive models for clinic visit attendance at six weeks postpartum*

Model 1: 95% adherence (nonadherence=<95%medication adherence)		
Factor	**Adjusted OR (95% CI)**	**p-value**
Previous HIV diagnosis	1.58 (0.85, 2.95)	0.150
Adherent in ANC	1.71 (1.02, 2.85)	0.041
Model 2: 95% adherence (nonadherence=<95% adherence or returned without pill box/did not return)		
Maternal age	1.43 (0.89, 2.30) 3.25 (0.92, 11.53)	0.136 0.067
Previous PMTCT	0.53 (0.30, 0.93)	0.028
Previous HIV diagnosis	1.87 (1.04, 3.36)	0.038
Partner counseled/tested for HIV	1.62 (0.88, 2.99)	0.124
PSS group attendance	1.67 (0.82, 3.42)	0.159
Adherent in ANC	1.70 (1.07, 2.71)	0.024
Model 3: 80% adherence (nonadherence= <80% medication adherence)		
Maternal age	1.43 (0.85, 2.40) 2.38 (0.66, 8.55)	0.183 0.183
Previous PMTCT	0.65 (0.35, 1.21)	0.174
Previous HIV diagnosis	1.64 (0.88, 3.08)	0.120
Adherent in ANC	1.61 (0.88, 2.95)	0.120
Model 4: 80% adherence (nonadherence= <80% adherence or returned without pill box/did not return)		
Maternal age	1.48 (0.92, 2.37) 3.29 (0.93, 11.59)	0.106 0.064
Previous PMTCT	0.52 (0.29, 0.90)	0.022
Previous HIV diagnosis	1.91 (1.06, 3.45)	0.031
Partner counseled/tested for HIV	1.63 (0.88, 3.01)	0.118
PSS group attendance	1.69 (0.83, 3.46)	0.151
Adherent in ANC	1.67 (1.04, 2.68)	0.033

*Reference groups: 1) Previous HIV diagnosis: No; 2) Adherent in ANC: No; 3) Maternal age: 18-24 years; 4) Previous PMTCT: No; 5) Partner counseled/tested: No; 6) PSS group attendance: None

Clinic visit attendance at six months postpartum

Table 5 in Appendix E summarizes the results of the univariate and multivariate logistic regression models looking at the effects of different factors on clinic attendance at six months postpartum. In the univariate analyses, older women in the 25 to 34 and 35 to 60 age groups were more likely to attend at six months postpartum than younger women ages 18-24 (unadjusted OR=1.60, p=0.053 and unadjusted OR=9.67, p=0.028, respectively), but these association became nonsignificant in the multivariate analysis (adjusted OR=1.33, p=0.431 and adjusted OR=5.18, p=0.140, respectively). Similarly, HIV-infected pregnant women and mothers who had attended at least one psychosocial support group meeting between ART initiation and six months postpartum were more than three and a half times more likely than women who had attended no psychosocial support group meetings to attend the clinic at six months postpartum in the

univariate analysis (unadjusted OR=3.56, p=0.002), but this association was no longer significant in the multivariate analysis (adjusted OR=2.02, p=0.159). HIV-infected pregnant women who had spent more than 30 days on ART in pregnancy were almost three times more likely than those who had spent 30 days or less on ART in pregnancy to attend the clinic at six months postpartum (unadjusted OR=2.88, p<0.0001) in the univariate analysis and more than three and a half times more likely to attend clinic at six months postpartum in the multivariate analysis (adjusted OR=3.58, p<0.001). HIV-infected pregnant women who were adherent in ANC based on the 80% cutoff were more than two times as likely as women who were not adherent in ANC to attend the clinic at six months postpartum in the univariate analysis (unadjusted OR=2.11, p=0.002), but this association was not significant in the multivariate analysis (adjusted OR=1.51, p=0.233). The strongest predictor of clinic attendance at six months postpartum was clinic attendance at six weeks postpartum. HIV-infected mothers who attended the clinic at six weeks postpartum were more than six times as likely as HIV-infected mothers who did not attend the clinic at six weeks postpartum to attend the clinic at six months postpartum in the univariate analysis (unadjusted OR=6.75, p<0.001), and this association remained strong and significant in the multivariate analysis (adjusted OR=5.19, p<0.001).

Predictive models for clinic visit attendance at six months postpartum

Table 8 lists the factors included in the predictive models obtained from the backwards selection process for each definition of adherence. Employment, marital status, psychosocial support group meeting attendance, time spent on ART in pregnancy and attendance at six weeks postpartum were all predictive of attendance at six months postpartum in all four models. Women who reported being employed were approximately 40% less likely than women who reported not being employed to attend the clinic at six months postpartum. Women who reported being married almost three times more likely than women who reported not being married to attend the

clinic at six months postpartum, women who attended at least one psychosocial support group meeting between ART initiation and six months postpartum were more than twice as likely as women who had not attended a psychosocial support group meeting to attend the clinic at six months postpartum, women who had initiated ART more than 30 days before delivery were over three times as likely as women who had initiated ART less than or equal to 30 days before delivery to attend the clinic at six months postpartum and women who had attended the clinic at six weeks postpartum were more than five times as likely as women who had not attended the clinic at six weeks postpartum to attend the clinic at six months postpartum.

Table 8: Predictive models for clinic visit attendance at six months postpartum*

Model 1: 95% adherence (nonadherence=<95%medication adherence)		
Factor	**Adjusted OR (95% CI)**	**p-value**
Employment	0.61 (0.33, 1.13)	0.113
Marital status	2.92 (0.97, 8.77)	0.056
PSS group attendance	2.23 (0.87, 5.73)	0.097
Time on ART in pregnancy	3.30 (1.68, 6.49)	0.001
Attendance at six weeks postpartum	5.95 (3.14, 11.28)	0.000
Model 2: 95% adherence (nonadherence=<95% adherence or returned without pill box/did not return)		
Employment	0.56 (0.30, 1.06)	0.073
Marital status	2.65 (0.87, 8.08)	0.088
PSS group attendance	2.19 (0.85, 5.62)	0.103
Time on ART in pregnancy	3.20 (1.60, 6.36)	0.001
Adherent in ANC	1.65 (0.88, 3.09)	0.115
Attendance at six weeks postpartum	5.14 (2.68, 9.85)	0.000
Model 3: 80% adherence (nonadherence= <80% medication adherence)		
Employment	0.61 (0.33, 1.13)	0.113
Marital status	2.92 (0.97, 8.77)	0.056
PSS group attendance	2.23 (0.87, 5.73)	0.097
Time on ART in pregnancy	3.30 (1.68, 6.49)	0.001
Attendance at six weeks postpartum	5.95 (3.14, 11.28)	0.000
Model 4: 80% adherence (nonadherence= <80% adherence or returned without pill box/did not return)		
Employment	0.58 (0.31, 1.09)	0.091
Marital status	2.66 (0.87, 8.17)	0.087
PSS group attendance	2.15 (0.84, 5.52)	0.113
Time on ART in pregnancy	3.18 (1.59, 6.34)	0.001
Adherent in ANC	1.63 (0.86, 3.06)	0.131
Attendance at six weeks postpartum	5.18 (2.70, 9.94)	0.000

*Reference groups: 1) Employment: Housewife/not employed; 2) Marital status: Not married; 3) PSS group attendance: None; 4) Time on ART in pregnancy: ≤30 days; 5) Attendance at six weeks postpartum: No; 6) Adherence in ANC: No

Clinic visit attendance at six weeks and six months postpartum

Table 6 in Appendix E summarizes the results of the univariate and multivariate logistic regression models looking at the effects of different factors on clinic attendance at both six weeks and six months postpartum. In the univariate analysis, women between 35 and 60 years old were approximately three and a half times more likely than women between 18 and 24 years old to attend the clinic at both time points (unadjusted OR=3.55, p=0.024), but this association was not as significant in the multivariate analysis (adjusted OR=3.44, p=0.071). In the univariate analysis, women who had previously received PMTCT treatment or prophylaxis were 39% less likely than women who had not previously received any PMTCT treatment or prophylaxis to attend the clinic at both time points (unadjusted OR=0.61, p=0.060), but this association was also not significant in the multivariate analysis (adjusted OR=0.63, p=0.207). Women who were previously diagnosed with HIV before the current pregnancy were twice as likely as women who were newly diagnosed with HIV to attend the clinic visit at both time points in the univariate and multivariate analyses (unadjusted OR=2.04, p=0.006 and adjusted OR=2.03, p=0.031). Similarly, women who had spent more than 30 days on ART during pregnancy were more than twice as likely as women who had spent 30 days or less on ART during pregnancy to attend the clinic at both time points, and the association was significant in the univariate and multivariate analyses (unadjusted OR=2.19, p=0.002 and adjusted OR=2.05, p=0.020). Having a partner who was counseled and test for HIV in ANC, having attended at least one psychosocial support group meeting between ART initiation and six months postpartum and 95% or 80% adherence at the first ANC visit post-ART initiation were all associated with clinic visit attendance at both time points (unadjusted OR=1.66, p=0.065, unadjusted OR=1.75, p=0.043, unadjusted OR=1.91, p=0.002 and unadjusted OR=1.82, p=0.005, respectively) , but these associations were not significant in the multivariate analysis.

Predictive models for clinic visit attendance at six weeks postpartum and months postpartum

Table 9 lists the factors included in the predictive models obtained from the backwards selection process for each definition of adherence. Previous PMTCT program experience, having been previously diagnosed with HIV, having a partner who was counseled and tested for HIV in ANC and time spent on ART in pregnancy were predictive of attendance at both time points in all four models. Previous PMTCT program experience was associated with between a 39% (model 4) and 32% (model 2) decreased odds of attendance at both clinic visits while women who had been diagnosed with HIV prior to the current pregnancy were approximately twice as likely as women who were newly diagnosed with HIV to attend the clinic at both time points. Having a partner who was counseled and tested for HIV in ANC was associated with between a 71% (model 1) and 85% (model 2) increased odds of clinic attendance at both time points and women who had initiated ART more than 30 days before delivery were approximately twice as likely as women who had initiated ART later in pregnancy to attend the clinic at both time points. Higher education level was actually associated with a 32% decreased odds of attendance at both clinic visits in models 1, 2 and 3 while attending at least one psychosocial support group meeting between ART initiation and six months postpartum predicted attendance at both clinic visits in every model with the exception of model 1. Good adherence in ANC was associated with an approximately 50% increased odds of attendance at both time points in model 2 and model 4.

Table 9: Predictive models for clinic visit attendance at six weeks and six months postpartum*

Model 1: 95% adherence (nonadherence=<95%medication adherence)		
Factor	**Adjusted OR (95% CI)**	**p-value**
Education	0.68 (0.43, 1.07)	0.095
Previous PMTCT	0.65 (0.38, 1.13)	0.127
Previous HIV diagnosis	1.94 (1.13, 3.44)	0.017
Partner counseled/tested for HIV	1.71 (0.97, 3.03)	0.063
Time on ART in pregnancy	2.10 (1.24, 3.57)	0.006
Model 2: 95% adherence (nonadherence=<95% adherence or returned without pill box/did not return)		
Education	0.68 (0.43, 1.10)	0.114
Previous PMTCT	0.68 (0.39, 1.20)	0.181
Previous HIV diagnosis	1.81 (1.04, 3.15)	0.037
Partner counseled/tested for HIV	1.85 (1.02, 3.35)	0.043
PSS group attendance	1.73 (0.94, 3.20)	0.079
Time on ART in pregnancy	2.01 (1.16, 3.46)	0.012
Adherent in ANC	1.49 (0.95, 2.34)	0.084
Model 3: 80% adherence (nonadherence= <80% medication adherence)		
Education	0.68 (0.43, 1.08)	0.102
Previous PMTCT	0.62 (0.36, 1.08)	0.094
Previous HIV diagnosis	1.98 (1.15, 3.43)	0.014
Partner counseled/tested	1.74 (0.98, 3.08)	0.058
PSS group attendance	1.63 (0.90, 2.98)	0.108
Time on ART in pregnancy	1.99 (1.17, 3.40)	0.011
Model 4: 80% adherence (nonadherence= <80% adherence or returned without pill box/did not return)		
Previous PMTCT	0.61 (0.36, 1.04)	0.069
Previous HIV diagnosis	1.78 (1.06, 3.00)	0.030
Partner counseled/tested for HIV	1.83 (1.03, 3.26)	0.039
PSS group attendance	1.81 (1.02, 3.23)	0.044
Time on ART in pregnancy	1.82 (1.07, 3.11)	0.027
Adherent in ANC	1.51 (0.96, 2.36)	0.072

*Reference groups: 1) Education: None/primary; 2) Previous PMTCT: No; 3) Previous HIV diagnosis: No; 4) Partner counseled/tested: No; 5) Time on ART in pregnancy: ≤ 30 days; 6) PSS group attendance: None; 7) Adherent in ANC: No

DISCUSSION

This study found that of the 1,106 HIV-infected pregnant women who required ART initiation, 79% were enrolled in the Option B+ program and of these, only 68% attended more than one visit in ANC. These findings were consistent with the Malawi Option B+ program in 2014 which resulted in approximately 80% of HIV-infected pregnant women being initiated on treatment.[15] However, these results also highlight the gaps that continue to exist in the PMTCT care and treatment cascade, even under the Option B+ approach.

Trends and predictors of adherence

This study found that ART adherence decreased over time from 52.1% in ANC to 44.8% at six months postpartum using the 95% adherence cutoff and from 64.4% in ANC to 56.9% at six months postpartum using the 80% adherence cutoff. This decrease in ART adherence over time from pregnancy to the postpartum period is consistent with findings from the meta-analysis conducted by Nachega et al. looking at PMTCT adherence over time that reported a drop in medication adherence from 73.5% during pregnancy to 53% in the postpartum period.[16] Similarly, a study in western Uganda also looking at Option B+ adherence in 2014 found that only 51% HIV-infected women who initiated ART exhibited greater than or equal to 95% adherence during pregnancy.[11] While it is possible that adherence to ART under Option B+ has improved in the three years since this cohort of women was enrolled into the program, the low proportion of adherent women at both time points as well as the significant decrease in adherence over time merit an in-depth exploration of the factors associated with poor adherence as well as interventions targeted at improving and sustaining adherence over time. This study also found that 17.1% of HIV-infected pregnant women and 14.8% of HIV-infected mothers had unknown adherence at ANC and six months postpartum, respectively. Pill count adherence could not be calculated for these women if they had not brought back their pill boxes or if the number of pills dispensed at the last clinic visit could not be determined by the PMTCT counselor at the current visit. Pill counts have been found in the literature to correlate more significantly with viral load and CD4 counts than patient self-report[17] and are often used in resource limited settings where viral load and CD4 count measures are not routinely performed. This study indicates that additional counseling about the importance of returning to clinic with the pill box or interventions to improve the pill box return rate may be necessary if this measure of adherence is to be relied upon in the future. Furthermore, additional training of PMTCT counselors may be beneficial to improve the pill box return rate and to assist counselors with successfully measuring and

recording pill count adherence at each clinic visit. Adherence at six months postpartum could also not be determined for 18.3% of women who did not return within the established five to seven month visit window. This finding was in line with results of other studies looking at retention in care under Option B+, where loss to follow-up ranged from 11.2% in Malawi[18] to 38% Mozambique[19] by six months since ART initiation and 24% in South Africa[20] by 12 months after delivery.

This study found that adherence could not be calculated for the majority of HIV-infected mothers presenting for care at six weeks postpartum because the number of pills dispensed at labor and delivery (i.e. the last visit before six months postpartum) could not be ascertained for 51.7% of women and 21.5% did not return to the clinic at six weeks postpartum. While the issue of unknown adherence at six weeks postpartum may be specific to Mulago National Referral hospital, it once again underlines the limitations of pill count procedures for determining medication adherence. Routine viral load testing for PMTCT is currently being rolled out at Mulago, but attention should be paid to the gap in pill count adherence at six weeks postpartum and data collection procedures at labor and delivery should be addressed and improved to address this gap.

The models obtained from this study found that baseline CD4 cell count, previous PMTCT experience, disclosure, education, employment status and HIV diagnosis prior to the current pregnancy were predictive of good adherence in ANC. Women with CD4 cell counts greater than 350 cells/mm^3 were 50% less likely than women with lower CD4 cell counts to be adherent in ANC and similarly, women with previous PMTCT program experience were 40% less likely than women who were completely ART-naïve to be adherent in ANC. These findings suggest that some challenges may have existed with respect to transitioning to Option B+ from the previous Option A approach where HIV-infected pregnant women with CD4 cell counts greater than 350 cells/mm^3 were counseled about and initiated on PMTCT prophylaxis as opposed

to lifetime treatment for their own health. These findings signify the importance of effective counseling at the time of ART initiation to ensure that pregnant women who may feel otherwise healthy or who have had experience with previous PMTCT guidelines are fully aware of the Option B+ treatment regimen and the importance of maintaining good adherence at all times. In this study, HIV status disclosure was associated with a 49% to 96% increased odds of adherence at the first ANC visit post-ART initiation. This result was consistent with findings in the PMTCT adherence literature. For example, one study in Zimbabwe looking at factors affecting uptake of PMTCT services found that women who had disclosed their status were 30% more likely to obtain treatment or prophylaxis for PMTCT.[21] In this study, women with at least a secondary level of education were between 50% and 90% more likely to be adherent in ANC than women with lower levels of education. This finding was consistent with the study from Western Uganda that found higher education level to be associated with increased odds of retention in care under the Option B+ program.[11] This study found that having been diagnosed with HIV prior to the current pregnancy was associated with a 47% to 66% increased odds of adherence in ANC but that 74.2% of HIV-infected pregnant women presenting for ANC were obtaining their HIV status for the first time. These findings are relevant to the Option B+ test-and-treat approach where HIV-infected pregnant women are expected to initiate ART immediately after diagnosis and consistent with findings from qualitative studies that have shown same-day initiation of treatment, to be a challenge for successful Option B+ program implementation.[22] In this study, women who reported being employed were between 31% and 48% less likely to be adherent in ANC than women who were not employed at the first ANC visit post-ART initiation. While this result may seem counterintuitive at first, qualitative studies have shown that fear of stigma or discrimination is associated with poor medication adherence.[23] It is possible that women who work outside of the home are fearful of having their HIV status exposed at work and therefore do not take ART at work. Similarly, women enrolled in the Option B+ program are counseled by

PMTCT counselors to take ART at the same time every day. It is possible that being employed outside of the home is more disruptive to a daily routine that allows for consistent adherence.

The only factor found to predict adherence at six months postpartum in this study, regardless of the definition for adherence that was used in the prediction model, was adherence at the first ANC visit post-ART initiation. Women who were adherent at the first ANC visit post-ART initiation were at least twice as likely to be adherent at six months postpartum than women who were not adherent in ANC. One systematic review looking at interventions to improve postpartum retention in PMTCT and ART care found that interventions using phone calls or text messages improved early postpartum retention in PMTCT care and treatment, different levels of integration of PMTCT and ART services had mixed effects on postpartum program retention and that several other trials aimed at improving postpartum retention in care were ongoing but had yet to publish results.[24] However, the results of this study indicate that long-term postpartum ART adherence might be significantly improved if efforts are focused on continued improvement of adherence in the antenatal period, especially since only 52.1% and 64.4% of women were at least 95% and 80% adherent, respectively, in this study.

The only factor in this study found to predict sustained adherence in ANC and at six months postpartum regardless of the definition of adherence specified in the prediction model, was disclosure in the antenatal period, by the first visit post-ART initiation. HIV-infected pregnant women who had disclosed their HIV status to at least one person by this clinic visit were up to two times more likely than women who had not disclosed their status to be adherent in ANC and sustain this good adherence at six months postpartum. Since only 58.3% of HIV-infected pregnant women had disclosed their HIV status by the first ANC visit post-ART initiation, interventions aimed at facilitating early disclosure may be beneficial for improving adherence in the antenatal period and sustaining good adherence through at least six months postpartum.

Trends in clinic visit attendance

Of the 480 women included in this study at the first ANC visit post-ART initiation, 71.9% of women presented for care at six weeks postpartum and 73.8% presented for care at six months postpartum. Predictive models for clinic visit attendance at six weeks postpartum found that having been diagnosed with HIV prior to the current pregnancy and having good adherence in ANC were strong predictors of clinic visit attendance at six weeks postpartum. HIV diagnosis prior to the current pregnancy was associated with 58% to 91% increased odds of attendance at six weeks postpartum. This trends was consistent with the study from Western Uganda that found women who were previously diagnosed with HIV before the current pregnancy to be more than three times as likely as women who were newly diagnosed with HIV to be retained in care.[11] Good adherence in ANC was associated with a 61% to 70% increased odds of attendance at six weeks postpartum. Although little has been presented in the literature about the association between adherence in pregnancy and clinic visit attendance in the postpartum period, this study suggests that more research should be conducted to explore the validity and reliability of this association. In most of the prediction models resulting from this study, older age was also predictive of attendance at six weeks postpartum. This result was similar to what was found in a study in Zimbabwe looking at factors affecting program retention where older women were less likely to be lost to follow-up than younger women initiating Option B+ for PMTCT.[25] This suggests that specifically targeting younger women for PMTCT counseling and support services may lead to improved program retention in the postpartum period. Most of the prediction models in this study also found that previous PMTCT program experience was associated with an approximately 50% decreased odds of attendance at six weeks postpartum. Some research has found that facility resource constraints and a lack of client-friendly services are barriers to successful PMTCT program implementation.[26] It is possible that negative experiences with previous PMTCT programs may have affected program retention in the postpartum period in this

study, but a more in-depth understanding of the previous experiences of HIV-infected women with PMTCT programs may be necessary to better understand this association.

Predictive models for attendance at six months postpartum found a number of factors predicting attendance at this time point, including employment status, psychosocial support group meeting attendance, time since ART initiation in pregnancy and attendance at six weeks postpartum. Similarly to the association with adherence, employment outside of the home predicted an approximately 40% decreased odds of attendance at six months postpartum. It is possible that inflexible work schedules or financial need took precedence over clinic visit attendance at six months postpartum, but these results indicate that more should be done to support the HIV care and treatment of working pregnant women and mothers. Although only 18% of women attended at least one psychosocial support group meeting between treatment initiation in pregnancy and six months postpartum, women who did attend are more than twice as likely as women who did not attend to present for a clinic visit at six months postpartum. While it is possible that receiving this psychosocial support has an effect on program retention, it is also possible that women who were more likely to attend psychosocial support group meetings were the same women who would likely attend regularly scheduled clinic visits. It would therefore be necessary to conduct additional research specifically isolating the effects of psychosocial support interventions on program retention in order to better understand this association. HIV-infected pregnant women who initiated ART more than 30 days before delivery were more than three times as likely as women who had initiated ART less than 30 days before delivery to attend the clinic at six months postpartum. It is possible that initiating ART earlier in pregnancy allows for women to become more accustomed with the Option B+ program or that initiating ART earlier in pregnancy facilitates stronger relationships between the HIV-infected women and the care providers, therefore leading to improved clinic visit attendance at six months postpartum. It was also found in this study that attendance at six weeks postpartum was a strong predictor of

attendance at six months postpartum, signifying that interventions aimed at improving early postpartum program retention could have long-lasting effects on program retention in the later postpartum period and that more should be done to improve attendance at six weeks postpartum.

This study also found previous PMTCT program experience, previous diagnosis with HIV, time since ART initiation in pregnancy and psychosocial support group meeting attendance to be strong predictors of sustained clinic visit attendance at both six weeks and six months postpartum. In addition, although only 20% of women had partners who had been counseled and tested for HIV in ANC, partner counseling and testing was associated with between 71% and 85% increased odds of attending both clinic visits in the postpartum period. This finding is supported in the literature, where male partner involvement in ANC was found to be associated with improved uptake of PMTCT interventions[27] and decreased infant HIV infection.[28] The study findings support the need for a more in-depth understanding of the barriers to male partner involvement and interventions targeted at increasing male partner involvement in PMTCT programs.

Limitations

It is important to address the various limitations of this study. First, this study did not include information about the HIV-infected pregnant women who were enrolled in care during the antenatal period but who did not return for a second visit before delivery or who were lost to follow-up after this initial ANC visit. For the purposes of program retention, it would have been useful to analyze and compare the baseline characteristics of these women to those included in the study to gain an improved understanding of the factors that affect early program retention during pregnancy. Similarly, baseline clinical and demographic information for women who did not return for a second ANC visit would have been helpful to assess potential confounding in the study.

Next, utilization of pill counts as the measure of medication adherence was prone to measurement errors and resulted in incomplete adherence data at six weeks postpartum. The six week postpartum visit is crucial in the PMTCT care and treatment cascade since this is when infant testing most commonly occurs, and an understanding of adherence in the early postpartum period is crucial for improving the current understanding of when adherence is most challenging and when the risk for nonadherence and/or vertical HIV transmission is highest under the Option B+ approach. Similarly, pill counts could not be performed for women who did not bring back their pill boxes, and it is possible that these women were less likely to be adherent than women who successfully brought back the pill boxes at each visit, thus biasing the adherence results of the study. Nevertheless, pill counts are commonly relied upon in resource-limited settings are considered to be more objective and more closely associated with viral load measures than patient self-report techniques.

Another limitation of this study is that the effects of time-varying exposures on adherence and program retention could not be captured utilizing the data regularly collected and entered into the PMTCT database. For example, it is possible for factors such as disclosure and male partner involvement to change over time, potentially impact changes in adherence and program retention in the postpartum period. This limitation was brought up to PMTCT clinic staff at Mulago and has led to preliminary discussions about updating the PMTCT visit forms to include questions about changes to disclosure and male partner involvement over time.

Next, this study was not explicitly powered to detect the effects of the various factors of interest on adherence and clinic visit attendance since the study population came from the existing PMTCT program in 2014. For instance, only 18% of HIV-infected women included in this study had ever attended a psychosocial support group meeting between ART initiation in pregnancy and six months postpartum and only 20% had a partner who was counseled and test for HIV in ANC, so the effects of these factors on adherence and clinic visit attendance may be

uncertain. However, the low rate of psychosocial support group meeting attendance as well as the low level of male partner involvement in ANC are important findings that merit additional research to better understand how rates of psychosocial support group utilization and male partner involvement may be improved in the future.

A final limitation of this study is that pill count adherence measures greater than 100% were counted as adherent in this study. This was only the case for approximately 3% of adherence measures in ANC and 5% of adherence measures at six months postpartum. Further exploration of the pill count practices of PMTCT counselors, potentially through qualitative research, may be helpful to understand the significance of a pill count measure greater than 100%.

CONCLUSION

The goal of this study was to improve the current understanding of changes to Option B+ medication adherence and clinic visit attendance over time from pregnancy through six months postpartum for a cohort of HIV-infected women at Mulago National Referral Hospital who were first-time initiators of Option B+ for PMTCT in 2014. This study found that Option B+ adherence was relatively low and decreased over time while clinic visit attendance at six weeks postpartum and six months postpartum remained consistent at just over 70%. Since the large majority of women enrolled into the PMTCT program at Mulago are done so during pregnancy and few additional HIV-infected women present for care in the postpartum period, it is crucial to continue efforts to improve adherence during pregnancy in this setting and to tailor adherence and program retention interventions for the antenatal period. It is also equally important to continue efforts for further understanding the barriers and facilitators to postpartum HIV care and treatment in the early and late postpartum periods, especially as Option B+ implementation continues throughout sub-Saharan Africa.

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PART THREE:

"It is the only way to stay healthy, live longer and have a child who is HIV negative": Understanding the programmatic and adherence experiences of HIV-infected women receiving Option B+ for preventing mother-to-child transmission of HIV from ART initiation through six weeks postpartum in Kampala, Uganda

ABSTRACT

Option B+ is the current strategy for eliminating vertical HIV transmission in resource-limited settings. Long-term adherence and program retention are two important outcomes to measure when considering the success of Option B+ program implementation. A number of studies have reported Option B+ adherence and program retention rates at different time points and in various settings, yet limited research exists aimed at gaining an in-depth understanding of the factors affecting Option B+ ART adherence and program retention over time. This study utilized a series of longitudinal in-depth interviews with 16 HIV-infected women in the first month of ART initiation during pregnancy and again at six weeks postpartum to examine the changes in Option B+ adherence and clinic visit experiences for women seeking care for PMTCT at the Mulago National Referral Hospital in Kampala, Uganda. Adherence and clinic visit attendance for all participants remained consistently high throughout pregnancy and the early postpartum period, and a number of themes emerged: 1) effective messaging and counseling at the time of HIV testing and treatment initiation; 2) reliance on health workers for support between clinic visits; 3) disclosure to an HIV-infected person; 4) variability of male partner involvement; 5) modified behaviors to prioritize health and ART adherence; 6) concern with unwanted HIV status exposure and 7) a desire for a healthy baby and a healthy life. Interviews at six weeks postpartum uncovered a number of factors that continued to affect the ART adherence and Option B+ program experiences of the participants: 1) consistent support from health workers; 2) limitations of the health facility; 3) ongoing support after disclosure; 4) variability of male partner involvement; 5) normalization of daily ART and 6) a continued desire for a healthy baby and a healthy life. As Option B+ program implementation continues, emphasis should be placed on continued training of health workers, the importance of counseling and support services at the facility level, ensuring satisfactory health service delivery, promoting HIV status disclosure and persistent HIV education beginning in pregnancy and through the early postpartum period.

INTRODUCTION

Option B+ is the current World Health Organization (WHO) strategy for eliminating vertical HIV transmission. Considered a universal strategy for the treatment of HIV-infected pregnant women and prevention of mother-to-child transmission (PMTCT), it includes the provision of triple antiretroviral therapy (ART) for HIV-infected pregnant women at the antenatal clinic (ANC) regardless of clinical stage or CD4 cell count, to be continued for life.[1] Under this recommendation, HIV-exposed infants are expected to receive nevirapine (NVP) or zidovudine (AZT) syrup from birth through six weeks postpartum. The first HIV test for HIV-exposed infants is also generally administered at the six-week postpartum clinic visit. Based on preliminary PMTCT data from Malawi[2], it was originally believed that the Option B+ approach could help overcome operational and programmatic complexities that countries had been experiencing with PMTCT program implementation and that had been obstacles for meeting the 2015 deadline for eliminating maternal-to-child transmission (MTCT) set by the Global Plan.[3] The Uganda Ministry of Health (MoH) began implementing Option B+ for PMTCT as the national approach for HIV treatment and prophylaxis of pregnant women and mothers in October 2012. While Option B+ has been scaled nationally and across sub-Saharan Africa, adherence to life-long ART initiated during pregnancy and continued in the postpartum period continues to be a challenge in many settings throughout the country and in the region, and rates of program retention may vary. For example, in its first year of implementation the Option B+ program in Malawi reported a large proportion of women lost to follow-up six months after ART initiation, with most losses occurring in the first three months of therapy and many women recorded as initiating treatment, accepting their first month of ART and then never returning for care.[4] Similarly, data from the Mulago National Referral Hospital in Kampala showed that while a majority of pregnant women were presenting for ANC, only 70% of HIV-infected pregnant women who were initiated on Option B+ returned for at least one visit in six weeks.[5]

As Option B+ implementation progresses across sub-Saharan Africa, data continue to be collected about long-term medication adherence and program retention in various settings, including Uganda. However, quantitative research studying ART adherence and Option B+ program retention should be coupled with qualitative studies exploring the changing experiences of HIV-infected pregnant women and mothers with the Option B+ program over time. One qualitative report addressing HIV-infected women on Option B+ in Malawi and Uganda found that community engagement, income-generating activities and male partner involvement may be key factors affecting the success of Option B+ program implementation.[6] Similarly, the PURE Malawi Consortium found through in-depth interviews with women enrolled in Option B+ and focus group discussions with health care workers that lack of male involvement, concerns with the test-and-treat approach and fears surrounding lack of privacy and confidentiality at the health centers may be contributing to the rates of loss to follow-up observed in some areas of Malawi.[7] A different qualitative study in western Kenya looking specifically at health facility challenges surrounding Option B+ implementation found that same-day initiation of treatment, insufficient health worker training, lack of health worker confidence in the Option B+ program, facility resource constraints and a lack of client-friendly services were challenges to success of the Option B+ program.[8]

The existing qualitative Option B+ research highlights some important factors that may be affecting medication adherence and program retention at specific time points, usually at ART initiation. However, little is known about the experiences of HIV-infected women enrolled in Option B+ in the postpartum period and how their experiences with the program have changed since pregnancy. This study aims to qualitatively explore the changing experiences of HIV-infected women enrolled in the Option B+ program from pregnancy through six-weeks postpartum at Mulago National Referral Hospital in Kampala, Uganda and to further understand

how these changing experiences may affect Option B+ medication adherence and program retention over time.

METHODS

In-depth interviews were conducted with 16 HIV-infected pregnant women who were at least 18 years old and in the last trimester of pregnancy at the time of their first ANC visit. All participants were first-time initiators of Option B+ for PMTCT at Mulago National Referral Hospital and part of the "Friends for Life Circles" study, a randomized controlled trial aimed at assessing the effects of a community peer support group intervention on long-term clinic visit attendance, ARV drug adherence and viral suppression for HIV-infected pregnant women and mothers. For this qualitative study, the first 16 HIV-infected pregnant women in their last trimester of pregnancy who provided informed consent were purposively sampled from the control arm of the "Friends for Life Circles". Participants in the control arm received the MoH standard of care for PMTCT. A sample size of 20-30 individuals has been recommended to reach saturation of themes for in-depth interviews,[9] but a smaller sample size can be justified when the same participants are being interviewed at multiple time points.[10]

For each participant, basic demographic and clinical information was collected from the PMTCT database at Mulago National Referral Hospital. Adherence information for each participant at each study visit was also recorded. As per the "Friends for Life Circles" study protocol, a visual analog scale (VAS) was used for participants to indicate their adherence in the last 30 days. As part of routine data collection at Mulago, clinic counselors measure and record pill count adherence in every patient chart. This routinely recorded adherence measure was entered into the PMTCT database starting in 2015 and this information was also utilized to assess adherence of each participant. Participants were interviewed first during pregnancy, one month after their first ANC visit, and again at six-weeks postpartum. Interviews lasted between 30

minutes to one hour and took place upon completion of all other study activities. Interviews conducted during pregnancy focused on experiences with HIV testing and ART initiation, clinic visits and health workers, male partner involvement, HIV status disclosure, stigma and social networks and understanding how these experiences might relate to ART adherence and program retention. Interviews conducted six-weeks postpartum focused on experiences with infant HIV testing and initiation of infant prophylaxis, clinic visits and health workers, male partner involvement, HIV status disclosure, stigma and social networks and understanding how changes in experiences between pregnancy and six-weeks postpartum might relate to ART adherence and program retention. All interviews were conducted with the aid of semi-structured field guides. Transcript summaries were also provided to the interview team prior to conducting the six-week postpartum interviews so that appropriate, participant-specific probes and follow-up questions could be asked at the time of each follow-up interview.

All interviews were conducted by one of the local co-investigators or one of two study counselors who had received training on proper interview techniques, use of the semi-structured field guides and the goals of the study prior to study initiation. The semi-structured field guides can be found in Appendix F. All interviews were conducted in Luganda and digitally recorded after obtaining approval from each participant. Interviews were then directly transcribed and translated into English for analysis by a trained qualitative analysis consulting team with experience in previous NIH or PEPFAR-supported qualitative research studies. The in-depth interview team consisting of the study coordinator and the three interviewers met weekly with the first author prior to and during the initial data collection period and then monthly as data collection progressed, to practice interviewing techniques, discuss arising themes and refine the interview guides for a more iterative research process.

Thematic analysis was used to analyze the transcripts.[11] Transcripts were reviewed and read over multiple times as they were received, and analytic memos were written to reflect on

developing patterns, categories, themes and concepts in the data. The analytic memos were then coded and categorized according to their content. The coding and categorization process was based both on emergent themes from the data and a priori themes based on the interview guides. All transcripts were coded using the scheme developed from the analytic memos, with additional codes added as they appeared, if considered relevant to addressing the study goal. Transcripts from interviews at pregnancy and six-weeks postpartum were coded and analyzed separately, and another series of analytic memos and codes were developed to reflect the changes in experiences of participants over time from pregnancy to six-weeks postpartum. Coding was performed manually and tracked through the use of multiple Excel spreadsheets.

Ethical approval to conduct this research was obtained from the institutional review boards of the Johns Hopkins University School of Medicine, the University of California San Francisco, the Joint Clinical Research Centre and the Uganda National Council for Science and Technology.

FINDINGS

Demographics, adherence and clinic visit attendance

At the time this manuscript was written, a total of 16 ANC interviews and eight six-week postpartum interviews were completed, transcribed and translated for analysis. Table 1 below summarizes the demographic characteristics and pill count adherence of each participant. The age of the participants ranged from 18 to 33 and the median participant age was 24. All participants resided in either the Kampala District or the Wakiso District of the Central Region of Uganda. 12 of the 16 participants reported being married, three reported being single and marital status for one participant was missing. The majority of the participants reported a secondary education and were either housewives or self-employed. This was the first pregnancy for only four participants. The median CD4 count at ART initiation was 367.5 cells/mm^3.

Table 1: Socio-demographic characteristics of participants

Characteristic	N (%)
Age (years)	
Median	24
Mean (SD)	25.3 (4.5)
Range	18-33
Education	
None/primary	3 (18.8)
Secondary	10 (62.5)
Post-secondary	1 (6.3)
Missing	2 (12.5)
Occupation	
Housewife	6 (37.5)
Self-employed	3 (18.9)
Not employed	1 (6.3)
Other	4 (25.0)
Missing	2 (12.5)
Marital Status	
Married	12 (75)
Single	3 (18.9)
Missing	1 (6.3)
Place of residence	
Kampala	8 (50%)
Wakiso	7 (43.8)
Missing	1 (6.3)
Gravidity	
First pregnancy	4 (25)
Two or more pregnancies	11 (68.8)
Missing	1 (6.3)
Median Baseline CD4 (cells/mm$^{3)}$	
Median	367.5
Mean (SD)	376.6 (147.7)
Range	173-670
Pill-count adherence at ANC visit	
100% adherence	7 (43.8)
95-99% adherence	3 (18.8)
<95% adherence	0 (0.0)
Could not be calculated	5 (31.2)
Missing	1 (6.3)
Pill count adherence at 6 weeks postpartum	
100% adherence	3 (37.5)
95-100% adherence	1 (12.5)
<95% adherence	0 (0.0)
Could not be calculated	4 (50.0)
Missing	0

According to the VAS adherence measure, all participants reported 100% medication adherence at the ANC visit one month post-ART initiation and at six weeks postpartum. Using the pill count approach, all participants for whom adherence was able to be measured displayed

an adherence rate of 95% or better at both study visits, but adherence could not be calculated for five participants in ANC and 4 visits at six weeks postpartum.

Based on information uncovered in the interviews, six of the 16 participants reported having missed one dose at the time of the study visit. Only two participants had ever missed a scheduled clinic visit. For the eight participants for whom the six-week postpartum in-depth interview transcripts could be reviewed, three out of eight participants reported having missed one dose at the time of the study visit, and in all three cases it was on the day of labor and delivery. One participant reported missing one scheduled clinic visit since her baby was born.

Option B+ in the antenatal period

Some factors were found to notably influence the experiences of HIV-infected women with Option B+ during pregnancy. These factors could be grouped into seven key themes: 1) effective messaging and counseling at the time of HIV testing and treatment initiation; 2) reliance on health workers for support between clinic visits; 3) disclosure to an HIV-infected person; 4) variability of male partner involvement; 5) modified behaviors to prioritize health and ART adherence; 6) concern with inadvertent HIV status disclosure and 7) a desire for a healthy baby and a healthy life. The Option B+ program logistics was also a factor affecting the PMTCT experience during pregnancy.

<u>Effective messaging and counseling at the time of HIV testing and treatment initiation</u>

15 of the 16 participants interviewed during pregnancy stated that the positive HIV test result was unexpected, and most expressed fear, shock or sadness upon receiving their results. As one participant describes:

> *Health worker, I never expected it because in December on the 15th I went to Nsambya Hospital and I was tested and found HIV negative and didn't have HIV…When I was told*

> *[that I am HIV positive], I got shocked and broke down and cried…* (27-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-09)

In addition to results being unexpected, a number of participants also described confusion about the implications of a positive HIV test and difficulties with ART initiation due to the size of the tablet. As one participant explained:

> *"When I was pregnant, I came here and I was tested and was told that I am HIV positive, but I first denied the results and I requested the health worker to re-do the test. She tested me again and confirmed to me that I was HIV positive…I was told to start medication but I first felt that the tablets were too big and I never started on that day…I would keep asking myself, "Who has infected me? How come that I am HIV positive yet I do not have support!"* (22-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-06)

Despite these feelings of fear and uncertainty, the counseling services provided on this day and the messaging surrounding being HIV positive and initiating ART provided encouragement to the participants. With respect to overcoming the distress associated with being found HIV positive, participants consistently reported that hearing from health workers about others who were also infected with HIV and doing well helped them to overcome their initial fear about their own HIV status. For example, one participant talks about how speaking with health workers who were themselves infected with HIV helped her to gain confidence:

> *They counseled me in a special way and I went home confident…What I mean is that they explained to me that they were also going through the same, that I will live a good life, I will be able to give birth to an HIV-negative baby, "That's how I am too." And I got encouraged. I got to know I am not alone. Even health workers get infected…something I didn't know.* (24-year old HIV-infected pregnant woman with 100% pill count adherence at study visit IDI-08)

Another participant described a similar experience in which health workers encouraged her after she received her HIV test result by talking to her about others who are also infected:

> *They told me that I should calm down and start taking drugs. I first got some fear and asked myself, "Up to when will I be taking this medicine?" A health worker told me, "You are not the only infected person; you are so many; others are coming."…I calmed down and the health worker counseled me and gave me drugs.* (30-year old HIV-infected pregnant woman with missing pill count adherence at study visit, IDI-07)

The same participant went on to describe the effective way in which health workers were able to implement the test-and-treat approach associated with the Option B+ program requiring HIV-infected pregnant women to initiate treatment on the day they were found to be HIV positive, as well as additional messaging that was often used to motivate the HIV-infected pregnant women to initiate treatment:

> *The health workers helped me so much…so much…because I had refused and the counselor had already put on my file that I am not ready to start, but she kept on asking, "Are you sure?" I said, "Yes…" and she repeated it three times, "Aren't you going to take medicine?" And I said, "No…" They later got another health worker who took me aside and started counselling me, "You have to take your medication because you will give birth to an HIV positive baby. Yet now it's easy for you to take medication without anyone noticing. If you give birth to an HIV positive baby we shall give you medication for your baby and everyone will be able to tell that you are infected, yet if you had started taking, it would have saved the baby." I then was able to start taking my medicine...At first I felt bad because it was as though they were forcing me, "Take the medication." But later I realised that it was going to help me and my baby. I calmed down and accepted that they should give me the medicine and I started taking. I first felt bad and I wasn't listening to anything they were saying. I later felt good because they were helping me and my baby. They were not benefiting anything; they do not know me, they do not know where I come from, they just wanted to save my life and the life of the child inside.* (30-year old HIV-infected pregnant woman with missing pill count adherence at study visit IDI-07)

The excerpt above highlights the persistence of the health workers with respect to initiating treatment for HIV-infected pregnant women but also hints at the challenge that may arise if HIV-infected pregnant women feel forced into making a decision to initiate ART. In this case and in the case of many participants, the persistence exhibited by the health workers was viewed as a positive characteristic of the overall HIV test-and-treat experience that promoted ART initiation. The passage above also illustrates additional messaging put forth by the health workers attending to the HIV-infected pregnant women that participants described as convincing with respect to ART initiation. Most of the participants stated the desire to give birth to an HIV-negative baby as a strong motivator for initiating ART and throughout the ANC interviews, a number of participants expressed a desire to keep their HIV status hidden from others, feelings that were

taken into account by health workers when counseling their clients about the benefits of initiating ART for PMTCT right away.

In contrast, another participant described a different counseling approach used by the health workers to ensure ART treatment initiation. Although the approach was different, it was clear that the goal of the counseling and the general message of ART adherence for the purpose of preventing vertical transmission remained the same.

> *I was first given some time to cool down…later I was sent to another room where I also received counselling. But all those counselling sessions were pointing at one aim; having to take ARVs in case I want to give birth to an HIV negative baby. I was told that I have to take ARVs to help me stay healthy and protect my baby, and I accepted*. (33-year old HIV-infected pregnant woman with missing pill count adherence at study visit, IDI-015)

In the same interview, the participant talked about the positive effect counseling had on her clinic experience the day she tested positive for HIV. In this interview as in others, receiving immediate counseling and support from health workers was described as an effective strategy for initiating HIV-infected pregnant women on treatment and promoting ART adherence.

> *I felt good and when I went back home I told them that I had met health workers who are so nice that I had never met before. If it were not for them I would have either refused to take medicine or did abortion. They counseled me that I can be able to give birth to an HIV negative baby if I take my ARVs well. It gave me courage to start taking ARVs and do what I had been told, which I accept and started doing it.* (33-year old HIV-infected pregnant woman with missing pill count adherence at study visit, IDI-015)

<u>Reliance on health workers for support between clinic visits</u>

The large majority of participants described having good relationships with the health workers at the PMTCT and ANC clinics during their pregnancies and many identified the health workers as their primary source of support for their pregnancies or HIV status. The health workers often called participants between clinic visits and participants also felt comfortable to call the health workers. As one participant explained when asked about seeking support outside of the hospital:

> *Apart from going back to the health workers, I do not go anywhere else. I usually call health workers and explain the problem I have and they advise me on what to do. At*

> *whatever time you call them, because they gave me their telephone number. You can call and explain how you feel and she tells you what to do, asks you to go to the clinic if the situation does not change* (30-year HIV-infected pregnant woman with missing pill count adherence at study visit, IDI-07).

Maintaining contact by phone between clinic visits helped participants to feel close to the health workers and allowed them to view the health workers as more than health care providers. Many participants described forming meaningful relationships with the health workers that served as motivation for staying adherent to ART.

> *They [the health workers] do call me…one thing that has made it easy is that some of the health workers became my friends. I felt that since a health worker has taken her time to call and counsel me, I should be strong and take my medication.* (24-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-013)

In one instance, a participant described how her husband worked together with the health worker between clinic visits to ensure the participant was adhering to ART. The health worker would maintain phone contact with the participant through her husband and work with him to support her with HIV treatment:

> *Participant: And a nurse from this side who would also call my husband and remind him about the time we chose for ARVs.*
> *Interviewer: Your husband and the nurse?How did they do it?*
> *Respondent: The nurse would keep calling my husband on the time we agreed to be taking ARVs. She would remind him and then he also reminds me.*
> *Interviewer: And tell him what?*
> *Respondent: "It is time."*
> *Interviewer: Even when it is at night?*
> *Respondent: Yes.* (18-year old with 96% pill count adherence, IDI-01)

The relationships formed with the health workers also served as a great motivator for the participants in this study to return for their scheduled clinic visits. Most of the participants explained that they were motivated to return to the clinic on time to receive helpful health updates from the health workers and because they are treated very well by them during their clinic visits:

> *I feel good when I am with them because they know my status and I also know my own status. When I am with them they do encourage me and they do not make me lose energy.* (24-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-013)

Disclosure to an HIV-infected person

In this study, every participant had disclosed her HIV status to at least one person during pregnancy. Approximately half of the participants had disclosed to their male partners and half had disclosed to a friend or family member. While the nature of the relationship between each participant and the person to whom she disclosed her status varied by participant, the more productive disclosure experiences appeared to take place when the person to whom HIV status was being disclosed was also known by the participant to be infected with HIV or to have had first-hand experience with HIV. In one example, a participant who had not disclosed to her husband described her disclosure experience with a friend:

> *How she got to know, one time I left home early, I had left my husband and yet he had the key and I asked her to help keep for me the drugs. That is when she got to know. I had nowhere to keep the medicine yet my husband was around and he had the key. I told her, "These drugs have been given to me in the hospital. Keep them for me until my husband opens." That is how she came to know. I already knew that she was also infected and that is why I kept with her my medicine. If she wasn't infected, I wouldn't have kept it with her, but I knew that she was too infected. She got astonished and asked, "Are you also infected?" I told her, "I have been tested and found HIV positive." And she told me, "Be strong and take your medication." She used to comfort me and whenever medicine would treat me badly I would go to her and she said, "Be strong, all that will stop. Just be strong and take your medication."* 30-year old HIV-infected pregnant woman with missing pill count adherence at study visit, IDI-07)

In another instance, a participant disclosed to her mother because she believed her mother would be able to assist with obtaining ART refills. HIV-infected pregnant women receiving the standard of care at Mulago National Referral Hospital were asked to bring a "treatment buddy," usually a friend or partner, to support them with adherence to clinic visits and ART treatment. Like other participants, she felt the burden of keeping her HIV status a secret and chose to disclose to someone who understood what she was going through:

> *I decided to tell my mother because I can fall sick or have no time to line up for medicine and my mother can help. I went there because it is not easy to know such a secret alone, and in case you don't say it out to someone, then it can all the time be in your heart…she encouraged me to take medicine because my mother…my dad died of the same disease and my mother is also on the same treatment.* (24-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-014)

The participant said that her mother supported her ART adherence by calling every two days and asking, *"How are you feeling? Do you take your medicine?"* She also explained that even though she has many friends, the participant seeks support from her mother because, "*She is the only person I can tell everything on my heart without leaving out anything."* In a different clinic experience, one participant described being paired with a fellow HIV-infected pregnant woman at the clinic on the day of her HIV test. While this was a unique situation described by only one participant, it emphasized the benefits of disclosing to a peer who is also infected with HIV and demonstrated the difficulties associated with trying to talk about being HIV positive with others who are not infected with HIV:

> *It was clear that both of us were infected and there was nothing to hide…and it helped me because she was given her ARVs and I was given mine as well. We sat outside and discussed [our status]. And she told me, "I will come and pay you a visit" and I also told her that I would also want to see where she stays…I had been told to bring someone I knew but I feared telling any of my people. The only person who is like me that I would have told is not around, she is my sister and she is in the village. And yet we had been told that we have to choose someone who is nearby so that in case you are sick she can help to pick up your medicine if you are unable. If you failed to pick up the medicine she can pick it for you. Yes…even last week on Wednesday, we were both here. She stays in Mpererwe. I stay in Ndejje. She came from Mperewe and paid a visit. She is a great person!*
>
> *By the way to decide and tell someone [about your HIV status] is not easy. There are those who can frighten you and you lose focus. You can be having a conversation with people and if one says, "If you get infected with that HIV that would be the end of you." And you try to cover it up and say, "Medication is available…" But they say, "No…you are at the point of death any time." And you lose hope. You might have been at the point of disclosing but you decide not to* (32-year old HIV-infected pregnant woman with 96.4% pill count adherence at study visit, IDI-04)

Variability of male partner involvement

The extent of male partner involvement in the health and HIV treatment of the participants varied from none to extensive and seemed linked to whether or not participants were aware of the HIV status of their partners, felt able to disclose their own status or were living together with their partners. Only six of the 16 participants were aware of their partners' status

and the rest either did not know if their partners had been tested or had partners who refused HIV testing. Most of the participants who had not disclosed their HIV status to their partners were living separately and male partner involvement was non-existent or limited to providing money for food, transportation or general expenses. In the interview excerpt below, one participant described the lack of support she received from her husband in the first month since testing positive for HIV and initiating treatment and the circumstances surrounding this lack of involvement:

> *When he is around and has not gone up country, I stay with him…my husband works but when you ask him to go to the clinic he becomes rude just like other men, so I decide to let that go. My father-in-law refused me to show him [not to disclose to him] and told me that in case he gets to know it he will completely refuse to go for testing, yet if we hide it from him he [father-in-law] can convince him to go for testing…he has never accepted to do so. My father-in-law told him, "Why don't you want to go for testing?" But he completely refused…I do not tell him that I am coming for ARVs; I tell him I am going for antenatal services and he thinks I have come to give birth…I kept telling my husband to come with me to the hospital but he refused. He kept on saying. "You can go, it is not me who is going to push the baby…" Such things..."It is you who is carrying a baby." I then asked him, "What should I do?" And he said, "You can go on your own and tell them I am not around."* (27-year old with 100% pill count adherence at study visit, IDI-09)

The same participant also explained that she thought about separating from her husband but then decided to stay together because, "*He is never around. When he goes for work he only comes back once a week or even not appearing at all and just sends money for home use."*

In a different interview, a participant described how her husband provides no support or communication during the current pregnancy:

> *I last saw my husband when this pregnancy was just a month. He left from where we used to stay and he told me that he was going to the village, but when I checked in the village he wasn't there and his phone is also off. I do not know where he is and where he is staying. At this moment I am on my own, I am not with any man. I stay with my sister and that is where I come from to go for my medicine… I do not know where he is. We were together but then I do not know what happened, I hear rumors that he got another wife and even has a child with her. I do not know whether that was part of the reasons he decided to disappear.* (33-year old HIV-infected pregnant woman with missing pill count adherence at study visit, IDI-015)

In contrast, HIV-infected pregnant women who did disclose to their male partners often found that their partners expressed a desire to help and exhibited more extensive involvement, even if the couple was found to be discordant:

> *So I told him, "Eeehhh it didn't go well today at the clinic. So they tested our blood but mine didn't come out well…here is the result…"I gave him the result and then he was, "Eeehhh…this is an accident, something which already happened has happened…me I cannot refuse you…I cannot divorce you…this is my blood, I cannot refuse my child…so I will help you for the rest of my life." He started giving me advice and counseling me but he also told me that next time we shall go together. Yes…that is when today we came together…we tested together and it was negative.* (28-year old with 100% pill count adherence at study visit, IDI-05)

The same participant also spoke about how her husband reminds her to take ART, despite testing negative for HIV:

> *It was only one day when my husband asked, "Have you swallowed your medicine?" Then I also ask him, "What is the time?" And then he said, "It's remaining four minutes to time…" Then I told him, "It is okay I am going to swallow." From then up until now I don't forget.* (28-year old with 100% pill count adherence at study visit, IDI-05)

In addition to receiving ART adherence support, HIV-infected pregnant women who disclosed to their partners were also able to find financial and emotional support from their male partners. As on participant described:

> *He has helped me because when it reaches time for taking drugs, he reminds me, "Have you taken your medicine?" He keeps asking me…whenever it clocks time he says, "Go and take your drugs." The second thing, he has encouraged me a lot. He tells me about real life situations like, "People have diabetes or cancers, but for our scenario, we have medicine to reduce it. So we can be sick but be able to stay alive for quite some time."…He looks after me. He works and I do not work. He goes for work and provides everything at home.* (27-year old with 100% pill count adherence at study visit, IDI-10)

<u>Modified behaviors to prioritize health and ART adherence</u>

Often in the study, participants reported having to make adjustments to their behaviors and lifestyle choices to prioritize their health and ART adherence. For some participants, this meant discontinuing alcohol consumption. For instance:

> *I used to take alcohol before I had been tested. Whenever I would get annoyed I would leave home and go take a bottle. One day I got annoyed and went to have one. I used to take one and I would not get drunk, but this time I got drunk. I asked myself, "Why has*

> *this happened yet ever since I have never experienced this!" I got on my phone and called a health worker and she told me, "That is so wrong and never do it again." I then got to know that I am not supposed to do that again.* (24-year old HIV-infected pregnant woman with 100% pill count adherence at study visit at study visit, IDI-08)

For other participants, modifying social behaviors was an essential change to ensure they remained healthy and adherent to ART. In some cases, this included changing the social environment. As one participant described:

> *Because before, I used to go clubbing…But I never do that these days. I stopped doing that because whenever I take my medicine I have to go and rest. I also realised that in case I took it [ARVs] and go out to have fun it will still make me lose energy. But when I stay home and sleep I wake up without feeling any problem. I decided to stop doing that and I used to take alcohol but I eventually stopped.* (24-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-08)

In other instances, participants described having to make sure to be home by a certain time to ensure being able to take ART. They also mentioned having to take into account balancing visitors in the home with taking ART and attending scheduled clinic visits. As seen from the interview below:

> *I automatically know that I have to take medicine…Unless I have left home and gone somewhere. But even so, I first get to know the time. I do not exceed 8pm before I set off for home because I do not move with ARVs…Or when you receive a visitor who is an adult and you can't leave him/her around yet you have to return to the clinic."* (27-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-010)

In every case of a participant reporting having missed a dose of ART, the circumstances surrounding the missed dose had to do with disruptions to the daily routine that had been established to prioritize ART adherence. In one example, a participant explained that she remembers to take her ART every day by setting an alarm on her cell phone. When the alarm did not go off, she forgot to take her ART.

> *On Friday, I was sick and slept early…the children had played with my phone…and the alarm set off…only to wake up at 3am. And I forgot to take it. I woke up in a shock because I had never done it before. I was in fear but I had nothing to do. I resumed the following day.* (28-year old HIV-infected pregnant woman with 95% pill count adherence at study visit, IDI-02)

On a different occasion, one participant described missing an ART dose because she had decided to spend the night outside the home with her sister to be in closer proximity to the clinic.

> *I had spent a night somewhere else and I had forgotten the medicine at home. The following day I was supposed to come back to the clinic but the tablets I had carried were missing that tablet and I told the health worker…Anyway I feared and I really wanted to swallow it but time had passed, I had nothing to do. And when I came today I asked the health worker and she said…Actually she asked, "Why is it that this tablet remained?" And I explained it to her. She said, "Okay that is fine but the reasons why women take medicine is because of this and that…"* She told me all the reasons and I told her, "*I encourage myself [to take the medicine] but it only happened once by mistake." I thought I had packed it but when I reached where I had gone I realised I had left behind one tablet*. (27-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-09)

For many participants, being HIV infected during pregnancy had a significant effect on their work. Of the nine participants who worked to generate income, four described having to stop working during this pregnancy and those who continued to work described challenges integrating their work schedules with their ART schedules. As one participant described, fatigue was the most common reason for stopping work:

> *Health worker, I do not have much work to do…What might have been much work is that I used to walk to work but now I do not work. I do not walk to work these days. I closed the business because I do not have energy to walk to work and then walk home…When it reached a time and I couldn't do it anymore I decided to rest until I give birth and then resume work…it has affected me because yesterday I saw the landlord yet I haven't worked this month.* (27-year old HIV-infected pregnant woman, 100% pill count adherence at study visit, IDI-09)

However, in some cases the emotional impact an HIV-positive diagnosis also caused participants to stop working. One participant explained why after receiving her diagnosis, she initially stopped working:

> *Everyone I would come across, I would think that probably he/she knows my status. I would feel ashamed and spent days without working. But later I got used to it and went back to my work…I spent like four days without working…I would stay home thinking that maybe everyone knows about me. But then I had to go back to work and start again.* (24-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-08)

The same participant also described difficulties incorporating her ART schedule into her routine once deciding to go back to work. This experience was mostly due to the rigidity of the ART schedule and the participant wishing to follow instructions about taking ART at the same time every night. In the example below, the participant prepared and sold tea from a taxi park. She described needing to re-evaluate when she takes her ART every night because of excessive traffic on the way home from work.

> *Sometimes I find a lot of jam along the way back home and find myself that it clocks 9:55 PM and I have yet to cross a road, yet cars are at high speed…I leave work at exactly 9PM. I travel for one hour but sometimes I meet a lot of jam. If there is no jam it can take me about 25 to 30 minutes. I move with it [drugs] but sometimes I fear swallowing it from the taxi where people are seeing me. Sometimes I use a lot of money to use a boda boda to be able to make it on time at home without taking a taxi because of the jam…But ever since health workers emphasized that when I chose 10 PM it has to be that, and in case I take it an hour later I give it [HIV] an opportunity of multiplying, I try my best and I feel I should change that time. I can take it at 8PM because I can excuse myself and run to my small office, take it and come back to continue with my work. It will help to reduce the tension whether jam is there or not.* (24-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-08)

<u>Concern with inadvertent HIV status disclosure</u>

While practically every participant reported that being told they are just one of many infected with HIV or knowing others who are HIV-positive but otherwise healthy as motivating factors for ART adherence and clinic visit attendance, they also consistently brought up concerns surrounding having their HIV status exposed to others. This concern revealed itself in a number of situations. For example, one participant talked about traveling the long distance from her home in Entebbe to Mulago National Referral Hospital because she did not want to encounter anyone she knows at her community clinic.

> *Participant: The area is bad. You might go and find someone who knows you very well and she informs everyone. But this side [clinic], when you come, sometimes you do not find anyone who knows you. You just get your medicine and go home…It would be of importance to collect ARVs from a place where you are not known. It is like say in Lweza, whoever goes there you hear people saying, "Here she comes, she is already HIV infected, she is also entering…she has come, she is HIV infected…"*
> *Interviewer: So, you advising that HIV infected people should go to…*

> *Participant: To general clinics where you are not known [offer holistic care] as opposed to HIV-specific clinics.*
> *Interviewer: Like the way you are doing it whereby you stay in Entebbe and then come to Mulago…*
> *Participant: Hhhmm [Yes] because they don't know who I am. But if I receive ARVs from my area they will say, "Eeehhh…Even XXXXX [name withheld] was found going to TASO. She goes to TASO to pick ARVs."* (32-year old HIV infected pregnant woman with 96.4% pill count adherence at clinic visit, IDI-04)

A different participant talked about a similar concern regarding having to involuntarily disclose her HIV status at the clinic. She was worried that when she returned to the clinic after giving birth, she would be asked to reveal that she is HIV positive to strangers before receiving care.

> *But the problem we have encountered, if you are not pregnant you might face many challenges because at the entrance you can't keep telling everyone, "I have come for ARVs." Those who are pregnant just move straight inside but when you are not pregnant, what will we do! They request some documents to look at before you enter, they need to know why you have come…Do they want us to disclose our status that we have come for ARVs? I do not know what we shall do for that. That is what they do at the Kampala City Council Authority [KCCA] clinics.* (27 year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-010)

In addition to having implications for where and when participants seek health care and treatment, fearing HIV status exposure also affected the relationships of participants with their friends and family. As one participant explained, she isolated herself from friends and family so that she could take her ART without having her HIV status discovered:

> *I have a big challenge about that because my people do not know that I am HIV positive and I do not visit them. Even back home; I do not go there because I fear to be seen. My dad and mum are old now but I have never seen any drug [ARVs] at home, not even my brothers or sisters…I do not even want visitors at home; I want to be free at my home swallowing my medicine without worries.* (24 year old, HIV-infected participant with 100% pill count adherence at study visit, IDI-08)

<u>A desire for a healthy baby and a healthy life</u>

The predominant motivation for initiating ART and adhering to the Option B+ treatment program was ensuring the health and HIV-negative status of the unborn child. Every participant expressed this desire above all else. In addition to delivering a healthy baby, the majority of

participants were also driven to adhere to ART and attend their scheduled clinic visits to continue living a healthy life. As one participant responded:

> *What encourages me? Trying to protect my baby inside the womb. And to keep my life moving on [well]. To have a longer life…To have a longer joyous life without having any worries.* (20-year old HIV-infected pregnant woman with 95% pill count adherence at study visit, IDI-03)

Even when the participants felt fear or stress about initiating treatment and adhering for life, a desire to stay healthy and to protect the baby overcame these feelings. For example, when one participant reflected on initiating ART, she explained:

> *I thought it was going to be harmful to me but…When they give me advice…what what…I just feel, "I am okay…" and I am getting the ARV…I am swallowing the ARVs to protect me and my baby…Yes…I want my baby to come out when…the baby is negative.* (25-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-05)

In a different interview, one participant also explained that she is motivated to continue taking ART so her unborn child will not have to go through the same process of always taking medicine and going to the hospital:

> *So what encouraged me was because I want to have an HIV negative baby. I wasn't ready to keep going to hospitals because of my child and since I didn't like medicine I also didn't wish it for my baby. That in a way encouraged me to sacrifice and take medicine to give birth to an HIV negative baby.* (27-year old HIV-infected pregnant woman with 100% adherence at study visit, IDI-010)

<u>Other factors affecting Option B+ experiences during pregnancy</u>

Additional factors identified by only a few participants as influencing their PMTCT experiences were specific to the Option B+ program logistics and treatment schedule. For example, one participant who had attended health talks prior to Option B+ expressed a desire for this previous PMTCT program when ART was not necessarily initiated immediately upon testing positive during pregnancy and was not required to be taken for life. It is unclear from the interview if this participant was referring specifically to the old WHO recommendation calling only for single-dose nevirapine to be administered at the onset of labor, or if she is speaking about

some other approach. Nevertheless, it is clear that that the concept of initiating ART immediately during pregnancy and continuing therapy for life was not the option of choice for this participant.

> *I was told that I have to take that medicine [ARVs] for the rest of my life when I start it, without missing any day, and it should be at the same time…Some time back they taught us that you are given a tablet which you will swallow at the onset of labour before 24 hours elapse. I wish it was maintained like that…during health talks, they used to tell us that if you are found to be HIV positive, you are given a tablet and you keep it and then take it at labour. If 24 hours elapse before giving birth, you are then given another tablet. However, you do not start right away from the day you are found to be HIV positive.* (20-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-012)

A different participant also expressed surprise about the Option B+ treatment schedule being for life. In this case the participant expected to be following the Option A approach previously implemented in Uganda that differentiated HIV-infected pregnant by CD4 count to decide if they qualified to receive treatment for their own health or prophylaxis for PMTCT.

> *The other thing we were told was that I am going to be on treatment forever, yet I thought in case I gain some energy I stop for a while…You know some time back we used to hear rumours that when one gains energy she is asked to rest medications for some time and then resume when the CD4 count falls down. However, we were told that we shall stay on medication forever, which is something that is different from what I expected…*(27-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-010)

The same participant was uneasy about taking ART every day for the rest of her life due to the risk of unknown long-term side effects that may develop over time. The participant explained that she would prefer a different treatment schedule that only required taking a pill once a week or once a month.

> *What I wish to change is that issue of taking medicine every day...If they can come up with another type which you can take once in a month…Yes…where you take it once in a week or a month…Because taking every day…and within me I feel medicine is a chemical substance…As time goes on, the chemical is not good in your blood. I feel it has some effect apart from curing…you know everything has a side effect…Apart from eliminating viruses I feel it must be having side effects…Maybe within the liver, within me and maybe reach a time and it causes abnormality…I sometimes think about it…Those long term effects…That when you take ARVs for a long time what do you get…Do you stay normal…You know…I don't know those long term effects.* (27-year old HIV-infected pregnant woman with 100% pill count adherence at study visit, IDI-010)

Option B+ at six weeks postpartum

Clinic visit attendance, maternal ART adherence and adherence to infant prophylaxis remained high from the time of labor and delivery through six week postpartum and all HIV-exposed infants in the study received an HIV test at this study visit. Nevertheless, a variety of factors had an impact on the Option B+ program experience of the participants. These factors could be grouped into six themes: 1) consistent ongoing support from health workers; 2) health facility constraints; 3) continued support after disclosure; 4) variability of male partner involvement; 5) normalization of daily ART and 6) a continued desire for a healthy baby and a healthy life. During the course of the study, the location of some health services, including obstetrics and gynecology, were transferred from Mulago National Referral Hospital to Kawempe General Referral Hospital to allow for renovations at the Mulago site. This change in location also factored into the experiences of participants as described in the first two sections below.

Consistent support from health workers

Each of the eight participants interviewed at six weeks postpartum described reliable health worker involvement in PMTCT from the time of labor and delivery. One participant described her satisfaction with the health workers during labor and delivery:

> *Participant: They treated me well since I was unconscious, but they made sure my baby does not get infected with HIV…they cleaned me so fast so that the blood does not mix with the baby. I got so happy and I learned a lesson*
> *Interviewer: What lesson did you learn?*
> *Participant: Helping others.*

The health worker support from labor and delivery through six weeks postpartum was also found to be consistent with respect to ART adherence, clinic visit attendance and infant prophylaxis. In the same interview, the participant talked about the support provided to her by the health workers in the last six weeks since her baby was born and the way it made her feel:

> *The relationship I have with health workers; they have handled me like a person. A person, not like a child. Which has made me not go to that level of saying, "Why did I get infected to this virus?"… They have helped me not get worried and taking my medication at the right time.*

She also mentioned that when health workers visited her at home, *"they encourage me which gives me more energy that they care about me and my life"* (28-year old HIV-infected breastfeeding mother with missing pill count adherence at the six-week postpartum study visit, IDI-02). In addition to providing support at the clinic, health workers continued to maintain regular phone contact with participants after labor and delivery. The phone calls included reminders of upcoming clinic appointments to pick up drugs as well as advice and answers to questions. It was also clear that in addition to making phone calls, health workers were receptive to receiving calls from HIV-infected mothers between clinic visits. As one participant described:

> *Health workers do remind me the days for my clinic visit and it makes me feel so good because you never know, I might forget. It encourages me when they remind me to come and pick it and also take it at the right time…I call health workers and explain to them what I am going through and what my child is experiencing and they tell me what to do or take her here and there…health workers help me that whenever I call them they handle me well. Sometimes they actually call and inquire about my health. That also encourages me and I do not feel like an infected person.* (24-year old HIV-infected breastfeeding mother with missing pill count adherence at the six-week postpartum study visit, IDI-08*)*

In one instance, a participant arrived at the Mulago clinic site and found it closed. The participant explained how the health workers continued to be helpful, even in this unique case. She also echoed the feelings of the other interviewees with respect to the role of the health worker and the relationship between health workers and HIV-infected women in the early postpartum period.

> *When I reached where we used to have antenatal clinic the place was all closed and some roads are closed. Health workers picked me and came with me to the right place. It made me feel great knowing that health workers are helping me and think about me…*
>
> *…They help me by providing medicine to me and deciding to counsel me to take my medication so that I will live longer. They make it easy whenever I come here to get hope that I will live longer and see my baby grow. The relationship is not bad at all, it is not bad. They care so much and they even call reminding us to come for medication. They give you a call and even go to the extent of picking you in case you are lost. They make me feel happy and that my life in future will go on.* (32-year old HIV-infected

breastfeeding woman with missing pill count adherence at the six-week postpartum study visit, IDI-04)

Health facility constraints

Although participants exhibited good adherence to ART and infant prophylaxis and regular clinic visit attendance in the early postpartum period, a majority of the interviews at the six-week postpartum study visit noted some unanticipated barriers to a satisfactory clinic experience at this time point. First, practically every participant expected to receive the infant HIV test results on the same day as the test was administered. As one participant explained:

> *What I expected, I thought you get the results there and then but that never happened, they just took off the sample. So, I am waiting for the results so I don't know whether my baby is infected or not.* (27-year old HIV-infected breastfeeding woman with 100% pill count adherence at the six-week postpartum study visit, IDI-09)

While this participant was able to remain patient for the results, in some instances participants described stress and anxiety associated with having to wait to receive the infant test results.

> *I felt bad health worker, because when they were getting off blood from him yesterday they went on to tell me that results are not received immediately. I thought I was going to go back with the results…not receiving the test results on the same day…it keeps you worried every day.* (28-year old HIV-infected breastfeeding woman with missing pill count adherence at the six-week postpartum study visit, IDI-02)

Next, many of the HIV-infected mothers interviewed found long waiting times and overcrowding at the six-week postpartum visit. As one participant described:

> *Participant: We are always many patients. You have to first wait [be patient] for the one who came first to be served first. Because the working space is small yet the patients are many.*
> *Interviewer: Which working space are you talking about?*
> *Participant: The side where we shifted…Where Mulago shifted…In Kawempe [Mulago Women Hospital for Obstetrics and Gynecology in Kawempe].*
> *Interviewer: The working space is small? How do you find it? When you say that it is small, what do you mean?*
> *Participant: We have to first wait for those inside…we move step by step. You first see the doctor for the baby and then move to another place for medicine…Yes we spend a lot of time…It depends on the number of patients you have found there. They have to first counsel everyone. It can take about one hour or about 40 minutes.* (22-year old HIV-infected breastfeeding woman with 100% pill count adherence at the six-week postpartum study visit, IDI-06)

In addition to feeling crowded, participants also believed that it took longer to get to Kawempe and were concerned about the quality of care they received due to unfamiliarity with the clinic staff at this site.

> *There is a lot of jam in Kawempe, the journey is far, and you might get there and find other health workers who you don't know and you do not get the help you thought you would get.* (32-year old HIV-infected breastfeeding woman with missing pill count adherence at the six-week postpartum study visit, IDI-04)

In one example, a participant described feeling uncomfortable sharing a health concern with a new doctor who was unfamiliar. In this case, the participant was not able to see her regular doctor because the PMTCT team she was expecting were all in a meeting on the day of her clinic visit.

> *For the skin rash, I went to Kawempe Hospital and told a health worker because here, like I told you, it was a new doctor and I wasn't open to tell her a lot about it. I just talked about it just a little and she also didn't give me a solution. She just said, "It will clear…"*(27-year old HIV-infected breastfeeding woman with 100% pill count adherence at the six-week postpartum study visit, IDI-09)

Although the circumstance was unique to this participant, it emphasized the impact that a lack of trust can have on the relationship between the patient and the health worker, as well as the importance placed on establishing long-lasting relationships with health workers by the HIV-infected mothers receiving care.

<u>Ongoing support after disclosure</u>

All participants interviewed at six weeks postpartum described receiving continued support from the people to whom they had disclosed their HIV status during pregnancy. The most common forms of support received included encouragement of ART and infant prophylaxis adherence, having someone to talk to about being HIV positive and gaining courage from the experiences of others. In one interview, the participant had disclosed to a close female friend who had an HIV-infected mother and was therefore familiar with the infection and the importance of adhering to treatment. The friend had been disclosed to while the participant was still pregnant,

and provided adherence support as well as encouragement from pregnancy through six weeks postpartum. In the follow passage, the participant talked about this disclosure experience:

> *She calls me over the phone and sometimes she comes home and we talk about it, she advises me and tells me that I have to take it, and gives me examples of different people and I a way I get contented [relieved]…I think she checked my stuff because she sent me a message saying, "I want you to tell me the truth…feel free with me, do not hide anything away from me…" And I told her, "That is fine, I will come and tell you the truth." I then later told her and we sat and discussed about it and she told me, "You always have to take your ARVs on time and you have to go to the clinic as requested."…She gave me advice and gave me some examples of people…Like her mother who is also infected. She is still alive and she looks so well to the extent that you can't tell what she is…Yes it gave me confidence.* (22-year old HIV-infected breastfeeding woman with 100% pill count adherence at the 6-week postpartum study visit, IDI-06)

This experience also tied into earlier themes affecting the Option B+ program experience during pregnancy. In pregnancy, significant support was received from disclosing to someone who was also HIV-infected and participants gained strength from learning about others who were HIV-infected but appeared healthy. In this case, significant support was received from an HIV-negative friend who had first-hand experience with the infection through her mother. Similarly, learning about someone who was HIV-infected but able to remain healthy by adhering to ART treatment continued to serve as a source of inspiration for the participant in this case. A different participant who had also disclosed to a close female friend during pregnancy described a similar experience with receiving continued support in the early postpartum period:

> *She is a very good friend of mine, I told her about the results that had come out of the testing. Sometimes she sends me a message to remind me about the time of taking medicine. She is the only person who knows [about my status]…She felt so bad and she kept on encouraging me, she has done a lot to encourage me.* (24-year old HIV-infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-08)

The majority of participants revealed that at six weeks postpartum they had not disclosed to any new individuals since choosing to disclose during pregnancy. The reasoning behind this warrants further exploration but may be due to participants feeling they did not need to take the

unnecessary risk of disclosing to someone who may react poorly when ample support was being consistently received by participants from the individuals to whom they had disclosed their HIV status during pregnancy. As one participant who had disclosed to her husband and sister during pregnancy responded when asked why she had not disclosed to anyone new since giving birth, "*Now I cannot go telling all people that I am positive." (*28-year old HIV-infected breastfeeding mother with 98% pill count adherence at six-week postpartum study visit, IDI-05)

In the time between interviews, one participant did newly disclose to her husband, however the disclosure still happened during pregnancy and not in the postpartum period. In this case as in many of the others in this study, the husband continued to provide financial and emotional support throughout the pregnancy and the early postpartum period, even when his HIV test results came back negative. Despite the participant thinking the couple should separate because of their HIV discordance, her husband would not leave and continued to provide encouragement.

> *He gave me support…he never left me alone…on that day, he came on the day we were discharged and he was also tested but he was negative. I told him "Let us separate" and he said "It's not possible XXXX, The time we have spent with you we cannot separate. We shall ask health workers to direct us on what to do but we cannot separate after this long."* (32-year old HIV-infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-04)

Variability in male partner involvement

The variability in male partner involvement with the health of the participants and their new infants continued through six weeks postpartum. On one side of the spectrum, one male partner provided extensive adherence support and attended clinic visits with the participant. In this case, the couple was married and the husband had been tested for HIV in the antenatal period and was found to be uninfected.

> *I don't see any problem with him [husband], he still cares the way he used to…sometimes he comes back home to see if I have taken my medication. Sometimes he reminds me to give the baby…hhhmmm…he can remind you, "Have you taken your medicine? Have you*

> *given the baby syrup? He comes back and reminds me…even when he is driving [taxi driver] he will park the car and come to remind me and see if you took your medication…It felt good because he accepted to escort me to have the baby tested so that we come to know the truth whether he is sick or not, as opposed to having a baby whom we are not sure whether is infected or not.* (18-year old, HIV-infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-01)

On the other side of the spectrum, one participant reported receiving no financial or emotional support from her male partner at the time of the six-week postpartum study visit. In this case, the participant had not disclosed her HIV status to her partner and they were not living together. The participant chose not to disclose to her husband because she was worried he would think she had infected him, despite not knowing whether or not he was currently infected with HIV.

> *He sends money though right now we have some misunderstandings…there are some people who I do not know who went and told him that the baby I have is not his. He got angry and does not come home anymore…of course he is not sending any help but before that, he would send money.* (20 year-old HIV-infected breastfeeding woman with 100% pill count adherence at six-week postpartum study visit, IDI-03).

A different participant described mixed levels of support with respect to the involvement of her male partner with her HIV care and the health of their baby. In this situation, the husband provided financial and adherence support to both the participant and the baby but continued to refuse initiating ART for his own HIV infection. In the excerpt below, the participant described her struggle with her husband's disregard for his own health:

> *Actually what is making me get so worried is that he knows I am HIV positive and he is HIV positive as well but he does not want to come and start taking drugs…I am not sure whether he is taking hiding…I do not know…Though I feel he is not taking because I would tell. But however much I tell him, he doesn't allow…Yes, he looks after me and in most cases he provides everything I request for, be it food or anything…It is my husband who helps me...One day he saw that I was not giving the baby syrup and he asked me and I told him that it had got finished and that is why he told me that, "You were told to go back on the 13th..." I feel good but at the same time feel bad because inside that bag, there are documents and medicine; he is aware that I take them and they are for HIV but still he refused to take medication…so I feel bad about that…I actually told him today that remember I asked you last time that when I am taking back the baby to the hospital we must go together, but he pretended that someone had called him which proved to me that he is just dodging. I thought about it but left it at that...I told him that, "Are you waiting to be bedridden to start taking ARVs? Sometimes it might even fail to work." He appeared as though he had understood and he said, "The day you go back to the hospital we shall go together." But whenever it gets to that day he refuses.* (28-year old HIV-

> infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-02)

Participants with male partners who were supportive and exhibited involvement in PMTCT care and treatment during pregnancy continued to show high levels of support and involvement in the early postpartum period. Interestingly, an improvement in male partner support after labor and delivery was noted by most of the participants who described their partners to be uninvolved during pregnancy. In the example below, the participant was single and had yet to disclose her HIV status to her male partner. During her pregnancy the participant described receiving no support from the father of her baby. In contrast, since the baby was born the participant received financial support for herself and the baby:

> *He now gives me support for the baby. He never used to care when I was still pregnant, but after giving birth he started caring about me…He gives me money for food and rent. He also provides money for treatment in case the baby is sick.* (22-year old HIV-infected breastfeeding woman with 100% pill count adherence at six-week postpartum study visit, IDI-06)

In a different interview, one participant talked about how her husband who was unaware of her HIV status and refused HIV testing for himself had been making an effort to control his alcohol consumption since the baby was born. When the participant was still pregnant, her husband would spend all his money on alcohol while they were apart. Now that they have a first born child together, his behavior has improved:

> *When I am not around he does not save anything. In case I am not around he earns 200,000, he will go in a bar and drink it all. When you call him about his baby or that just says, "I do not have money."…Ever since I gave birth he has a lot of love for me [laughs]. He also loves his child very much, his thoughts are all taken up by her. That is our first born. Yes…So, the baby has taken most of his thoughts. From work he comes straight home and he stopped taking alcohol…So from work he bathes and spends most of his time with the baby. So when he comes home he first refreshes himself to carry the baby. So, in case you want something you can go through the baby.* (27-year old HIV-infected breastfeeding woman with 100% pill count adherence at six-week postpartum study visit, IDI-09)

<u>Normalization of daily ART</u>

It was seen in the ANC interviews that feelings of shock and fear often accompanied receipt of positive HIV test results and the immediate initiation of ART for PMTCT under the Option B+ program. Similarly, many changes were made to daily routines and behaviors to accommodate ART adherence during pregnancy. Nevertheless, over time the daily ART routine became normalized and less concerted effort was need to remember to take ART and attend clinic visits. As one participant described:

> *At first I was just fearing, "Eeehhh will I really continue with this life, with this medicine for life?"…I was just expecting whether I would continue with it but now I am used to it and I know I will finish. I will continue. That thing is just normal now in my brain because I have to swallow it every day…it is within my mind.* (28-year old HIV-infected breastfeeding woman with 98% pill count adherence at six-week postpartum study visit, IDI-05).

Similarly, a different participant talked about being able to easily remember her ART every night and having less reliance on health workers for clinic visit reminders.

> *Even when I am doing something, I first put it aside and take my medication; I know the date but health workers also try their best to call and remind you to come for help.* (18-year old HIV-infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-01)

This normalization could have been due in part to subsiding ART side effects over time. During pregnancy, the majority of participants described experiencing some degree of dizziness, nausea, exhaustion or hallucinations in the first month on ART. All but one participant interviewed at six weeks postpartum noted that these side effects had significantly subsided or completely stopped over time, and many described themselves as feeling as healthy as they had felt before becoming infected with HIV.

> *I feel so so so good…I actually feel as though I am not infected with HIV. But still I take my ARVs. Whenever it clocks the time, I take it…But I feel the same way I was before I got infected with it. I do not have any problems with it.* (24-year old HIV-infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-08)

<u>Continued desire for a healthy baby and a healthy life</u>

In spite of discrepancies in clinic visit experiences and male partner involvement, the desire for a healthy baby and a healthy life continued to be a driving force behind clinic visit attendance, maternal ART adherence and infant prophylaxis adherence throughout the early postpartum period for all participants. As one participant described, keeping clinic visit appointments was the only way to receive the ART and infant prophylaxis necessary to stay alive and keep the baby healthy:

> *I come to get medicine and medicine for my baby as well as immunization. To help him feel better…That he might not go through what I am going through.* (18-year old HIV-infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-01)

The same participant also explained that she is motivated to take her ART to stay alive for as long as it takes to find a cure for HIV. She also felt that her baby was actually healthier than other HIV unexposed infants:

> *Participant: I hope that if I continue taking it, I might live to see the cure, but in case you do not take it you might not be around when a cure is discovered…*
> *Interviewer: And ever since you gave birth to your baby, what motivates you to take your medicine?*
> *Participant: Seeing my baby not falling sick so often yet babies for those who are not infected keep falling sick.* (18-year old HIV-infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-01)

A different participant also described the sentiments that came through in every interview with respect to ART adherence in the first six weeks postpartum:

> *I feel so good and I have no problem. I take it at the right time to be able to get encouraging results the next time they take off blood from me…And my child is not in bad shape, she looks so healthy. Those made me choose to take my ARVs so that I do not infect her.* (24-year old HIV-infected breastfeeding woman with missing pill count adherence at six-week postpartum study visit, IDI-08)

DISCUSSION

This study aimed to explore the factors affecting the PMTCT adherence and program experiences of HIV-infected women under the Option B+ recommendation and how these factors

and experiences may change from pregnancy to six weeks postpartum through longitudinal in-depth interviews with HIV-infected pregnant women receiving the standard of care at Mulago National Referral Hospital. ART adherence and clinic visit attendance were consistently high throughout the study for all participants. In the antenatal period, seven key themes related to the Option B+ experiences of HIV-infected pregnant women were identified: 1) effective messaging and counseling at the time of HIV testing and treatment initiation; 2) reliance on health workers for support between clinic visits; 3) disclosure to an HIV-infected person; 4) variability of male partner involvement; 5) modified behaviors to prioritize health and ART adherence; 6) concern with inadvertent HIV status disclosure and 7) a desire for a healthy baby and a healthy life. At six weeks postpartum, six additional themes representing the changes and consistencies experienced by HIV-infected mothers from pregnancy through the early postpartum period were also identified: 1) consistent support from health workers; 2) health facility challenges; 3) ongoing support after disclosure; 4) variability of male partner involvement; 5) normalization of daily ART and 6) a continued desire for a healthy baby and a healthy life.

The reliable health worker support received by HIV-infected women from HIV testing and ART initiation through labor, delivery and the early postpartum period definitively impacted the PMTCT experiences of all participants and positively affected ART initiation, adherence and clinic visit attendance. In addition to providing support during clinic visits, the health workers also often served as a primary source of support between clinic visits in this study. This finding is in line with previous qualitative research that identified same-day initiation of treatment, health care providers being unconvinced of the benefits of Option B+ and insufficient health care provider training as barriers to the provision of Option B+.[8] The findings of this study illustrate the value of well-trained and passionate PMTCT health workers and the need for continued training and support of health workers to effectively implement the Option B+ program.

Some barriers to successful Option B+ program implementation at the facility level in the early postpartum period were identified by participants in this study. These barriers were primarily due to the shift in services from the Mulago National Referral Hospital location to Kawempe General Referral Hospital in the middle of the study, and included longer waiting times to receive treatment and services, overcrowding and unfamiliar clinic staff. A systematic literature review assessing the barriers and facilitators to uptake of ART for PMTCT in sub-Saharan Africa also identified high patient volume and long wait times resulting from a shortage of trained clinic staff as a health systems barrier to the acceptance of ART.[12] Although this study finding was due mostly to a specific disruptive event, it still demonstrates the potential impact of health systems barriers on long-term Option B+ adherence and program retention. At the six-week postpartum study visit, many of the participants expected to receive the infant HIV test results on the same day and were surprised to learn that it would take weeks to obtain results. Indeed, a recent report outlining the impact of Option B+ on the infant PMTCT cascade in Malawi found that in comparison to the PMTCT program prior to Option B+ implementation, no change was found with respect to the median time for delivery of infant HIV test results to caregivers.[13] This study indicates that communication at the health facility about the time it takes to receive infant HIV test results could be improved to ensure that expectations about the turnaround time for infant HIV test results are made clear to mothers prior to the date of testing.

HIV status was successfully disclosed to at least one person during the antenatal period by the majority of participants in the study. Often times the person to whom HIV status was disclosed was also known to be HIV-infected or known to have experience supporting other HIV-infected people and provided the participant with adherence and emotional support. Moreover, very few new disclosure events occurred for participants in the early postpartum period. These findings may serve to justify the utilization of either clinic-based peer support models such as Mothers2Mothers in South Africa[14] or community-based peer support models such as one in

Malawi training "expert mothers" experienced in PMTCT to provide education and psychosocial support to other HIV-infected pregnant women and mothers in the community.[15] On the other hand, most of the participants in this study were able to disclose to someone in their natural social network such as a husband, friend or family member, indicating that a targeted approach should be utilized for peer-based support models to ensure that the HIV-infected pregnant women and mothers receiving the intervention are truly those with an unmet need for HIV status disclosure and support.

In this study, the degree of male partner involvement in the HIV care and treatment of the participants varied greatly by participant. In some cases male partners were willing to be tested for HIV and provided continuous support to the mother and child through the early postpartum period, independent of their own serostatus. In other cases, participants received little to no support from their male partners throughout pregnancy and through six weeks postpartum. In a few cases, male partner involvement improved over time with the birth of the child, but support was purely financial in nature. In this study, lack of male partner involvement seemed to have little effect on the ability of participants to maintain good ART adherence, administer infant prophylaxis and attend clinic visits due mostly to support received from other individuals such as friends, family members or health workers. While some studies, such as a systematic review of interventions to improve PMTCT outcomes, have found that male partner involvement is associated with reductions in infant HIV transmission,[16] the degree to which male partners affect PMTCT outcomes warrants further qualitative and quantitative exploration.

Although most of the participants described having to modify their routine behaviors to accommodate ART adherence during pregnancy, many reported a normalization of this process over time, resulting in favorable adherence and clinic visit attendance experiences that were maintained through the early postpartum period. This is an interesting finding since existing literature suggests PMTCT ART adherence and program retention decrease over time. For

example, a meta-analysis of adherence to ART during and after pregnancy in low-income, middle-income and high-income settings found that while 73.5% of pregnant women exhibited good adherence, only 53% exhibited good adherence in the postpartum period.[17] It is possible that the participants in this study were uniquely good adherers due to strong support networks provided by the health facility and created by the participants themselves. Alternatively, it may be the case that adherence in the late postpartum period may decrease as predicted by previous research.

The health of the baby and a desire to live a healthy life consistently motivated the participants of the study to maintain good ART adherence, provide infants with HIV prophylaxis and attend scheduled clinic visits throughout pregnancy and in the early postpartum period. Participants were specifically interested in updates about their own CD4 count and viral load results and expected that sustaining good ART adherence would result in an HIV-negative baby and allow for a healthy, normal life. This finding indicates the positive impact that effective HIV counseling and education can have on long-term Option B+ adherence and program retention.

One limitation to this study is that only eight of the 16 six-week postpartum interviews were fully translated and transcribed for analysis at the time of manuscript preparation, suggesting that saturation at six weeks postpartum has yet to be reached. Nevertheless, a repetition of codes was becoming apparent within these first eight interviews, allowing for some conclusions to be made about the changes in experiences with the Option B+ program and ART adherence over time from pregnancy through the early postpartum period. The interview, translation and transcription process of the final eight interviews is ongoing and results will be added to the analysis as they become available. Similarly, this study is limited to the early postpartum period and does not explore the longitudinal changes in Option B+ adherence and program experiences in the later postpartum period. To address this limitation, a third set of interviews at six months postpartum with all sixteen study participants is currently under way.

The interviews completed at this third time point will allow for further exploration of the barriers and facilitators to successful ART adherence and program retention under Option B+ in the postpartum period and will illustrate the effects of infant HIV test results on adherence and program retention.

An additional limitation of this study is that adherence was high for all participants in the study so comparisons cannot be made between the experiences of adherent and non-adherent HIV-infected pregnant women and mothers with the Option B+ program. Similarly, pill count adherence measures were missing for many interview participants. If pill counts cannot be conducted by the PMTCT counselors, it is usually because patients have not returned with the pill box or the number of pills last dispensed cannot be determined by the counselor based on information in the medical chart. It is feasible that the adherence of participants for whom pill counts could not be conducted was lower than indicated using the VAS. As a result, the experiences of non-adherent HIV-infected pregnant women and mothers or the experiences of HIV-infected pregnant women and mothers who are lost to follow-up along the PMTCT cascade are not reflected in this study.

Another limitation of this study is that it does not sufficiently explore the effects of stigma on Option B+ ART adherence and program retention. Throughout the study, participants noted that learning about other individuals who were also HIV-infected but successfully managing the virus through good ART adherence was a source of motivation and encouragement. At the same time, many of the same participants also expressed concern with their own HIV status exposure. More probing on this topic area during the course of the interview process would have been helpful to better understand the sources and the role of stigma in the lives of the participants. As interviews continue in the postpartum period, updates to the field guides and suggest probes will be made to address this issue.

Finally, this study was also limited by interviewing only HIV-infected women who were currently enrolled in the Option B+ program and were participating in the control arm of the "Friends for Life Circles" randomized controlled trial. The adherence and Option B+ program experiences of the participants included in the study may therefore be different from those of HIV-infected pregnant women who are not regularly engaged in health facility-level care or from women receiving Option B+ for PMTCT at Mulago National Referral Hospital but not enrolled in the "Friends for Life" study. For example, the desire to maintain good ART adherence and receive PMTCT care and treatment services may be lower among HIV-infected pregnant women who declined to participate in the randomized controlled trial. Nonetheless, the experiences of the study participants do reflect the standard of care received at facilities such as Mulago National Referral Hospital and contribute to the limited body of research exploring the changes in PMTCT experiences under Option B+ that take place from pregnancy through the early postpartum period. As Option B+ program implementation continues, emphasis should be placed on continued training of health workers, the importance of counseling and support services at the facility level, ensuring satisfactory health service delivery, promoting HIV status disclosure and persistent HIV education beginning in pregnancy and through the early postpartum period.

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DISCUSSION AND PUBLIC HEALTH IMPLICATIONS

Summary of study findings

Substantial progress has been made over the last two and a half decades in reducing the rates of vertical HIV transmission. Nevertheless, program implementation challenges persist, especially in resource-limited settings. Under the Option B+ approach, long-term medication adherence and program retention are key outcomes that deserve attention. The goal of this project was to provide findings that could be useful for improving the current understanding of Option B+ adherence and program retention in pregnancy and the postpartum period.

Systematic review of maternal ART adherence and program retention under Option B+

The aim of this systematic review was to provide a summary of the maternal medication adherence and program retention literature since the beginning of the Option B+ era. The 19 studies included in this review were conducted in seven countries in sub-Saharan Africa. 15 of them evaluated retention in care, with loss to follow-up as the most common primary outcome, and 10 studies assessed medication adherence, with patient-self report and pill counts as the most commonly used measures of adherence. Rates of loss to follow-up ranged from 11.2% to 48.5% and that the proportion of adherent women ranged from 51.3% to 97.8%. Studies comparing program retention or adherence under the previous Option A recommendation to the current Option B+ approach found an increased risk of loss to follow-up and poorer adherence under Option B+. Women initiating antiretroviral therapy (ART) on the same day as HIV diagnosis were also more likely than women who initiated treatment at least one day after HIV diagnosis to be lost to follow-up. The majority of the included studies evaluated program retention or adherence at either pregnancy or in the postpartum period, but changes to program retention or adherence over time in a single cohort of women were not reported in any study.

Changes to Option B+ adherence and program retention at Mulago National Referral Hospital

The aim of this longitudinal cohort study was to assess changes in rates of Option B+ medication adherence and clinic visit attendance from pregnancy through six months postpartum, as well as factors that might be associated with these outcomes, for a cohort of HIV-infected women presenting for care at Mulago National Referral Hospital in 2014. This study found that utilizing a 95% cutoff, only 52.1% of HIV-infected pregnant women were adherent at the first antenatal care (ANC) visit post-ART initiation and only 44.8% were adherent at six months postpartum. 64.4% and 56.8% were adherent at the first ANC visit post-ART initiation and at six months postpartum, respectively, when an 80% adherence cutoff was used. Disclosure, having been previously diagnosed with HIV and higher education level were predictive of good adherence in ANC while higher baseline CD4 cell count, employment and previous prevention of mother-to-child transmission (PMTCT) experience were predictive of poor adherence in ANC. Good adherence at the first ANC visit post-ART initiation was the strongest predictor of good adherence at six months postpartum, while disclosure was the strongest predictor of maintaining good adherence at both time points.

71.9% of women included in this study attended the clinic at six weeks postpartum and 73.8% attended the clinic at six months postpartum. Good adherence in ANC and having been diagnosed with HIV prior to the current pregnancy were both strong predictors of clinic visit attendance at six weeks postpartum. Older mothers were also more likely than younger mothers to attend the clinic at six weeks postpartum, while women who had previous PMTCT program experience were less likely than women who were new to the PMTCT program to attend the clinic at six weeks postpartum. Having attended at least one psychosocial support group meeting between ART initiation and six months postpartum, being married, initiating ART more than 30 days before delivery and attendance at six weeks postpartum were all strong positive predictors of

clinic attendance at six months postpartum. Being employed outside of the home was a strong negative predictor of attendance at six months postpartum. Having a partner who had been counseled and tested for HIV in ANC and having spent more than 30 days on ART before delivery were positively predictive of consistently attending the clinic at both six weeks and six months postpartum. Previous PMTCT program experience was associated with a decreased odds of attendance at both postpartum clinic visits.

Understanding experiences with the Option B+ program at Mulago National Referral Hospital

The aim of this qualitative work was to explore the changing experiences of HIV-infected women enrolled in the Option B+ program from pregnancy through six weeks postpartum at Mulago National Referral Hospital and how these experiences may affect adherence and program retention in pregnancy and the postpartum period. Longitudinal in-depth interviews in ANC and at six weeks postpartum were conducted with a subsample of women enrolled in the "Friends for Life Circles" randomized controlled trial (RCT) who had been assigned to receive the standard of care. The 16 women included in this study were found to have good adherence at the first monthly ANC visit post-ART initiation and at six weeks postpartum. In the antenatal period, seven key themes were identified: 1) effective messaging and counseling at the time of HIV testing and treatment initiation; 2) reliance on health workers for support between clinic visits; 3) disclosure to an HIV-infected person; 4) variability of male partner involvement; 5) modified behaviors to prioritize health and ART adherence; 6) concern with inadvertent status disclosure and 7) a desire for a healthy baby and a healthy life. At six weeks postpartum, six additional themes representing experiences of HIV-infected mothers in the early postpartum period were also identified: 1) consistent support from health workers; 2) limitations of the health facility; 3) ongoing support after disclosure; 4) variability in male partner involvement; 5) normalization of daily ART and 6) a continued desire for a healthy baby and a healthy life. The study results

emphasized the importance of having well-trained health workers providing continued counseling and support services throughout the ANC and early postpartum period for sustaining good medication adherence and program retention among HIV-infected pregnant women and mothers enrolled in the Option B+ program. This study also demonstrated that early HIV status disclosure, specifically to individuals who were also infected with HIV or who had a good understanding of HIV care and treatment, could be a key facilitator of sustained adherence from pregnancy through six weeks postpartum.

Study strengths and limitations

The studies included in this dissertation have a number of limitations. First, time and financial constraints prevented double data abstraction from being performed in the systematic review. Although double data abstraction is not a requirement for a methodologically sound systematic review, it might have improved the consistency and accuracy of the study screening process. Next, the longitudinal data analysis of adherence was meant to include three time points: pregnancy, six weeks postpartum and six months postpartum. However, limitations in the way data were collected and recorded in labor and delivery prevented adherence calculations from being conducted at six weeks postpartum for more than half of the study population. As a result, adherence at the first ANC visit post-ART initiation and at six months postpartum were the only time points included in the analysis. Similarly, adherence could not be calculated for women who did not return to clinic with their pill boxes, thus highlighting a limitation of the pill count method for measuring adherence. In addition, because the study utilized program data from 2014, challenges surrounding missing or incomplete adherence measures were difficult to resolve two years later. In the qualitative study, one limitation was that all of the study participants reported good adherence in ANC and at six weeks postpartum so comparisons between experiences of adherers and non-adherers could not be compared in the study. In addition, delays in study start-

up and enrollment for the "Friends for Life Circles" RCT meant that in-depth interviews for all participants at all three time points could not be included in this dissertation. Finally, although conducted at a single site, the quantitative and qualitative studies in this dissertation utilized different study populations so the findings from the in-depth interviews with new initiators of Option B+ enrolled in the control arm of a randomized trial in 2016 may not be completely generalizable to the new initiators of Option B+ enrolled in the Mulago PMTCT program in 2014 who were included in the longitudinal cohort study.

Despite the limitations described above, the studies included in this project provide a unique perspective on the issue of medication adherence and program retention in the Option B+ era. At the time this dissertation was written, no other systematic reviews focusing specifically on adherence and program retention under the Option B+ approach existed in the literature. This systematic review provides a good first look at rates of adherence and loss to follow-up and the disparities that exist across different PMTCT care and treatment settings with respect to these outcomes. This review could also serve as a reference point for future PMTCT adherence and program retention research to assess whether or not adherence and program retention are improving over time with Option B+ or with future PMTCT recommendations. Similarly, relatively little is currently known about longitudinal changes in medication adherence and program retention from pregnancy through the postpartum period. The longitudinal data analysis of adherence and clinic visit attendance was able to utilize the rich PMTCT database that exists at Mulago National Referral Hospital to look at changes in adherence and clinic visit attendance over time, as well as a number of different important factors that may be affecting these outcomes in pregnancy and the postpartum period. This information could be particularly useful to the PMTCT clinic at Mulago as they evaluate the program strengths and limitations but may also be useful for the broader PMTCT research and program implementation communities as they consider appropriate interventions to improve medication adherence and program retention under

the Option B+ approach. The longitudinal in-depth interviews also provided a novel approach to understanding the experiences of HIV-infected pregnant women and mothers enrolled in Option B+ for PMTCT from pregnancy and through the postpartum period. By interviewing the same cohort of women in ANC and at six weeks and six months postpartum, this study will be able to look comprehensively at 16 individual experiences and provide 16 different stories while drawing conclusions about the collective challenges associated with successfully completing the PMTCT care and treatment cascade under Option B+ as well as potential strategies to address these challenges and improve health outcomes.

Public health implications

The results of this dissertation may be useful as PMTCT clinical care and research teams continue to strive toward the goals of eliminating vertical HIV transmission and meeting the 90-90-90 targets put forth by the Joint United Nations Program on HIV/AIDS (UNAIDS) that consist of 90% of people living with HIV diagnosed, 90% of diagnosed people on ART and 90% of people on ART achieving full viral suppression by the year 2020.[1] First, this project underscores the need for continued monitoring and evaluation of maternal medication adherence and program retention as well as interventions aimed at improving these outcomes. For example, the longitudinal data analysis of PMTCT program data included in this dissertation found that while a number of factors such as disclosure, having been previously diagnosed with HIV, employment and previous PMTCT experience affected adherence in ANC, having good adherence during pregnancy was the strongest predictor for having good adherence later in the postpartum period. In addition, the longitudinal in-depth interviews supported these findings since fear surrounding immediate initiation of ART after HIV diagnosis, balancing work with prioritizing ART adherence and reconciling past PMTCT recommendations with the revised Option B+ recommendation were challenges for many of the women interviewed, while status

disclosure to individuals who were also infected with HIV or who had a good understanding of HIV care and treatment seemed to provide a great deal of support to the participants. It could be concluded from these findings that interventions aimed at improving adherence during pregnancy may be the most effective for improving and sustaining good adherence in the postpartum period. More specifically, interventions aimed at increasing effective status disclosure, supporting health workers to provide appropriate guidance during HIV testing and ART initiation as well as throughout pregnancy and addressing the specific needs of HIV-infected pregnant women who work outside the home or desire to work outside the home may be appropriate for improving adherence and program retention in pregnancy and the postpartum period.

The studies included in this dissertation also emphasize the limitations associated with pill count adherence measures. Patient self-report and pill count are the common methods for determining adherence in resource-limited settings, but these methods have often been associated with lower reliability and overestimation of adherence in comparison to other options such as measuring plasma drug levels or viral load.[2] As seen in this dissertation, self-report and pill count adherence measures varied greatly between studies included in the systematic review and pill count adherence could not be assessed in the longitudinal data analysis for women who did not return to clinic with their pill boxes. Similarly, while all women participating in the in-depth interviews were thought to have good adherence based on self-report or pill count measures, pill count measures could not be established for all participants and in some cases, the interviews revealed that adherence may not be as good as implied from these adherence measurements. A gold standard for measuring adherence, especially in developing countries, has yet to be established, and while one study looking at a composite score of pill count, self-report and medication event monitoring systems (MEMS) adherence found good correlation with treatment response,[3] the feasibility of a MEMS approach in resource-limited settings remains uncertain. The ability to accurately measure treatment adherence is critical for understanding the problems

associated with adherence and for measuring the effects of interventions aimed at improving adherence. Recently, the limitations of pill count measures have been taken into account at Mulago National Referral Hospital and viral load measurements are now routinely collected. This change in practice may provide a more accurate depiction of medication adherence.

One of the perceived advantages of the Option B+ approach is that it does not require CD4 testing as a prerequisite for treatment initiation for PMTCT. Nevertheless, this study showed that HIV-infected pregnant women with CD4 cell counts higher than 350 cells/mm^3 were less likely to have good adherence in ANC than women with lower CD4 cell counts at baseline. This finding is important because it illustrates the potential importance of including a CD4 cell count assessment at baseline so that women with higher CD4 cell counts who may feel there is no need for ART are specifically targeted for additional counseling about the importance of good ART adherence. Similarly, although it has been found that transitioning to Option B+ has improved rates of ART initiation[4], the systematic review found that program retention and adherence were higher under Option A vs. Option B+ while the quantitative and qualitative studies included in this project found that having previous PMTCT program experience was a barrier for good adherence and clinic visit attendance under the Option B+ approach. These findings indicate that as guidelines and recommendations continue to be updated and changed, adequate resources must be set aside for education, training and support in the transition periods between recommendations for health workers as well as patients. It could also be helpful to utilize qualitative methods for formative research looking at best practices for the rollout of new guidelines prior to large-scale program implementation in the future.

Next steps and future research

A number of next steps may prove relevant with respect to the work completed for this dissertation. First, it may be useful to add a meta-analysis component to the systematic review so

the results of each included study can be combined in a statistical analysis. In addition, the systematic review focuses specifically on medication adherence and program retention but does not include outcomes measuring ART initiation, receipt of infant prophylaxis, breastfeeding practices, or infant testing and diagnosis under Option B+. As countries progress with Option B+ implementation, additional systematic reviews focusing specifically on each of these steps in the PMTCT care and treatment cascade could be useful for a more complete picture of the effectiveness of the Option B+ program at reducing vertical HIV transmission.

Next, there are a few directions in which the longitudinal data analysis of PMTCT medication adherence and clinic visit attendance could be taken to build upon the results of the study included in this dissertation. One relevant approach could be to compare the findings from 2014 to adherence and clinic visit attendance outcomes in 2015 and 2016. This could provide information about progress being made with Option B+ program implementation or reveal areas where additional interventions or support may be necessary. A prospective longitudinal cohort study focusing specifically on obtaining adherence outcomes at six weeks postpartum could also be helpful to improve the understanding of how adherence changes from the early postpartum period to the later postpartum period. Since viral load measures are now being regularly collected at Mulago, it could also be productive to compare pill count adherence measures to viral load measurements to assess agreeability between measures. Furthermore, since the Option B+ program eliminates the starting and stopping of ART between pregnancies but therefore requires good adherence to be maintained at all times, a longitudinal cohort study looking at rates of adherence and program retention between pregnancies may also be beneficial to understanding the feasibility of sustained levels of good adherence under the Option B+ approach. Finally, adding infant outcomes such as HIV testing, receipt of results, receipt of prophylaxis and infant HIV status would be the logical next step for assessing the effect of the Option B+ program on PMTCT.

The longitudinal in-depth interviews at six weeks and six months postpartum are currently under way and be completed in the coming months. The addition of these two time points to the interviews conducted in ANC will provide a more complete picture of the Option B+ program and adherence experiences at Mulago National Referral Hospital and will be useful for thinking about effective interventions aimed at improving adherence and program retention over time. Theoretically and with appropriate funding and human resources, additional in-depth interviews with the same cohort of women could be continued through two years postpartum since the "Friends for Life Circles" study follows participants up until this time point. In addition, further qualitative work aimed at understanding the experiences of PMTCT counselors with HIV-infected pregnant women and mothers as well as promoting and measuring adherence may provide insight into the challenges they face as well as what they have found to work well with regards to providing PMTCT care, treatment and adherence support.

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APPENDIX A: PREVIOUS WHO GUIDELINESS FOR PMTCT

Table 1: Recommendations for ART for women in resource-limited settings (2004)[131]

Clinical situation	Recommendation
A. HIV-infected women with indications for initiating ARV treatment who may become pregnant	First line regimens: ZDV+3TC+NVP or d4T+3TC+NVP EFV should be avoided in women of childbearing age, unless effective contraception can be ensured. Exclude pregnancy before starting treatment with EFV.
B. HIV-infected women receiving ARV treatment who become pregnant	Women: Continue with current regimen unless containing EFV, in which case substitute with NVP or PI if woman is in first trimester. Continue with ARV regimen during intrapartum period and after delivery. Infants: If born to women receiving first- or second-line ARV treatment regimens: ZDV for one week or sdNVP or sdNVP+ZDV for one week.
C. HIV-infected pregnant women with indications for ARV treatment	Women: Follow treatment guidelines as for non-pregnant adults except that EFV should not be given in first trimester. First line regimens: ZDV+3TC+NVP or d4T+3TC+NVP. Infants: ZDV for one week or sdNVP or sdNVP+ZDV for one week.
D. HIV-infected pregnant women without indications for ARV treatment	Women: ZDV starting at 28 weeks or as soon as feasible thereafter; continue during labor, plus sdNVP at onset of labor Infants: sdNVP+ZDV for one week Alternative regimens also provided in no specific order of preference.
E. HIV-infected pregnant women who have indications for starting ARV treatment when treatment is not yet available.	Follow recommendations in clinical situation D but use regimen that is most efficacious and available/feasible for use.
F. HIV-infected pregnant women with active tuberculosis	If ARV treatment is initiated, consider: ZDV+3TC+SQV/r or d4T+3TC+SQV/r If treatment initiated in third trimester, ZDV+3TC+EFV or d4T+3TC+EFV can be considered. If ARV treatment not initiated, follow recommendations in clinical situation D.
G. Pregnant women of unknown HIV status at time of labor or women in labor known to be HIV-infected who have not received ARV drugs before labor	Offer HIV testing/counseling if there is time and initiate intrapartum ARV prophylaxis if positive. If insufficient time for testing/counseling during labor offer as soon as possible postpartum and follow recommendations in clinical situation H. Women: sdNVP; if imminent delivery expected do not give dose but follow clinical situation H. Infants: sdNVP OR Women: ZDV+3TC in labor and ZDV+3TC for one week postpartum Infants: ZDV+3TC for one week
H. Infants born to HIV-infected women not receiving any ARV drugs	sdNVP as soon as possible after birth + ZDV for one week.

Table 2a: Recommendations for initiating ARV treatment in pregnant women based on clinical stage and availability of immunological markers (2006)[132]

WHO Clinical stage	CD4 testing available	CD4 testing not available
1	Do not treat	Treat if CD4 cell count < 200 cells/mm³
2	Do not treat	
3	Treat	Treat if CD4 cell count <350 cells/mm³
4	Treat	Treat irrespective of CD4 cell count

Table 2b: Recommended first-line ARV regimens for treating pregnant women and prophylactic regimens for infants (2006) [50]

Mother	
Antepartum **Intrapartum** **Postpartum**	AZT+ 3TC+NVP twice daily AZT+ 3TC+NVP twice daily AZT+ 3TC+NVP twice daily
Infant	
	AZT x 7 days; if mother receives less than four weeks of ART during pregnancy then four weeks instead of one week of infant AZT is recommended.

Table 2c: Recommended prophylactic ARV regimens for pregnant women who are not yet eligible for ART (2006) [50]

Mother	
Antepartum **Intrapartum** **Postpartum**	AZT starting at 28 weeks of pregnancy or as soon as feasible thereafter. sdNVP+AZT/3TC AZT/3TC x 7 days
Infant	
	sdNVP+AZT x 7 days; if mother receives less than four weeks of ART during pregnancy then four weeks instead of one week of infant AZT is recommended.

Table 3a: Eligibility criteria for initiating antiretroviral treatment or prophylaxis in HIV infected pregnant women (2010)[38]

WHO Clinical stage	CD4 cell count not available	CD4 cell count available	
		CD4≤ 350 cells/mm3	**CD4 >350 cells/mm3**
1	ARV prophylaxis	ART	ARV prophylaxis
2	ARV prophylaxis	ART	ARV prophylaxis
3	ART	ART	ART
4	ART	ART	ART

Table 3b: Antiretroviral treatment options recommended for HIV-infected pregnant women who are eligible for treatment (2010)[38]

Maternal ART	Infant ARV prophylaxis
Maternal antepartum daily ART starting as soon as possible irrespective of gestational age and continued during pregnancy, delivery and thereafter. Recommended regimens include: **AZT+3TC+NVP or** **AZT+3TC+EFV* or** **TDF+3TC (or FTC) +NVP or** **TDF+3TC (or FTC) + EFV*** ***Avoid use of EFV in the first trimester and use NVP instead.**	Daily NVP or twice-daily AZT from birth until 4 to 6 weeks of age (irrespective of the mode of infant feeding)

Table 3c: ARV prophylaxis options recommended for HIV-infected pregnant women not eligible for treatment for their own health (2010)[38]

Maternal AZT + infant ARV prophylaxis (Option A)	Maternal triple ARV prophylaxis (Option B)
Mother Antepartum twice-daily AZT starting from as early as 14 weeks gestation and continued during pregnancy. At onset of labor, sdNVP and initiation of twice-daily AZT+3TC for 7 days postpartum. (If maternal AZT was provided for more than 4 weeks antenatally, omission of sdNVP and AZT+3TC tail can be considered. In this case, continue maternal AZT during labor and stop at delivery.)	**Mother** Triple ARV prophylaxis starting from as early as 14 weeks gestation and continued until delivery, or if breastfeeding, continued until 1 week after all infant exposure to breast milk has ended. Recommended regimens include: AZT+3TC+LPV/r or AZT+3TC+ABC or AZT+3TC+EFV or TDV+3TC (or FTC) + EFV
Infant **For breastfeeding infants** Daily NVP from birth for at least 4-6 weeks, and until 1 week after all exposure to breast milk has ended. **For replacement feeding infants** Daily NVP or sdNVP+twice-daily AZT from birth to 4-6 weeks of age.	**Infant** Irrespective of infant feeding mode Daily NVP or twice-daily AZT from birth until 4-6 weeks of age.

APPENDIX B: PubMed search strategy

Option B+ countries concept:

Botswana[tiab] OR Burundi[tiab] OR Urundi[tiab] OR Cameroon[tiab] OR Cameroons[tiab] OR Cameron[tiab] OR Cameroun[tiab] OR Congo[tiab] OR Cote d'Ivoire[tiab] OR Ivory Coast[tiab] OR Eritrea[tiab] OR Ethiopia[tiab] OR Ghana[tiab] OR India[tiab] OR Kenya[tiab] OR Lesotho[tiab] OR Malawi[tiab] OR Mozambique[tiab] OR Namibia[tiab] OR Nigeria[tiab] OR Swaziland[tiab] OR Tanzania[tiab] OR "United Republic of Tanzania"[tiab] OR Uganda[tiab] OR Zambia[tiab] OR Zimbabwe[tiab] OR "Developing Countries"[Mesh] OR Africa[Mesh:NoExp] OR Africa, Northern[Mesh:NoExp] OR Africa South of the Sahara[Mesh:NoExp] OR Africa, Central[Mesh:NoExp] OR Africa, Eastern[Mesh:NoExp] OR Africa, Southern[Mesh:NoExp] OR Africa, Western[Mesh:NoExp] OR Asia[Mesh:NoExp] OR Asia, Central[Mesh:NoExp] OR Asia, Southeastern[Mesh:NoExp] OR "Southeast Asia"[Mesh] OR [Botswana[Mesh] OR Burundi[Mesh] OR Cameroon[Mesh] OR Congo[Mesh] OR "Cote d'Ivoire"[Mesh] OR "Democratic Republic of the Congo"[Mesh] OR Eritrea[Mesh] OR Ethiopia[Mesh] OR Ghana[Mesh] OR India[Mesh] OR Kenya[Mesh] OR Lesotho[Mesh] OR Malawi[Mesh] OR Mozambique[Mesh] OR Namibia[Mesh] OR Nigeria[Mesh] OR South Africa[Mesh] OR Swaziland[Mesh] OR Tanzania[Mesh] OR Uganda[Mesh] OR Zambia[Mesh] OR Zimbabwe[Mesh] OR "Southern African Development Community"[all fields] OR "East African Community"[all fields] OR "West African Health Organisation"[all fields] OR "Sub Saharan Africa "[all fields] OR "SubSaharan Africa "[all fields])

HIV concept:

("HIV"[mesh] OR "HIV"[all fields] OR AIDS[all] OR "HIV-1"[mesh] OR "HIV-2"[mesh] OR "Human immunodeficiency viruses"[all] OR "HTLV-III"[all] OR "Human Immunodeficiency Virus"[all fields] OR "Acquired Immune Deficiency"[all fields] OR "Acquired Immuno-Deficiency Syndrome"[all fields] OR "Acquired Immunodeficiency Syndrome"[Mesh] OR "Acquired Immunodeficiency"[all fields] OR "HIV Infections"[Mesh])

Mother-child concept:

Search "Mother-Child Relations"[Mesh] OR "Mother Child Relations"[tw] OR "Mother-Child Relation"[tw] OR "mother-to-child"[tw] OR "Mother baby"[tw] OR "Mother fetal"[tw] OR "Mother infant"[tw] OR (("Mother"[tw] OR "Mothers'[mesh] OR "Mothers"[tw] or "maternal'[tw]) AND ("Infant"[mesh] OR "infant"[tw] OR "infants"[tw] OR "neonate"[tw] OR "neonates"[tw] OR "Neo natal"[tw] OR "neonatal"[tw] OR "newborn"[tw] OR "newborns"[tw] OR "new-born"[tw] OR "new-borns"[tw] OR "Infant"[Mesh] OR "Infant, Newborn"[mesh] OR "baby"[tw] OR "babies"[tw] OR "child"[mesh] OR "child"[tw] OR "children"[tw])) OR "pregnancy"[mesh] OR "pregnancy"[tw] OR "pregnant"[tw] OR "antenatal"[tw] OR "ante natal"[tw] OR "prepartum"[tw] OR "pre partum"[tw] OR "Labor, Obstetric"[Mesh] OR "Obstetric Labor"[tw] OR "Parturition"[Mesh] OR "Parturition"[tw] OR Birth[tw] OR Births[tw] OR childbirth[tw] OR childbirths[tw] OR "Pregnant"[tw] OR "postpartum period"[mesh] OR "Puerperium"[tw] OR "Postpartum"[tw] OR" Post partum"[tw] OR "postnatal"[tw] OR "post natal"[tw] OR "intra-partum"[tw] OR "intrapartum"[tw]) OR "parent-to-child transmission"[tw] OR "parent-child"[tw] OR "parent to child"[tw]

Prophylaxis concept:

("B+"[tw] OR "B plus"[tw] OR "Option B+"[tw] OR "Option B plus"[tw] OR "Option B"[tw] OR "PMTCT"[tw] OR "Prevention of mother-to-child-transmission"[tw] OR "mother-to-child transmission"[tw] OR "vertical transmission"[tw])

Date filter: 1-Jan-2010 Searched on 29-Dec-16: 1618

APPENDIX C: Study characteristics and outcomes

Table 1: Characteristics of studies evaluating retention in care

Author year	Country	Study period*	Setting	Study design	Study population	Sample size*	Outcome definition
Auld et al. 2016[25]	Mozambique	January 2013-April 2014	Rural and urban	Prospective cohort	HIV+ adults and pregnant women	65,442	**Loss to follow-up**: ≥60 days late for next scheduled medication pick-up appointment
Chan et al. 2016[26]	Malawi	October 2011-March 2012	Rural	Retrospective cohort	Pregnant women seeking ANC	813	**Loss to follow-up**: not attending clinic for ≥ 2 months after date that last dispensed ART would run out
Dzangare et al. 2016[27]	Zimbabwe	January-March 2014	Rural	Retrospective cohort	HIV+ pregnant women	138	Attrition from care: death, stopped treatment or loss to follow-up
Ford et al. 2016[28]	Zimbabwe	September 2013-February 2015	Rural	Prospective cohort	HIV+ pregnant and breastfeeding women	435	**Loss to follow-up:** no clinic visit for 90 days
Garcia et al. 2016[29]	Mozambique	July 2013-June 2014	Unknown	Prospective cohort	HIV+ pregnant and breastfeeding women; ART-naïve and 15-50 years old	625	**Loss to follow-up:** did not return for >180 days after last visit **No Follow-up:** Missed 1st follow-up

							visit and did not return for >180 days
Author year	**Country**	**Study period***	**Setting**	**Study design**	**Study population**	**Sample size***	**Outcome definition**
Kamyuango et al. 2014[30]	Malawi	September 2008-September 2010 and September 2011-April 2012	Unknown	Retrospective cohort	HIV+ pregnant women	292	**Default:** not seen in ART clinic and off ART for more than 60 days
Kim et al. 2015[31]	Malawi	October 2009-March 2011 and October 2011-March 2013	Urban	Pre-post quasi-experimental	HIV+ pregnant women enrolled in ANC	2,546	**Loss to follow-up:** did not return for ≥60 days and cannot be traced **Withdrawal from enrollment**
Koss et al. 2016[32]	Uganda	March-September 2015	Rural	Cross-sectional	HIV+ adult women, ART-naïve and 12-28 weeks gestation	200	**Retention in care:** having attended HIV clinic in last 90 days
Landes et al. 2016[33]	Malawi	January 2012-September 2013	Rural and urban	Retrospective cohort	HIV+ adult women initiating ART	2,955	**Early default:** failed to visit clinic within 30 days of ART initiation
Mitiku et al. 2016[34]	Ethiopia	March 2013-April 2015	Urban	Retrospective cohort	HIV+ pregnant and breastfeeding women	346	**Loss to follow-up:** not seen for 90 days since last

							document ed visit
Price et al. 2014[35]	Malawi	July 2011-January 2013	Rural and Urban	Retrospecti ve cohort	HIV+ mothers who gave birth after July 1, 2011	43	**Retained in care:** no definition provided
Author year	**Country**	**Study period***	**Setting**	**Study design**	**Study population**	**Sample size***	**Outcome definition**
Schnack et al. 2016[36]	Uganda	Missing	Rural and urban	Prospective cohort	HIV+ mothers ≥ 18 years old	124	**Loss to follow-up:** Did not return for care after 1st visit
Schwartz et al. 2015[37]	South Africa	May-July 2013	Urban	Prospective cohort (pilot study)	HIV+ pregnant women ≥ 36 weeks gestation	50	**Retained in care:** active 12 months post-delivery, transferre d out or lost to follow-up
Tenthani et al. 2014[38]	Malawi	Septem ber 2011-March 2012	Rural and urban	Prospective cohort	HIV+ pregnant and breastfeedin g women, ART-naïve	11,534	**Lost to follow-up:** missed appointme nt and did not return for ≥60 days
Tweya et al. 2014[39]	Malawi	Septem ber 2011-Septem ber 2013	Urban	Retrospecti ve cohort	HIV+ pregnant and breastfeedin g women initiating ART	2.930	**Loss to follow-up:** missing next scheduled visit by ≥ 3 weeks

*Study period and sample size associated with period of Option B+ program implementation.

Table 2: Retention in care/loss to follow-up of HIV-infected pregnant women and mothers

Study	**Time at which endpoint evaluated**	**Rate of retention**	**Rate of LTFU/attrition /default**	**Associated factors**	**Effect size** (95% CI) p-value	**Factors investigated but not associated with outcome or association not assessed**
Malawi						
Chan et al.	6 months since ART initiation	N/A	15% LTFU	**PMTCT integration model** (full integration vs. HTC only) **Days between diagnosis and ART initiation** (same day vs. >1 day)	aOR=1.68 (0.98-2.88) p=0.0058 aOR=2.27 (1.34-3.85) P=0.002	Maternal age, parity, size of health facility
Kamyuan go et al.	1 year since ART initiation	N/A	2.6% default			PMTCT regimen: 3.9% default for HIV+ pregnant women receiving Option A
Kim et al.	6 months since ART initiation		11.2% LTFU	**PMTCT regimen** (Option A vs. Option B+)	5.8% LTFU under Option A X^2 test p-value=0.02	
Landes et al.	Not specified		16.4% default	**Maternal age** (>30 vs. <30) **Pregnancy status** (pregnant vs. breastfeeding) **WHO stage**	aOR= 1.27 (1.02-1.57) p=0.03 aOR=1.62 (1.28-2.05) p<0.001 aOR=0.62 (0.39-0.98)	Size of health facility, adherence

				(2 vs. 1) (3/4 vs. 1)	p=0.004 aOR=0.30 (0.15-0.60) p<0.001	
Study	**Time at which endpoint evaluated**	**Rate of retention**	**Rate of LTFU/attrition /default**	**Associated factors**		
Price et al.	6 months since ART initiation	81%		Not assessed		
Tenthani et al.	After 1st visit		39.8% LTFU	**Reason for ART** (B+ pregnant vs. own health) (B+ breastfeeding vs. own health) **Age** (30-39 vs. <30) (>40 vs. <30)	aOR=5.04 (4.16-6.10) aOR=2.24 (1.79-2.81) p<0.001 aOR=0.76 (0.65-0.88) aOR=0.59 (0.42-0.84) p=0.0002	Type of health facility
Tenthani et al.	After 3-6 months since ART initiation		17% LTFU	**Age** (30-39 vs. <30) (>40 vs. <30) **Health facility** (mission hospital vs. health center) (district hospital vs. health center) (central hospital vs. health center)	aOR=0.63 (0.46-0.87) aOR=0.76 (0.47-1.22) p=0.0153 aOR=0.51 (0.21-1.25) aOR=1.57 (0.90-2.71) aOR=1.24 (0.66-2.33) p=0.0129	Reason for ART
Tweya et al.	Not specified		20% LTFU	**Maternal age** (13-24 vs. ≥25)	aRRatio=1.29 (1.09-1.52) p<0.001	Employment status

				Pregnancy status at ART initiation (breastfeeding vs. pregnant) **Year of implementation** (2011 vs. 2012) (2013 vs. 2012)	aRRatio=0.63 (0.49-0.82) p<0.001 aRRatio=1.25 (1.06-1.49) aRRatio=0.41 (0.29-0.58) p<0.001	
Study	**Time at which endpoint evaluated**	**Rate of retention**	**Rate of LTFU/attrition /default**	**Associated factors**	**Effect size** (95% CI) p-value	**Factors investigated but not associated with outcome or association not assessed**
Mozambique						
Auld et al.	6 months since ART initiation		38% LTFU			ART status: 26% LTFU for HIV+ pregnant women not on Option B+; 18% LTFU for non-pregnant women
Garcia et al.	1 year since ART initiation		48.5% LTFU	**ART group** (B+ pregnant vs. own health) (B+ lactacting vs. own health) **Health center** (outpatient w/clinician vs. inpatient w/physician) **PMTCT regimen**	asHR=2.77 (2.18-3.50) p<0.001 asHR= 1.94 (1.37-2.74) p<0.001 asHR=1.45 (1.17-1.80) p<0.001	Maternal age, WHO stage, time from HIV diagnosis to ART start

				(Option B+ vs. Option A)	asHR= 1.91 (1.40-2.60) p<0.001	
Garcia et al.	1 year since ART initiation		25.6% no follow up	**ART group** (B+ pregnant vs. own health) (B+ lactating vs. own health) **PMTCT regimen** (Option B+ vs. Option A)	aOR=4.07 (2.53-6.56) p<0.001 aOR=2.36 (1.23-4.52) p=0.01 aOR=3.33 (1.50-7.40) p=0.003	Maternal age, WHO stage, time from HIV diagnosis to ART start, type of health center
Study	**Time at which endpoint evaluated**	**Rate of retention**	**Rate of LTFU/attrition /default**	**Associated factors**	**Effect size** (95% CI) p-value	**Factors investigated but not associated with outcome or association not assessed**
Uganda						
Koss et al.	Not specified	90%		Not assessed		
Schnack et al.	After 1st visit		36.3% LTFU	**Education** (Tertiary vs. below tertiary) **HIV status awareness** (previously unknown vs. previously known) **Status disclosure** (no vs. yes)	OR=0.127 (0.016-1.011) p=0.031 OR=3.059 (0.966-9.688) p=0.049 OR=3.396 (1.182-9.760) p=0.019	Maternal age, marital status, income, travel cost/distance to clinic, male partner involvement, gravidity, gestation, CD4 at initiation
Zimbabwe						
Dzangare et al.	6 months since ART initiation		17.4 % attrition (15.9% LTFU, <1% dead, <1% stopped treatment)	**Maternal age** (20-24 vs. 15-19)	aRR=0.2 (0.1-0.5) p=0.000 aRR=0.1	Gestational age, time from HIV diagnosis to ART initiation,

				(25-29 vs. 15-19) (30-34 vs. 15-19) (35+ vs. 15-19) **Gravidity** (2 vs. 1) (3 vs. 1) (≥4 vs. 1)	(0.0-0.5) p=0.001 aRR=0.2 (0.0-0.8) p=0.022 aRR=0.0 (0.0-0.4) p=0.004 aRR=5.4 (1.6-18.7) p=0.008 aRR=7.4 (1.7-32.5) p=0.008 aRR=8.8 (1.9-40.2) p=0.005	facility type
Study	**Time at which endpoint evaluated**	**Rate of retention**	**Rate of LTFU/attrition /default**	**Associated factors**	**Effect size** (95% CI) p-value	**Factors investigated but not associated with outcome or association not assessed**
Ford et al.	6 months and 1 year since ART initiation		13.7% LTFU at 6 months 14.2% LTFU at 12 months	**Maternal age** (per year increase)	aHR=0.94 (0.90-0.98) p=0.01	Pregnancy status at ART initiation, type of facility, initiation period, CD4 at initiation
Ethiopia						
Mitiku et al.	Study period		16.5% LTFU (28% of LTFU had no follow-up visit)	**Maternal age** (18-24 vs. 30-40) (25-29 vs. 30-40)	aHR=2.3 (1.2-4.5) aHR=0.67 (0.3-1.5) p=0.017 aHR=1.8 (1.1-3.2) p=0.039	Weight at enrollment

				Health facility (hospital vs. health center) **ART started on day of diagnosis** (yes vs. no) **CD4 test done 3 months before and 1 month after ART initiation** (no vs. yes)	aHR=1.9 (1.1-3.2) p=0.032 aHR=2.3 (1.2-4.4) p=0.010	
Study	**Time at which endpoint evaluated**	**Rate of retention**	**Rate of LTFU/attrition /default**	**Associated factors**	**Effect size** (95% CI) p-value	**Factors investigated but not associated with outcome or association not assessed**
South Africa						
Schwartz et al.	12 months after delivery	66%	24% LTFU 10% Transferred out	Not assessed		

*LTFU: Loss to follow-up; OR=odds ratio; aOR= adjusted odds ratio; aRR= adjusted relative risk; aRRatio=adjusted rate ratio, asHR=subdistribution hazard ratio, aHR= adjusted hazard ratio

Table 3: Characteristics of studies evaluating medication adherence

Author year	Country	Study period*	Setting	Study design	Study population	Sample size*	Outcome definition
Chan et al. 2016	Malawi	October 2011-March 2012	Rural	Retrospective cohort	Pregnant women seeking ANC	813	**Cumulative retention on ART:** % on ART
Ebuy et al. 2014[40]	Ethiopia	Missing	Rural and urban	Cross-sectional	HIV+ pregnant women in treatment ≥ 2 months and initiated ART during pregnancy	277	**Self-report** with 4-question multi-method tool; "No" to all questions = good adherence
Gill et al. 2016[41]	Rwanda	April 2013-January 2014	Urban	Prospective cohort	HIV+ pregnant women in 3rd trimester	608	**Self-report**: # missed doses in last 3 days; 0 doses missed = adherent
Kamyuango et al. 2014	Malawi	September 2008-September 2010 and September 2011-April 2012	Unknown	Retrospective cohort	HIV+ pregnant women	292	**Pill count:** ≤ 95% adherence at either of last two clinic visits during 1 year follow-up period= non-adherent
Landes et al. 2016	Malawi	January 2012-September 2013	Rural and urban	Retrospective cohort	HIV+ adult women initiating ART	2,955	**Self-report:** # pills remaining out of those prescribed at last visit; ≥95%= adherent
Phillips et al. 2016[42]	South Africa	April 2013-June 2014	Urban	Prospective cohort	HIV+ pregnant women > 18 years old making 1st ANC visit for current pregnancy	526	**Self-report:** # missed doses in last 30 days **Treatment discontinuation:** no doses for ≥ 30 days
Price et al. 2014	Malawi	July 2011-January 2013	Rural and Urban	Retrospective cohort	HIV+ mothers who gave birth after July 1, 2011	43	**Self-report:** on treatment at time of interview

Schnack et al. 2016	Uganda	Missing	Rural and urban	Prospective cohort	HIV+ pregnant women >18 years old	124	**Pill count adherence:** <80% = "inadequate"; 80-94.5%="moderate" and ≥95%="adequate" adherence
Author year	**Country**	**Study period***	**Setting**	**Study design**	**Study population**	**Sample size***	**Outcome definition**
Schwartz et al., 2015	South Africa	May-July 2013	Urban	Prospective cohort (pilot study)	HIV+ pregnant women ≥ 36 weeks gestation	50	**Prescription pick-up: ≥**1 ARV pick-ups after delivery (0-10 weeks postpartum)
Tsegaye et al. 2016[43]	Ethiopia	March-April 2016	Rural	Cross-sectional	HIV+ pregnant and lactating women	190	**Pill count:** missing ≥1 dose= non-adherent **Self-report:** missing 0 doses in last 4 weeks and answer ≥ 2 out of 4 questions correctly= good adherence

*Study period and sample size associated with period of Option B+ program implementation.

Table 4: Maternal ART adherence among HIV-infected pregnant women and mothers

Study	Time at which endpoint evaluated	Percent adherent	Associated factors	Effect size (95% CI) p-value	Factors investigated but not associated with outcome or association not assessed
Malawi					
Chan et al.	3 months since ART initiation	84%	**PMTCT integration model** (full integration vs. HTC only)	Full integration: 79% HTC only: 87% p=0.02	
Chan et al.	6 months since ART initiation	81%	**PMTCT integration model** (full integration vs. HTC only)	Full integration: 75% HTC only: 86% p=0.003	
Kamuyango et al.	1 year since ART initiation	95.8%			PMTCT regimen: 98% adherent for HIV+ pregnant women receiving Option A
Landes et al.	Not specified	97.8%			Pregnancy status at initiation: pregnant vs. breastfeeding
Price et al.	Time of interview (mean 4.3 months since initiation post-delivery)	88%	Not assessed		
Ethiopia					
Ebuy et al.	Time of interview (during pregnancy)	87.1%	**Counselled on side effects** (yes vs. no) **Status disclosure** (yes vs. no)	aOR= 4.75 (1.98-11.35) p<0.01 aOR=4.21 (1.07-16.33) p<0.05	WHO clinical stage, CD4 cell count, male partner involvement, knowledge on Option B+, attitude toward Option B+, place of residence
Tsegay et al.	Time of interview (pregnancy or breastfeeding)	87.9%	**Health facility** (hospital vs. health center) **Residence** (rural vs. urban)	aOR=0.30 (0.11-0.80) p<0.05 aOR=0.26 (0.09-0.73) p<0.05 aOR=0.08 (0.02-0.37) p<0.05	Age, marital status, education level, experienced side effects

			Challenges with same-day initiation (yes vs. no)		
Study	**Time at which endpoint evaluated**	**Percent adherent**	**Associated factors**	**Effect size** (95% CI) p-value	**Factors investigated but not associated with outcome or association not assessed**
South Africa					
Phillips et al.	Twice during pregnancy and immediately after delivery	68% missed 0 doses 28% missed 1-3 doses 4% missed ≥4 doses	**Side effect frequency** (# of side effects) **Side effect type** (any type vs. none) **Side effect severity** (low vs. high)	aOR=1.20 (1.12-1.29) p<0.001 aOR=2.65 (1.46-4.81) p=0.001 0.25 (0.14-0.45) p<0.001	
Schwartz et al.	12 months after delivery	90%	Not assessed		
Rwanda					
Gill et al.	At study enrollment (third trimester pregnancy or ≤2 weeks post-delivery)	90.9%	Not assessed		
Uganda					
Schnack et al.	Pre-delivery	51.3% with ≥95% adherence 27.6% with 80-94.9% adherence 21.1% with <80% adherence	**Education** (Tertiary vs. below tertiary)	OR=0.259 (0.064-1.048) p=0.047	Maternal age, income, travel cost/distance to clinic, HIV status awareness, disclosure, male partner involvement, gravidity, gestation, CD4 cell count

APPENDIX D: Quality assessment

Table 1a: Quality assessment of studies measuring program retention

Author year	Selection bias	Study design	Confounders	Blinding	Data collection methods	Withdra-wals or dropouts	Integrity of interven-tion*
Auld et al. 2016	Moderate	Moderate	Weak	Weak	Weak	Moderate	Weak
Chan et al. 2016	Moderate	Moderate	Weak	Moderate	Strong	N/A	Weak
Dzangare et al. 2016	Moderate	Moderate	Strong	Moderate	Weak	N/A	Moderate
Ford et al. 2016	Moderate	Moderate	Weak	Moderate	Weak	N/A	Weak
Garcia et al. 2016	Moderate	Moderate	Strong	Moderate	Strong	N/A	Moderate
Kamuyan go et al. 2014	Moderate	Moderate	Weak	Moderate	Weak	N/A	Weak
Kim et al. 2015	Moderate	Moderate	Weak	Moderate	Weak	N/A	Moderate
Koss et al. 2016	Strong	Moderate	Weak	Moderate	Strong	Strong	Moderate
Landes et al. 2016	Moderate	Moderate	Strong	Moderate	Strong	N/A	Moderate
Mitiku et al. 2016	Moderate	Moderate	Strong	Moderate	Weak	N/A	Moderate
Price et al. 2014	Moderate	Moderate	Weak	Moderate	Strong	N/A	Moderate
Schnack et al. 2016	Weak	Moderate	Weak	Moderate	Weak	N/A	Moderate
Schwartz et al. 2015	Moderate	Moderate	Strong	Moderate	Strong	N/A	Moderate
Tenthani et al. 2014	Moderate	Moderate	Weak	Moderate	Strong	N/A	Moderate
Tweya et al. 2014	Moderate	Moderate	Strong	Moderate	Strong	N/A	Weak

*In this review, the "intervention" refers to implementation of the Option B+ program.

Table 1b: Quality assessment of studies measuring adherence

Author year	Selection bias	Study design	Confounders	Blinding	Data collection methods	Withdra-wals or dropouts	Integrity of interven-tion*
Chan et al. 2016	Moderate	Moderate	Weak	Moderate	Strong	N/A	Weak
Ebuy et al. 2014	Strong	Weak	Weak	Moderate	Strong	N/A	Moderate
Gill et al. 2016	Moderate	Moderate	Strong	Moderate	Moderate	Weak	Moderate
Kamuyan go et al. 2014	Moderate	Moderate	Weak	Moderate	Weak	Strong	Weak
Landes et al. 2016	Moderate	Moderate	Strong	Moderate	Moderate	Moderate	Moderate
Phillips et al. 2016	Moderate	Moderate	Strong	Moderate	Moderate	Strong	Moderate
Price et al. 2014	Moderate	Moderate	Weak	Moderate	Moderate	Weak	Moderate
Schnack et al. 2016	Weak	Moderate	Weak	Moderate	Moderate	Moderate	Moderate
Schwartz et al. 2015	Moderate	Moderate	Strong	Moderate	Moderate	Strong	Moderate
Tsegaye et al. 2016	Moderate	Weak	Weak	Moderate	Strong	N/A	Moderate

*In this review, the "intervention" refers to implementation of the Option B+ program.

APPENDIX E: Logistic regression results

Table 1a: Univariate and multivariate logistic regression results for 95% adherence in ANC (nonadherence defined as medication adherence <95%)

Factor	Total not adherent (%)	Total adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	63 (38.9)	100 (61.4)	Reference group		Reference group	
25-34	59 (31.1)	131 (69.0)	1.40 (0.90, 2.17)	0.135	1.22 (0.69, 2.17)	0.485
35-60	7 (30.4)	16 (69.6)	1.44 (0.56, 3.70)	0.448	0.81 (0.26, 2.59)	0.726
Education						
None/primary	49 (40.5)	72 (59.5)	Reference group		Reference group	
Secondary/post-secondary	70 (31.5)	152 (68.5)	1.48 (0.93, 2.34)	0.096	1.73 (0.99, 3.02)	0.056
Parity						
0	46 (36.2)	81 (63.8)	Reference group		Reference group	
≥1	83 (33.3)	166 (66.7)	1.14 (0.73, 1.78)	0.577	1.21 (0.68, 2.15)	0.517
Employment						
Housewife/not employed	60 (34.5)	114 (65.5)	Reference group		Reference group	
Employed	58 (34.3)	111 (65.7)	1.01 (0.65, 1.57)	0.975	0.81 (0.47, 1.39)	0.449
Marital status						
Not married	11 (45.8)	13 (54.2)	Reference group		Reference group	
Married	110 (33.3)	220 (66.7)	1.69 (0.73, 3.90)	0.217	1.76 (0.64, 4.85)	0.277
Baseline CD4 (cells/mm$^{3)}$						
≤350						
>350	43 (29.9)	101 (70.1)	Reference group		Reference group	
	88 (37.3)	148 (62.7)	0.72 (0.46, 1.12)	0.140	0.55 (0.31, 0.96)	0.036
Previous PMTCT						
No	100 (32.3)	210 (67.7)	Reference group		Reference group	
Yes	29 (43.9)	37 (56.1)	0.61 (0.35, 1.04)	0.071	0.53 (0.26, 1.09)	0.086
Previous HIV diagnosis						
No	102 (36.7)	176 (63.3)	Reference group		Reference group	
Yes	29 (28.2)	74 (71.8)	1.48 (0.90, 2.42)	0.120	1.37 (0.76, 2.46)	0.295
Disclosure						
No	50 (39.4)	77 (60.6)	Reference group		Reference group	
Yes	71 (30.9)	159 (69.1)	1.45 (0.92, 2.29)	0.105	1.54 (0.89, 2.67)	0.122
Partner counseled/tested						
No						
Yes	109 (35.2)	201 (64.8)	Reference group		Reference group	
	23 (31.9)	49 (68.1)	1.16 (0.69, 2.00)	0.605	1.02 (0.52, 1.99)	0.962

Table 1b: Univariate and multivariate logistic regression results for 95% adherence in ANC (nonadherence defined as medication adherence <95% or did not return with pill box/did not return for clinic visit)

Factor	Total not adherent (%)	Total adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	102 (50.5)	100 (49.5)	Reference group		Reference group	
25-34	96 (42.3)	131 (57.7)	1.39 (0.95, 2.03)	0.089	1.32 (0.81, 2.14)	0.273
35-60	11 (40.7)	16 (59.3)	1.48 (0.65, 3.35)	0.343	0.84 (0.31, 2.30)	0.737
Education						
None/primary	87 (54.7)	72 (45.3)	Reference group		Reference group	
Secondary/post-secondary	109 (41.8)	152 (58.2)	1.69 (1.13, 2.51)	0.010	2.00 (1.23, 3.26)	0.005
Parity						
0	72 (47.1)	81 (52.9)	Reference group		Reference group	
≥1	138 (45.4)	166 (54.6)	1.07 (0.72, 1.58)	0.736	1.23 (0.75,2.04)	0.410
Employment						
Housewife/not employed	100 (46.7)	114 (53.3)	Reference group		Reference group	
Employed	95 (46.1)	111 (53.9)	1.02 (0.70, 1.50)	0.900	0.81 (0.51, 1.29)	0.383
Marital status						
Not married	13 (50.0)	13 (50.0)	Reference group		Reference group	
Married	182 (45.3)	220 (54.7)	1.21 (0.55, 2.67)	0.639	1.16 (0.43, 3.08)	0.772
Baseline CD4 (cells/mm$^{3)}$						
≤350						
>350	61 (37.7)	101 (62.4)	Reference group		Reference group	
	150 (50.3)	148 (49.7)	0.60 (0.40, 0.88)	0.009	0.53 (0.33, 0.86)	0.010
Previous PMTCT						
No	166 (44.2)	210 (55.9)	Reference group		Reference group	
Yes	43 (53.8)	37 (46.3)	0.68 (0.42, 1.10)	0.119	0.57 (0.30, 1.07)	0.083
Previous HIV diagnosis						
No	169 (49.0)	176 (51.0)	Reference group		Reference group	
Yes	44 (37.3)	74 (62.7)	1.61 (1.05, 2.48)	0.028	1.52 (0.91, 2.53)	0.112
Disclosure						
No	91 (54.2)	77 (45.8)	Reference group		Reference group	
Yes	109 (40.7)	159 (59.3)	1.72 (1.17, 2.54)	0.006	1.84 (1.15, 2.94)	0.011
Partner counseled/tested						
No						
Yes	173 (46.3)	201 (53.7)	Reference group		Reference group	
	41 (45.6)	49 (54.4)	1.03 (0.65, 1.63)	0.905	1.00 (0.56, 1.76)	0.988

Table 1c: Univariate and multivariate logistic regression results for 80% adherence in ANC (nonadherence defined as medication adherence <80%)

Factor	Total not adherent (%)	Total adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	32 (19.6)	131 (80.4)	Reference group		Reference group	
25-34	36 (19.0)	154 (81.1)	1.04 (0.61, 1.78)	0.871	0.89 (0.43, 1.81)	0.743
35-60	4 (17.4)	19 (82.6)	1.16 (0.37, 3.65)	0.799	0.70 (0.19. 2.86)	0.614
Education						
None/primary	22 (18.2)	99 (81.8)	Reference group		Reference group	
Secondary/post-secondary	44 (19.8)	178 (80.2)	0.90 (0.51, 1.59)	0.713	0.96 (0.47, 1.97)	0.910
Parity						
0	25 (19.7)	102 (80.3)	Reference group		Reference group	
≥1	46 (18.5)	203 (81.5)	1.08 (0.63, 1.86)	0.777	1.31 (0.65, 2.68)	0.446
Employment						
Housewife/not employed	29 (16.7)	145 (83.3)	Reference group		Reference group	
Employed	37 (21.9)	132 (78.1)	0.71 (0.42, 1.22)	0.221	0.58 (0.29, 1.14)	0.112
Marital status						
Not married	8 (33.3)	16 (66.7)	Reference group		Reference group	
Married	58 (17.6)	272 (82.4)	2.34 (0.96, 5.74)	0.062	2.48 (0.82, 7.47)	0.107
Baseline CD4 (cells/mm$^{3)}$						
≤350						
>350	22 (15.3)	122 (84.7)	Reference group		Reference group	
	50 (21.2)	186 (78.8)	0.67 (0.39. 1.16)	0.156	0.52 (0.25, 1.05)	0.070
Previous PMTCT						
No	56 (18.1)	254 (81.9)	Reference group		Reference group	
Yes	16 (24.2)	50 (75.8)	0.69 (0.37, 1.30)	0.249	0.93 (0.37, 2.34)	0.871
Previous HIV diagnosis						
No	55 (19.8)	223 (80.2)	Reference group		Reference group	
Yes	18 (17.5)	85 (82.5)	1.16 (0.65, 2.10)	0.611	0.99 (0.48, 2.04)	0.988
Disclosure						
No	28 (22.1)	99 (78.0)	Reference group		Reference group	
Yes	36 (15.7)	194 (84.3)	1.52 (0.88, 2.64)	0.133	1.78 (0.91, 3.48)	0.094
Partner counseled/tested						
No						
Yes	62 (20.0)	248 (80.0)	Reference group		Reference group	
	11 (15.3)	61 (84.7)	1.39 (0.69, 2.79)	0.360	0.76 (0.33, 1.76)	0.524

Table 1d: Univariate and multivariate logistic regression results for 80% adherence in ANC (nonadherence defined as medication adherence <80% or did not return with pill box/did not return for clinic visit)

Factor	Total not adherent (%)	Total adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	71 (35.2)	131 (64.9)	Reference group		Reference group	
25-34	73 (32.2)	154 (67.8)	1.14 (0.77, 1.71)	0.513	1.10 (0.66, 1.85)	0.712
35-60	8 (29.6)	19 (70.4)	1.29 (0.54, 3.09)	0.572	0.83 (0.29. 2.36)	0.725
Education						
None/primary	60 (37.7)	99 (62.3)	Reference group		Reference group	
Secondary/post-secondary	83 (31.8)	178 (68.2)	1.30 (0.86, 1.96)	0.214	1.46 (0.88, 2.42)	0.144
Parity						
0	51 (33.3)	102 (66.7)	Reference group		Reference group	
≥1	101 (33.2)	203 (66.8)	1.00 (0.66, 1.52)	0.981	1.27 (0.75, 2.15)	0.373
Employment						
Housewife/not employed	69 (32.2)	145 (67.8)	Reference group		Reference group	
Employed	74 (35.9)	132 (64.1)	0.85 (0.57, 1.27)	0.427	0.69 (0.42, 1.12)	0.134
Marital status						
Not married	10 (38.5)	16 (61.5)	Reference group		Reference group	
Married	130 (32.4)	272 (67.8)	1.31 (0.58, 2.96)	0.520	1.19 (0.44, 3.19)	0.735
Baseline CD4 (cells/mm$^{3)}$						
≤350						
>350	40 (24.7)	122 (75.3)	Reference group		Reference group	
	112 (37.6)	186 (62.4)	0.54 (0.36, 0.83)	0.005	0.55 (0.33, 0.92)	0.022
Previous PMTCT						
No	122 (32.5)	254 (67.8)	Reference group		Reference group	
Yes	30 (37.5)	50 (62.5)	0.80 (0.48, 1.32)	0.385	0.84 (0.43, 1.64)	0.601
Previous HIV diagnosis						
No	122 (35.4)	223 (64.6)	Reference group		Reference group	
Yes	33 (28.0)	85 (72.0)	1.41 (0.89, 2.23)	0.143	1.29 (0.74, 2.22)	0.367
Disclosure						
No	69 (41.1)	99 (58.9)	Reference group		Reference group	
Yes	74 (27.6)	194 (72.4)	1.83 (1.22, 2.75)	0.004	2.07 (1.28, 3.37)	0.003
Partner counseled/tested						
No						
Yes	126 (33.7)	248 (66.3)	Reference group		Reference group	
	29 (32.2)	61 (67.8)	1.07 (0.65, 1.75)	0.791	0.85 (0.47, 1.56)	0.601

Table 2a: Univariate and multivariate logistic regression results for 95% adherence at six months postpartum (nonadherence defined as medication adherence <95%)

Factor	Not adherent (%)	Adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	34 (28.57)	85 (71.4)	Reference group		Reference group	
25-34	42 (28.4)	106 (71.6)	1.01 (0.59, 1.72)	0.972	1.81 (0.79, 4.14)	0.157
35-60	4 (17.4)	19 (82.6)	1.90 (0.60, 6.00)	0.274	2.20 (0.44, 11.00)	0.337
Education						
None/primary	34 (33.3)	68 (66.7)	Reference group		Reference group	
Secondary/post-secondary	36 (21.8)	129 (78.2)	1.79 (1.03, 3.11)	0.039	1.53 (0.69, 3.36)	0.295
Parity						
0	18 (18.4)	80 (81.6)	Reference group		Reference group	
≥1	60 (31.1)	133 (68.9)	0.50 (0.28, 0.90)	0.022	0.39 (0.16, 0.97)	0.043
Employment						
Housewife/not employed	37 (28.0)	95 (72.0)	Reference group		Reference group	
Employed	34 (25.2)	101 (74.8)	1.16 (0.67, 1.99)	0.599	0.76 (0.36, 1.63)	0.486
Marital status						
Not married	3 (20.0)	12 (80.0)	Reference group		Reference group	
Married	73 (28.6)	182 (71.4)	0.62 (0.17, 2.27)	0.474	0.44 (0.08, 2.35)	0.335
Baseline CD4 (cells/mm$^{3)}$						
≤350	22 (19.8)	89 (80.2)	Reference group		Reference group	
>350	59 (32.4)	123 (67.6)	0.52 (0.29, 0.90)	0.020	0.66 (0.30, 1.44)	0.300
Previous PMTCT						
No	66 (27.6)	173 (72.4)	Reference group		Reference group	
Yes	14 (27.5)	37 (72.6)	1.01 (0.51, 1.98)	0.982	0.72 (0.25, 2.03)	0.530
Previous HIV diagnosis						
No	60 (26.7)	165 (73.3)	Reference group		Reference group	
Yes	21 (30.4)	48 (69.6)	0.83 (0.46, 1.50)	0.540	0.84 (0.36, 1.94)	0.678
Disclosure						
No	35 (33.0)	71 (67.0)	Reference group		Reference group	
Yes	43 (24.9)	130 (75.1)	1.49 (0.88, 2.54)	0.141	1.08 (0.50, 2.31)	0.852
Partner counseled/tested						
No	67 (28.9)	165 (71.1)	Reference group		Reference group	
Yes	14 (21.9)	50 (78.1)	1.45 (0.75, 2.80)	0.268	2.09 (0.79, 5.53)	0.137
PSS group attendance						
No	67 (28.6)	167 (71.4)	Reference group		Reference group	
Yes	14 (22.6)	48 (77.4)	1.38 (0.71, 2.66)	0.343	1.22 (0.45, 3.32)	0.703
Time on ART in pregnancy						
≤30 days	15 (30.0)	35 (70.0)	Reference group		Reference group	
>30 days	66 (26.8)	180 (73.2)	1.17 (0.60, 2.28)	0.647	0.49 (0.17, 1.40)	0.182
Adherent in ANC						
No	27 (33.3)	54 (66.7)	Reference group		Reference group	
Yes	37 (22.2)	130 (77.8)	1.76 (0.97, 3.17)	0.061	1.89 (0.90, 3.96)	0.092
Attended six week postpartum visit						
No	13 (29.6)	31 (70.5)	Reference group		Reference group	
Yes	68 (27.1)	183 (72.9)	1.13 (0.56, 2.28)	0.737	1.55 (0.59, 4.07)	0.377

Table 2b: Univariate and multivariate results for 95% adherence at six months postpartum (nonadherence defined as medication adherence <95% or did not return with pill box/did not return for clinic visit)

Factor	Not Adherent (%)	Adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	110 (56.4)	85 (43.6)	Reference group		Reference group	
25-34	118 (52.7)	106 (47.3)	1.16 (0.79, 1.71)	0.444	1.11 (0.64, 1.91)	0.720
35-60	8 (29.6)	19 (70.4)	3.07 (1.28, 7.35	0.012	1.97 (0.63, 6.14)	0.243
Education						
None/primary	89 (56.7)	68 (43.3)	Reference group		Reference group	
Secondary/post-secondary	127 (49.6)	129 (50.4)	1.33 (0.89, 1.98)	0.163	1.17 (0.68, 2.02)	0.569
Parity						
0	71 (47.0)	80 (53.0)	Reference group		Reference group	
≥1	164 (55.2)	133 (44.8)	0.72 (0.49, 1.07)	0.101	0.76 (0.43, 1.33)	0.330
Employment						
Housewife/not employed	115 (54.8)	95 (45.2)	Reference group		Reference group	
Employed	102 (50.3)	101 (49.8)	1.20 (0.81, 1.76)	0.358	0.85 (0.51, 1.43)	0.541
Marital status						
Not married	12 (50.0)	12 (50.0)	Reference group		Reference group	
Married	212 (53.8)	182 (46.2)	0.86 (0.38, 1.96)	0.717	0.86 (0.30, 2.51)	0.786
Baseline CD4 (cells/mm$^{3)}$						
≤350	70 (44.0)	89 (56.0)	Reference group		Reference group	
>350	169 (57.9)	123 (42.1)	0.57 (0.39, 0.85)	0.005	0.69 (0.41, 1.16)	0.160
Previous PMTCT						
No	195 (53.0)	173 (47.0)	Reference group		Reference group	
Yes	41 (52.6)	37 (47.4)	1.02 (0.63, 1.66)	0.946	1.18 (0.58, 2.43)	0.648
Previous HIV diagnosis						
No	177 (51.8)	165 (48.3)	Reference group		Reference group	
Yes	63 (56.8)	48 (43.2)	0.82 (0.53, 1.26)	0.359	0.80 (0.45, 1.42)	0.437
Disclosure						
No	93 (56.7)	71 (43.3)	Reference group		Reference group	
Yes	134 (50.8)	130 (49.2)	1.27 (0.86, 1.88)	0.231	0.96 (0.57, 1.61)	0.877
Partner counseled/tested						
No						
Yes	199 (54.7)	165 (45.3)	Reference group		Reference group	
	41 (45.1)	50 (55.0)	1.47 (0.93, 2.33)	0.101	1.59 (0.85, 2.95)	0.145
PSS group attendance						
No	209 (55.6)	167 (44.4)	Reference group		Reference group	
Yes	31 (39.2)	48 (60.8)	1.94 (1.18, 3.18)	0.009	1.39 (0.73, 2.63)	0.312
Time on ART in pregnancy						
≤30 days	46 (56.8)	35 (43.2)	Reference group		Reference group	
>30 days	154 (46.1)	180 (53.9)	0.58 (0.40, 0.84)	0.004	1.16 (0.63, 2.14)	0.637
Adherent in ANC						
No	126 (61.5)	79 (38.5)	Reference group		Reference group	
Yes	105 (44.7)	130 (55.3)	1.97 (1.35, 2.89)	0.000	2.00 (1.21, 3.30)	0.006
Attended six week postpartum visit						
No	73 (70.2)	31 (29.8)	Reference group		Reference group	
Yes	138 (43.0)	183 (57.0)	3.12 (1.94, 5.02)	0.000	2.78 (1.51, 5.12)	0.001

Table 2c: Univariate and multivariate logistic regression results for 80% adherence at six months postpartum (nonadherence defined as medication adherence <80%)

Factor	Not adherent (%)	Adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	11 (9.2)	108 (90.8)	Reference group		Reference group	
25-34	11 (7.4)	137 (92.6)	1.27 (0.53, 3.04)	0.593	1.58 (0.37, 6.80)	0.540
35-60	0 (0.0)	23 (100.0)			N/A	N/A
Education						
None/primary	10 (9.8)	92 (90.2)	Reference group		Reference group	
Secondary/post-secondary	9 (5.5)	156 (94.6)	1.88 (0.74, 4.81)	0.185	1.34 (0.34, 5.26)	0.676
Parity						
0	5 (5.1)	93 (94.9)	Reference group		Reference group	
≥1	17 (8.8)	176 (91.2)	0.56 (0.20, 1.56)	0.264	0.37 (0.07, 2.09)	0.262
Employment						
Housewife/not employed	11 (8.3)	121 (91.7)	Reference group		Reference group	
Employed	8 (5.9)	127 (94.1)	1.44 (0.56, 3.71)	0.446	2.22 (0.49, 10.06)	0.300
Marital status						
Not married	3 (20.0)	12 (80.0)	Reference group		Reference group	
Married	18 (7.1)	237 (92.4)	3.29(0.85, 12.74)	0.084	3.13 (0.42, 23.38)	0.266
Baseline CD4 (cells/mm$^{3)}$						
≤350	7 (6.3)	104 (93.7)	Reference group		Reference group	
>350	16 (8.8)	166 (91.2)	0.70 (0.28, 1.75)	0.445	1.41 (0.35, 5.72)	0.631
Previous PMTCT						
No	18 (7.5)	221 (92.5)	Reference group		Reference group	
Yes	4 (7.8)	47 (92.2)	0.96 (0.31, 2.96)	0.939	0.38 (0.05, 2.86)	0.347
Previous HIV diagnosis						
No	14 (6.2)	211 (93.8)	Reference group		Reference group	
Yes	9 (13.0)	60 (87.0)	0.44 (0.18, 1.07)	0.071	0.10 (0.23, 0.47)	0.003
Disclosure						
No	12 (11.3)	94 (88.7)	Reference group		Reference group	
Yes	11 (6.4)	162 (93.6)	1.88 (0.80, 4.43)	0.149	2.19 (0.55, 8.68)	0.264
Partner counseled/tested						
No	20 (8.6)	212 (91.4)	Reference group		Reference group	
Yes	3 (4.7)	61 (95.3)	1.92 (0.55, 6.67)	0.306	3.40 (0.35, 33.43)	0.293
PSS group attendance						
No	20 (8.6)	214 (91.5)	Reference group		Reference group	
Yes	3 (4.8)	59 (95.2)	1.84 (0.53, 6.40)	0.339	0.46 (0.07, 3.22)	0.433
Time on ART in pregnancy						
≤30 days	2 (4.0)	48 (96.0)	Reference group		Reference group	
>30 days	21 (8.5)	225 (91.5)	0.45 (0.10, 1.97)	0.287	0.42 (0.04, 4.27)	0.466
Adherent in ANC						
No	6 (14.6)	35 (85.4)	Reference group		Reference group	
Yes	12 (5.8)	195 (94.2)	2.79 (0.98, 7.91)	0.054	3.12 (1.54, 32.89)	0.012
Attended six week postpartum visit						
No	2 (4.6)	42 (95.5)	Reference group		Reference group	
Yes	21 (8.4)	230 (91.6)	0.52 (0.12, 2.31)	0.391	0.47 (0.03, 7.30)	0.587

Table 2d: Univariate and multivariate logistic regression results for 80% adherence at six months postpartum (nonadherence defined as medication adherence <80% or did not return with pill box/did not return for clinic visit)

Factor	Not adherent (%)	Adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	87 (44.6)	108 (55.4)	Reference group		Reference group	
25-34	87 (38.8)	137 (61.2)	1.27 (0.86, 1.87)	0.232	1.06 (0.60, 1.88)	0.836
35-60	4 (18.8)	23 (85.2)	4.64 (1.54,13.90)	0.006	2.61 (0.67, 10.11)	0.166
Education						
None/primary	65 (41.4)	92 (58.6)	Reference group		Reference group	
Secondary/post-secondary	100 (39.1)	156 (60.9)	1.10 (0.74, 1.65)	0.638	1.03 (0.58, 1.83)	0.917
Parity						
0	58 (38.4)	93 (61.6)	Reference group		Reference group	
≥1	121 (40.7)	176 (59.3)	0.91 (0.61, 1.36)	0.634	0.97 (0.54, 1.76)	0.931
Employment						
Housewife/not employed	89 (42.4)	121 (57.6)	Reference group		Reference group	
Employed	76 (37.4)	127 (62.6)	1.23 (0.83, 1.82)	0.306	0.98 (0.56, 1.69)	0.930
Marital status						
Not Married	12 (50.0)	12 (50.0)	Reference group		Reference group	
Married	157 (39.9)	237 (60.2)	1.51 (0.66, 3.45)	0.328	1.93 (0.65, 5.67)	0.234
Baseline CD4 (cells/mm$^{3)}$						
≤350	55 (34.6)	104 (65.4)	Reference group		Reference group	
>350	126 (43.2)	166 (56.9)	0.70 (0.47, 1.04)	0.077	0.82 (0.47, 1.43)	0.492
Previous PMTCT						
No	147 (40.0)	221(60.0)	Reference group		Reference group	
Yes	31 (39.7)	47 (60.3)	1.01 (0.61, 1.66)	0.974	1.27 (0.59, 2.76)	0.544
Previous HIV diagnosis						
No	131 (38.3)	211 (61.7)	Reference group		Reference group	
Yes	51 (46.0)	60 (54.0)	0.73 (0.47, 1.13)	0.154	0.54 (0.30, 0.98)	0.043
Disclosure						
No	70 (42.7)	94 (57.3)	Reference group		Reference group	
Yes	102 (38.6)	162 (61.4)	1.18 (0.80, 1.76)	0.407	0.88 (0.51, 1.53)	0.647
Partner counseled/tested						
No	152 (41.8)	212 (58.2)	Reference group		Reference group	
Yes	30 (33.0)	61 (67.0)	1.46 (0.90, 2.37)	0.127	1.46 (0.75, 2.86)	0.270
PSS group attendance						
No	162 (43.1)	214 (56.9)	Reference group		Reference group	
Yes	20 (25.3)	59 (74.8)	2.23 (1.29, 3.86)	0.004	1.31 (0.66, 2.61)	0.446
Time on ART in pregnancy						
≤30 days	33 (40.7)	48 (59.3)	Reference group		Reference group	
>30 days	109 (32.6)	225 (67.4)	1.42 (0.86, 2.34)	0.169	1.35 (0.71, 2.54)	0.358
Adherent in ANC						
No	77 (52.4)	70 (47.6)	Reference group		Reference group	
Yes	98 (33.5)	195 (66.6)	2.19 (1.46, 3.28)	0.000	2.00 (1.15, 3.47)	0.014
Attended six week postpartum visit						
No	62 (59.6)	42 (40.4)	Reference group		Reference group	
Yes	91 (28.4)	230 (71.7)	3.73 (2.35, 5.91)	0.000	2.81 (1.54, 5.13)	0.001

Table 3a: Univariate and multivariate logistic regression results for 95% adherence at ANC and six months postpartum (nonadherence defined as medication adherence <95%)

Factor	Not adherent (%)	Adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	50 (49.0)	52 (51.0)	Reference group		Reference group	
25-34	55 (44.7)	68 (55.3)	1.19 (0.70, 2.01)	0.520	1.65 (0.78, 3.41)	0.160
35-60	10 (52.6)	9 (47.4)	0.87 (0.32, 2.31)	0.773	0.51 (0.18, 2.85)	0.670
Education						
None/primary	45 (54.9)	37 (45.1)	Reference group		Reference group	
Secondary/post-secondary	59 (41.6)	83 (58.5)	1.71 (0.99, 2.96)	0.055	2.01 (0.99, 4.07)	0.051
Parity						
0	34 (41.5)	48 (58.5)	Reference group		Reference group	
≥1	80 (49.7)	81 (50.3)	0.72 (0.42, 1.23)	0.225	0.65 (0.31, 1.36)	0.252
Employment						
Housewife/not employed	47 (43.1)	62 (56.9)	Reference group		Reference group	
Employed	57 (49.6)	58 (50.4)	0.77 (0.46, 1.31)	0.334	0.53 (0.27, 1.03)	0.060
Marital status						
Not Married	9 (60.0)	6 (40.0)	Reference group		Reference group	
Married	98 (46.2)	114 (53.8)	1.74 (0.60, 5.08)	0.307	1.53 (0.40, 5.92)	0.537
Baseline CD4 (cells/mm$^{3)}$						
≤350	45 (44.1)	57 (55.9)	Reference group		Reference group	
>350	73 (50.3)	72 (49.7)	0.78 (0.47, 1.29)	0.335	0.69 (0.35, 1.33)	0.265
Previous PMTCT						
No	90 (45.5)	108 (54.6)	Reference group		Reference group	
Yes	25 (54.4)	21 (45.7)	0.70 (0.37, 1.33)	0.278	0.60 (0.25, 1.46)	0.261
Previous HIV diagnosis						
No	91 (48.9)	95 (51.1)	Reference group		Reference group	
Yes	26 (42.6)	35 (57.4)	1.29 (0.72, 2.31)	0.393	1.40 (0.67, 2.96)	0.374
Disclosure						
No	46 (51.0)	36 (43.9)	Reference group		Reference group	
Yes	65 (43.3)	85 (56.7)	1.67 (0.97, 2.88)	0.064	1.69 (0.86 3.32)	0.130
Partner counseled/tested						
No	99 (50.5)	97 (49.5)	Reference group		Reference group	
Yes	19 (36.5)	33 (63.5)	1.77 (0.94, 3.33)	0.075	1.35 (0.62, 2.95)	0.455
PSS group attendance						
No	95 (48.5)	101 (51.5)	Reference group		Reference group	
Yes	23 (44.2)	29 (55.8)	1.19 (0.64, 2.19)	0.587	1.11 (0.48, 2.57)	0.801
Time on ART in pregnancy						
≤30 days	22 (53.7)	19 (46.3)	Reference group		Reference group	
>30 days	96 (46.4)	111 (53.6)	1.34 (0.68, 2.62)	0.395	0.89 (0.38, 2.07)	0.779

Table 3b: Univariate and multivariate logistic regression results for 95% adherence at ANC and six months postpartum (nonadherence defined as medication adherence <95% or did not return with pill box/did not return for clinic visit)

Factor	Not adherent (%)	Adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	140 (72.9)	52 (27.1)	Reference group		Reference group	
25-34	147 (68.4)	68 (31.6)	1.25 (0.81, 1.91)	0.316	1.41 (0.82, 2.45)	0.217
35-60	16 (64.0)	9 (36.0)	1.51 (0.63, 3.64)	0.353	0.99 (0.32, 3.11)	0.988
Education						
None/primary	116 (75.8)	37 (24.2)	Reference group		Reference group	
Secondary/post-secondary	164 (66.4)	83 (33.6)	1.37 (1.01, 2.50)	0.047	1.79 (1.02, 3.14)	0.043
Parity						
0	97 (66.9)	48 (33.1)	Reference group		Reference group	
≥1	207 (71.9)	81 (28.1)	0.79 (0.51, 1.22)	0.286	0.89 (0.51, 1.55)	0.670
Employment						
Housewife/not employed	144 (69.9)	62 (30.1)	Reference group		Reference group	
Employed	136 (70.1)	58 (29.9)	0.99 (0.65, 1.52)	0.965	0.73 (0.43, 1.23)	0.241
Marital status						
Not Married	18 (75.0)	6 (25.0)	Reference group		Reference group	
Married	266 (70.0)	114 (30.0)	1.29 (0.50, 3.32)	0.604	1.21 (0.37, 3.95)	0.752
Baseline CD4 (cells/mm$^{3)}$						
≤350	100 (63.7)	57 (36.3)	Reference group		Reference group	
>350	208 (74.3)	72 (25.7)	0.61 (0.40, 0.93)	0.020	0.66 (0.40, 1.12)	0.122
Previous PMTCT						
No	247 (69.6)	108 (30.4)	Reference group		Reference group	
Yes	56 (72.7)	21 (27.3)	0.86 (0.49, 1.49)	0.584	0.70 (0.34, 1.46)	0.345
Previous HIV diagnosis						
No	237 (71.4)	95 (28.6)	Reference group		Reference group	
Yes	72 (67.3)	35 (32.7)	1.21 (0.76, 1.94)	0.420	1.23 (0.70, 2.18)	0.471
Disclosure						
No	125 (77.6)	36 (22.4)	Reference group		Reference group	
Yes	169 (66.5)	85 (33.5)	1.75 (1.11, 2.75)	0.016	1.84 (1.07, 3.16)	0.028
Partner counseled/tested						
No	257 (72.6)	97 (27.4)	Reference group		Reference group	
Yes	53 (61.6)	33 (38.4)	1.65 (1.01, 2.70)	0.047	1.44 (0.79, 2.65)	0.234
PSS group attendance						
No	262 (72.2)	101 (27.8)	Reference group		Reference group	
Yes	48 (62.3)	29 (37.7)	1.57 (0.94, 2.62)	0.087	1.33 (0.70, 2.55)	0.387
Time on ART in pregnancy						
≤30 days	59 (75.6)	19 (24.4)	Reference group		Reference group	
>30 days	212 (65.6)	111 (34.4)	0.72 (0.47, 1.08)	0.111	0.59 (0.36, 0.97)	0.039

Table 3c: Univariate and multivariate logistic regression results for 80% adherence at ANC and six months postpartum (nonadherence defined as medication adherence <80%)

Factor	Not adherent (%)	Adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	23 (22.6)	79 (77.5)	Reference group		Reference group	
25-34	25 (20.3)	98 (79.7)	1.14 (0.60, 2.16)	0.685	1.44 (0.60, 3.44)	0.413
35-60	4 (21.1)	15 (79.0)	1.09 (0.33, 3.61)	0.886	1.14 (0.24, 5.4)	0.870
Education						
None/primary	16 (19.5)	66 (80.5)	Reference group		Reference group	
Secondary/post-secondary	32 (22.5)	110 (77.5)	0.83 (0.43, 1.63)	0.596	1.05 (0.44, 2.48)	0.917
Parity						
0	17 (20.7)	65 (79.3)	Reference group		Reference group	
≥1	34 (21.1)	127 (78.9)	0.98 (0.51, 1.88)	0.944	0.92 (0.37, 2.27)	0.850
Employment						
Housewife/not employed	18 (16.5)	91 (83.5)	Reference group		Reference group	
Employed	30 (26.1)	85 (73.9)	0.56 (0.29, 1.08)	0.083	0.46 (0.20, 1.04)	0.061
Marital status						
Not Married	8 (53.3)	39 (18.4)	Reference group		Reference group	
Married	7 (46.7)	173 (81.6)	5.07(1.74, 14.81)	0.003	3.93 (1.03, 15.0)	0.045
Baseline CD4 (cells/mm$^{3)}$						
≤350	21 (20.6)	81 (79.4)	Reference group		Reference group	
>350	32 (22.1)	113 (77.9)	0.92 (0.49, 1.70)	0.780	0.87 (0.38, 1.95)	0.728
Previous PMTCT						
No	39 (19.7)	159 (80.3)	Reference group		Reference group	
Yes	13 (28.3)	33 (71.7)	0.62 (0.30, 1.29)	0.204	0.86 (0.30, 2.51)	0.788
Previous HIV diagnosis						
No	40 (21.5)	146 (78.5)	Reference group		Reference group	
Yes	13 (21.3)	48 (78.7)	1.01 (0.50, 2.05)	0.974	0.72 (0.29, 1.75)	0.464
Disclosure						
No	24 (29.3)	58 (70.7)	Reference group		Reference group	
Yes	26 (17.3)	124 (82.7)	1.97 (1.04, 3.73)	0.036	2.08 (0.94, 4.62)	0.072
Partner counseled/tested						
No	46 (23.5)	150 (76.5)	Reference group		Reference group	
Yes	7 (13.5)	45 (86.5)	1.97 (0.83, 4.67)	0.123	0.99 (0.37, 2.66)	0.979
PSS group attendance						
No	41 (20.9)	155 (79.1)	Reference group		Reference group	
Yes	12 (23.1)	40 (76.9)	0.88 (0.42, 1.83)	0.736	0.74 (0.27, 2.02)	0.554
Time on ART in pregnancy						
≤30 days	10 (24.4)	31 (75.6)	Reference group		Reference group	
>30 days	43 (20.8)	164 (79.2)	1.28 (0.58, 2.82)	0.542	0.91 (0.32, 2.63)	0.866

Table 3d: Univariate and multivariate logistic regression results for 80% adherence at ANC and six months postpartum (nonadherence defined as medication adherence <80% or did not return with pill box/did not return for clinic visit)

Factor	Not adherent (%)	Adherent (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	113 (58.9)	79 (41.2)	Reference group		Reference group	
25-34	117 (54.4)	98 (45.6)	1.20 (0.81, 1.78)	0.368	1.26 (0.76, 2.09)	0.373
35-60	10 (40.0)	15 (60.0)	2.15 (0.92, 5.02)	0.078	1.65 (0.60, 4.51)	0.328
Education						
None/primary	87 (56.9)	66 (43.1)	Reference group		Reference group	
Secondary/post-secondary	137 (55.5)	110 (44.5)	1.06 (0.70, 1.59)	0.784	1.14 (0.69, 1.88)	0.598
Parity						
0	80 (55.2)	65 (44.8)	Reference group		Reference group	
≥1	161 (55.9)	127 (44.1)	0.97 (0.65, 1.45)	0.885	1.14 (0.68, 1.92)	0.612
Employment						
Housewife/not employed	115 (55.8)	91 (44.2)	Reference group		Reference group	
Employed	109 (56.2)	85 (43.8)	0.99 (0.66, 1.46)	0.942	0.84 (0.52, 1.35)	0.473
Marital status						
Not Married	17 (70.8)	7 (29.2)	Reference group		Reference group	
Married	207 (54.5)	173 (45.5)	2.03 (0.82, 5.00)	0.124	2.00 (0.67, 6.00)	0.215
Baseline CD4 (cells/mm$^{3)}$						
≤350						
>350	76 (48.4)	81 (51.6)	Reference group		Reference group	
	167 (59.6)	113 (40.4)	0.63 (0.43, 0.94)	0.024	0.76 (0.47, 1.23)	0.260
Previous PMTCT						
No	196 (55.2)	159 (44.8)	Reference group		Reference group	
Yes	44 (57.1)	33 (42.9)	0.92 (0.56, 1.52)	0.757	0.98 (0.51, 1.90)	0.959
Previous HIV diagnosis						
No	186 (56.0)	146 (44.0)	Reference group		Reference group	
Yes	59 (55.1)	48 (44.9)	1.01 (0.50, 2.05)	0.974	0.88 (0.52, 1.50)	0.635
Disclosure						
No	103 (64.0)	58 (36.0)	Reference group		Reference group	
Yes	130 (51.2)	124 (48.8)	1.69 (1.13, 2.54)	0.011	1.91 (1.18, 3.12)	0.009
Partner counseled/tested						
No	204 (57.6)	150 (42.4)	Reference group		Reference group	
Yes	41 (47.8)	45 (52.3)	1.49 (0.93, 2.39)	0.097	1.19 (0.67, 2.18)	0.544
PSS group attendance						
No	208 (57.3)	155 (42.7)	Reference group		Reference group	
Yes	37 (48.1)	40 (52.0)	1.45 (0.89, 2.38)	0.139	1.19 (0.65, 2.20)	0.571
Time on ART in pregnancy						
≤30 days	47 (60.3)	31 (39.7)	Reference group		Reference group	
>30 days	159 (49.2)	164 (50.8)	0.58 (0.39, 0.86)	0.006	0.54 (0.34, 0.85)	0.007

Table 4: Univariate and multivariate logistic regression results for clinic visit attendance at six weeks postpartum

Factor	Did not attend (%)	Attended (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	53 (27.9)	137 (72.1)	Reference group		Reference group	
25-34	46 (20.7)	176 (79.3)	1.48 (0.94, 2.33)	0.090	1.41 (0.75, 2.65)	0.282
35-60	3 (10.3)	26 (89.7)	3.35 (0.97, 11.5)	0.055	3.39 (0.70, 16.43)	0.130
Education						
None/primary	35 (22.6)	120 (77.4)	Reference group		Reference group	
Secondary/post-secondary	61 (24.4)	189 (75.6)	0.90 (0.56, 1.45)	0.676	0.71 (0.38, 1.35)	0.299
Parity						
0	36 (24.2)	113 (75.8)	Reference group		Reference group	
≥1	68 (23.1)	226 (76.9)	1.06 (0.67, 1.69)	0.809	1.02 (0.54, 1.93)	0.946
Employment						
Housewife/not employed	52 (25.7)	150 (74.3)	Reference group		Reference group	
Employed	42 (20.8)	160 (79.2)	1.32 (0.83, 2.10)	0.240	1.20 (0.66, 2.19)	0.547
Marital status						
Not Married	7 (28.0)	18 (72.0)	Reference group		Reference group	
Married	88 (22.6)	301 (77.4)	1.33 (0.54, 3.29)	0.537	1.11 (0.35, 3.46)	0.863
Baseline CD4 (cells/mm$^{3)}$						
≤350	34 (21.8)	122 (78.2)	Reference group		Reference group	
>350	71 (24.5)	219 (75.5)	0.86 (0.54, 1.37)	0.524	1.08 (0.59, 1.99)	0.802
Previous PMTCT						
No	76 (20.9)	287 (79.1)	Reference group		Reference group	
Yes	26 (33.3)	52 (66.7)	0.53 (0.31, 0.90)	0.020	0.49 (0.23, 1.03)	0.059
Previous HIV diagnosis						
No	87 (25.9)	249 (74.1)	Reference group		Reference group	
Yes	17 (15.2)	95 (84.8)	1.95 (1.10, 3.46)	0.022	2.37 (1.09, 5.13)	0.029
Disclosure						
No	43 (26.7)	118 (73.3)	Reference group		Reference group	
Yes	59 (22.5)	203 (77.5)	1.25 (0.80, 1.97)	0.329	0.87 (0.47, 1.59)	0.645
Partner counseled/tested						
No	87 (24.2)	272 (75.8)	Reference group		Reference group	
Yes	18 (19.8)	73 (80.2)	1.30 (0.73, 2.29)	0.371	1.46 (0.69, 3.06)	0.321
PSS group attendance						
No	93 (24.0)	294 (75.8)	Reference group		Reference group	
Yes	12 (19.1)	51 (81.0)	1.34 (0.69, 2.63)	0.387	1.50 (0.63, 3.59)	0.364
Time on ART in pregnancy						
≤30 days	21 (25.6)	61 (74.4)	Reference group		Reference group	
>30 days	67 (19.1)	283 (80.9)	1.45 (0.83, 2.55)	0.192	1.21 (0.61, 2.40)	0.590
Adherent in ANC (95%)						
No	61 (30.4)	140 (69.7)	Reference group		Reference group	
Yes	43 (18.1)	194 (81.9)	1.97 (1.26, 3.07)	0.003	1.58 (0.89, 2.82)	0.117
Adherent in ANC (80%)						
No	45 (31.3)	99 (68.8)	Reference group		Reference group	
Yes	59 (20.1)	235 (79.9)	1.81 (1.15, 2.85)	0.010	1.63 (0.90, 2.96)	0.108

Table 5: Univariate and multivariate logistic regression results for clinic visit attendance at six months postpartum

Factor	Did not attend (%)	Attended (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	48 (25.7)	139 (74.3)	Reference group		Reference group	
25-34	39 (17.7)	181 (82.3)	1.60 (0.99, 2.58)	0.053	1.33 (0.66, 2.69)	0.431
35-60	1 (3.4)	28 (96.6)	9.67 (1.28, 73.0)	0.028	5.18 (0.58, 46.09)	0.140
Education						
None/primary	34 (22.2)	119 (77.8)	Reference group		Reference group	
Secondary/post-secondary	48 (19.4)	200 (80.7)	1.19 (0.73, 1.95)	0.490	1.26 (0.60, 2.65)	0.540
Parity						
0	28 (19.3)	117 (80.7)	Reference group		Reference group	
≥1	61 (20.8)	232 (79.2)	0.91 (0.55, 1.50)	0.712	1.05 (0.50, 2.22)	0.893
Employment						
Housewife/not employed	39 (19.7)	159 (80.3)	Reference group		Reference group	
Employed	42 (20.8)	160 (79.2)	0.93 (0.57, 1.52)	0.785	0.47 (0.29, 0.96)	0.038
Marital status						
Not Married	8 (32.0)	17 (68.0)	Reference group		Reference group	
Married	74 (19.3)	309 (80.7)	1.97 (0.82, 4.73)	0.131	2.53 (0.74, 8.60)	0.137
Baseline CD4 (cells/mm$^{3)}$						
≤350	31 (19.8)	126 (80.3)	Reference group		Reference group	
>350	60 (21.2)	223 (78.8)	0.91 (0.56, 1.49)	0.718	1.05 (0.52, 2.11)	0.891
Previous PMTCT						
No	71 (19.8)	288 (80.2)	Reference group		Reference group	
Yes	17 (22.1)	60 (77.9)	0.87 (0.48, 1.58)	0.648	1.77 (0.63, 4.98)	0.282
Previous HIV diagnosis						
No	73 (21.9)	261 (78.1)	Reference group		Reference group	
Yes	18 (16.5)	91 (83.5)	1.41 (0.80, 2.50)	0.232	0.94 (0.42, 2.08)	0.875
Disclosure						
No	38 (23.6)	123 (76.4)	Reference group		Reference group	
Yes	51 (19.8)	207 (80.2)	1.25 (0.78, 2.02)	0.351	0.85 (0.43, 1.70)	0.652
Partner counseled/tested						
No	78 (21.9)	278 (78.1)	Reference group		Reference group	
Yes	13 (14.6)	76 (85.4)	1.64 (0.87, 3.11)	0.129	1.72 (0.70, 4.26)	0.240
PSS group attendance						
No	84 (23.5)	273 (76.5)	Reference group		Reference group	
Yes	7 (8.0)	81 (92.0)	3.56 (1.58, 8.00)	0.002	2.02 (0.76, 5.38)	0.159
Time on ART in pregnancy						
≤30 days	26 (31.7)	56 (68.3)	Reference group		Reference group	
>30 days	48 (13.9)	298 (86.1)	2.88 (1.65, 5.03)	0.000	3.58 (1.75, 7.32)	0.000
Adherent in ANC (95%)						
No	29 (22.8)	98 (77.2)	Reference group		Reference group	
Yes	36 (15.6)	195 (84.4)	1.60 (0.93, 2.77)	0.090	1.65 (0.84, 3.23)	0.147
Adherent in ANC (80%)						
No	42 (29.6)	100 (70.4)	Reference group		Reference group	
Yes	48 (16.6)	241 (83.4)	2.11 (1.31, 3.39)	0.002	1.51 (0.76, 3.02)	0.233
Attended six week postpartum visit						
No	48 (47.5)	53 (52.5)	Reference group		Reference group	
Yes	40 (11.8)	298 (88.2)	6.75(4.05,11.25)	0.000	5.19 (2.56, 10.51)	0.000

Table 6: Univariate and multivariate logistic regression results for clinic visit attendance at six weeks and six months postpartum

Factor	Did not attend (%)	Attended (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Maternal age (years)						
18-24	67 (36.2)	118 (63.8)	Reference group		Reference group	
25-34	65 (30.1)	151 (69.9)	1.32 (0.87, 2.00)	0.194	1.34 (0.76, 2.36)	0.312
35-60	4 (13.8)	25 (86.2)	3.55 (1.18, 10.6)	0.024	3.44 (0.88, 13.39)	0.071
Education						
None/primary	43 (28.5)	108 (71.5)	Reference group		Reference group	
Secondary/post-secondary	82 (33.6)	162 (66.4)	0.79 (0.51, 1.22)	0.287	0.68 (0.38, 1.21)	0.186
Parity						
0	45 (31.3)	99 (68.8)	Reference group		Reference group	
≥1	93 (32.3)	195 (67.7)	0.95 (0.62, 1.47)	0.827	1.03 (0.57, 1.85)	0.921
Employment						
Housewife/not employed	59 (30.1)	137 (69.9)	Reference group		Reference group	
Employed	64 (32.3)	134 (67.7)	0.90 (0.59, 1.38)	0.634	0.77 (0.45, 1.33)	0.349
Marital status						
Not Married	10 (40.0)	15 (60.0)	Reference group		Reference group	
Married	118 (31.2)	260 (68.9)	1.47 (0.64, 3.37)	0.363	1.33 (0.47, 3.76)	0.584
Baseline CD4 (cells/mm$^{3)}$						
≤350	45 (29.2)	109 (70.8)	Reference group		Reference group	
>350	96 (34.2)	185 (65.8)	0.80 (0.52, 1.22)	0.293	0.87 (0.50, 1.52)	0.621
Previous PMTCT						
No	105 (29.7)	249 (70.3)	Reference group		Reference group	
Yes	31 (40.8)	45 (59.2)	0.61 (0.37, 1.02)	0.060	0.63 (0.31, 1.29)	0.207
Previous HIV diagnosis						
No	117 (35.6)	212 (64.4)	Reference group		Reference group	
Yes	23 (21.3)	85 (78.7)	2.04 (1.22, 3.41)	0.006	2.03 (1.07, 3.86)	0.031
Disclosure						
No	57 (35.9)	102 (64.2)	Reference group		Reference group	
Yes	81 (31.8)	174 (68.2)	1.20 (0.79, 1.82)	0.391	0.86 (0.50, 1.49)	0.590
Partner counseled/tested						
No	120 (34.2)	231 (65.8)	Reference group		Reference group	
Yes	21 (23.9)	67 (76.1)	1.66 (0.97, 2.84)	0.065	1.70 (0.87, 3.35)	0.122
PSS group attendance						
No	121 (34.4)	231 (65.6)	Reference group		Reference group	
Yes	20 (23.0)	67 (77.0)	1.75 (1.02, 3.03)	0.043	1.31 (0.67, 2.55)	0.427
Time on ART in pregnancy						
≤30 days	36 (43.9)	46 (56.1)	Reference group		Reference group	
>30 days	90 (26.3)	252 (73.7)	2.19 (1.33, 3.61)	0.002	2.05 (1.12, 3.76)	0.020
Adherent in ANC (95%)						
No	80 (40.4)	118 (59.6)	Reference group		Reference group	
Yes	60 (26.2)	169 (73.8)	1.91 (1.27, 2.87)	0.002	1.56 (0.93, 2.63)	0.093
Adherent in ANC (80%)						
No	59 (41.8)	82 (58.2)	Reference group		Reference group	
Yes	81 (28.3)	205 (71.7)	1.82 (1.19, 2.78)	0.005	1.46 (0.85, 2.51)	0.171

APPENDIX F: Semi-structured in-depth interview guides

MAKERERE UNIVERSITY – JOHNS HOPKINS UNIVERSITY RESEARCH COLLABORATION
FRIENDS FOR LIFE CIRCLES FOR OPTION B$^+$ STUDY
IN DEPTH INTERVIEW (IDI) GUIDE FOR VISIT 0 (FIRST MONTHLY ANC VISIT) FOR MATERNAL PARTICIPANT ONLY.

Barriers to Option B+ program adherence for PMTCT in Uganda: a mixed methods study
Interview guide for Visit 0 (first monthly ANC visit): Exploring factors affecting the Option B+ adherence experiences of pregnant women living with HIV in the ANC period

Introduction: Thank you for agreeing to talk with us today about your experiences as a pregnant woman living with HIV. During this interview I would like you to tell me in your own words about your experiences with HIV treatment and prevention services during your pregnancy. The interview will last about one hour and with your permission, will be recorded. I will ask you several questions about your experiences with HIV testing and HIV medications since you got to know that you are HIV positive. I will also ask you about the people and things that have made taking your HIV medicine and coming to the clinic for scheduled visits easy or difficult. Remember that you may decline to answer any question if you feel uncomfortable and we can stop the interview at any point. Do you have any questions at this time?

Part 1: Experiences with HIV status discovery

i. To start with, can you tell me a little about how you came to know of your HIV status?
    a. **Probe:** When and where did you find out your HIV status?
    b. **Probe**: Who was involved and how did they affect your experience?

Part 2: Experiences with ART and the HIV clinic

i. Now, can you tell me about your first experiences in the antenatal clinic and what it has been like to start taking ART during this pregnancy?
    a. **Probe**: Who was involved in the process of helping you start ART and how did they help or hurt the starting process?
    b. **Probe**: Can you describe your interactions with care providers? Who were they and how did they make you feel?
    c. **Probe**: What were your expectations for starting ART during this pregnancy and were they fulfilled, or were things you would have liked to be different?

ii. Can you tell me specifically about what happened at your last visit to the clinic?
    a. **Probe**: How did you get there/how was the travel experience?
    b. **Probe**: Who were the clinic staff involved in your visit, how were you treated and how did they make you feel?
    c. **Probe**: How did you feel about your overall experience?
    d. **Probe**: What were your expectations for the visit and were they fulfilled, or were there things you would have liked to be different?

iii. Can you tell me about your experiences taking ART over the last week?

a. **Probe**: What were your experiences with beginning to take ART and were they fulfilled or were there things you would have liked to be different?
b. **Probe**: Can you tell me about any side effects you have experienced and how this has affected your ability to take your ART?

iv. How do you remember to take your ART and attend your scheduled clinic visits?
a. **Probe**: Can you describe your daily routine if you have one?
b. **Probe**: Can you describe a time when your routine changed and how this affected your ability to remember to take your ART or attend the clinic?

v. Can you tell me about a time since you became pregnant when you missed taking your ART or missed a clinic visit?
vi. During your pregnancy, what keeps you motivated to take your HIV medication and/or keep your clinic visit appointments?

Part 3: Experiences with male partners and disclosure to other people.

i. Does anyone in your family or outside your family know about your HIV status, and how did she/he/they come to find out about your status?
a. **Probe**: What was the process of telling this person like for you?
b. **Probe**: What was the reaction of the person you were telling?

ii. What experiences have you had discussing HIV with your partner during this pregnancy?
c. **Probe**: Can you describe the process of your partner being tested for HIV?
d. **Probe**: Can you describe the involvement of your partner with helping you manage your HIV status, either at your ANC/ART clinic visits or outside of the clinic?

iii. Can you describe a time during this pregnancy when those who knew your HIV status made it easier or more difficult to take your ART and/or keep your clinic visit appointments?

Part 4: Experiences with stigma and social networks

i. Thinking about your experiences with HIV during your pregnancy, who do you go to for support with your pregnancy and HIV?
a. **Probe**: When are these people/is this person most helpful and how do they help?

ii. Can you describe a time during this pregnancy when you felt rejected or were treated differently due to your HIV status and how this affected your ability to take your ART or attend your scheduled clinic visits?

iii. Can you describe a time when you felt shame or embarrassment about your HIV status and how this affected your ability to take your ART or attend your scheduled clinic visits?

iv. Can you describe a time during this pregnancy when someone made it more difficult for you to take your ART and/or keep your scheduled clinic visits?

a. **Probe**: What did they do and how did it make you feel?

v. Can you describe a time during this pregnancy when someone helped you take your ART and/or keep your scheduled clinic visits?
   a. **Probe**: What did they do and how did it make you feel?

Conclusion: This is the end of our interview today. Thank you very much for your time. Do you have any questions for me [*answer any questions*]? If you have additional thoughts or questions, please feel free to contact me or a member of our study team.

MAKERERE UNIVERSITY – JOHNS HOPKINS UNIVERSITY RESEARCH COLLABORATION
FRIENDS FOR LIFE CIRCLES FOR OPTION B$^+$ STUDY
IN DEPTH INTERVIEW (IDI) GUIDE FOR VISIT 1 (6 WEEKS POSTPARTUM) FOR MATERNAL PARTICIPANT ONLY.

Barriers to Option B+ program adherence for PMTCT in Uganda: a mixed methods study
Interview guide for Visit 1 (6 weeks postpartum): Exploring factors affecting the Option B+ adherence experiences of women at the time of infant HIV testing and diagnosis

Introduction: Welcome back and thank you for agreeing to talk with us today about your experiences living with HIV and a new infant. During this interview I would like you to tell me in your own words about your experiences with HIV treatment and services since giving birth to your child. This interview will last about one hour and with your permission, will be recorded. I will ask you several questions about your experiences with HIV in the time since your baby was born and how these experiences may have changed since you were pregnant. I will also ask you about the people and things that have made taking your HIV medicine, giving medicine to your baby and coming to clinic visits easy or difficult. Remember that you may decline to answer any question if you feel uncomfortable and we can stop the interview at any point. Do you have any questions at this time?

Part 1: Experiences with HIV testing for the baby

i. To start out, can you tell me about your experiences getting your new baby tested for HIV?
   a. **Probe**: When and where did your baby receive an HIV test?
   b. **Probe**: Who was involved and how did they affect your experience?
   c. **Probe**: What were your expectations for getting your new baby tested and were they fulfilled, or were there things you would have liked to be different?

Part 2: Experiences with ART and the HIV clinic

i. Now, can you tell me about your experiences in the clinic and what it has been like to receive ART for yourself since your baby was born?
   a. **Probe**: Who has been involved in the process and how do they help or hurt the process?

b. **Probe**: Can you describe your interactions with care providers since your baby was born? Who were they and how did they make you feel?
c. **Probe**: What were your expectations for continuing ART after your baby was born and were they fulfilled, or were there things you would have liked to be different?

ii. Can you tell me about your experiences in the clinic and what it has been like to receive HIV prevention medicine for your baby since your baby was born?
   a. **Probe**: Who has been involved in the process and how do they help or hurt the process?
   b. **Probe**: Can you describe your interactions with care providers with regards to getting HIV prevention medicine for your baby? Who were they and how did they make you feel?
   c. **Probe**: What were your expectations for getting HIV prevention medicine for your baby and were they fulfilled, or were there things you would have liked to be different?

iii. Can you tell me specifically about what happened at your last visit to the clinic?
   a. **Probe**: How did you get there/how was the travel experience?
   b. **Probe**: Who were the clinic staff involved in your visit, how were you treated and how did they make you feel?
   c. **Probe**: How did you feel about your overall experience?
   d. **Probe**: What were your expectations for the visit and were they fulfilled, or were there things you would have liked to be different?
   e. **Probe**: Have your experiences at the clinic changed in any way since the time your baby was born, and if so, in what way(s)?

iv. Can you tell me about your experiences taking ART over the last week?
   a. **Probe**: What were your expectations with beginning to take ART and were they fulfilled or were there things you would have liked to be different?
   b. **Probe**: Can you tell me about any side effects you have experienced and how this has affected your ability to take your ART?
   c. **Probe**: Have your experiences taking ART changed in any way since the time your baby was born, and if so, in what way(s)?

v. How do you remember to take your ART and attend your scheduled clinic visits since your baby was born?
   a. **Probe**: Can you describe your daily routine since your baby was born, if you have one?
   b. **Probe**: Can you describe a time when your routine changed and how this affected your ability to remember to take your ART or attend the clinic?

vi. Can you tell me about a time since your baby was born when you missed taking your ART, you missed giving your baby HIV prevention medicine or missed a clinic visit?

vii. Since your baby was born, what keeps you motivated to take your HIV medication and/or keep your clinic visit appointments?
   a. **Probe**: Have your motivations changed in any way since the time your baby was born, and if so, in what way(s)?

Part 3: Experiences with male partners and disclosure to other people.

i. Since the last time we spoke and especially in the time since your baby was born, do any new people in your family or outside your family know about your HIV status, and how did she/he/they come to find out about your status?

   a. **Probe**: What was the process of telling this person like for you?
   b. **Probe**: What was the reaction of the person you were telling?

ii. Since the last time we spoke and especially since the time since your baby was born, what experiences have you had discussing HIV with your partner?
   a. **Probe**: Can you describe your partner's involvement with helping you manage your HIV status and how it may have changed since the last time we spoke?
   b. **Probe**: Can you describe your partner's involvement with the health of your baby?

iii. Can you describe a time since your baby was born when those who know your HIV status made it easier or more difficult to take your ART, give medicine to your baby and keep your clinic visit appointments?

Part 4: Experiences with stigma and social networks

i. Thinking about your experiences with HIV since your baby was born, who do you go to for support with keeping yourself and your baby healthy?
   a. **Probe**: When are these people/this person most helpful and how do they help?

ii. Can you describe a time since your baby was born when you felt rejected or were treated differently due to your HIV status and how this affected your ability to take your ART, give your baby HIV prevention medicine or attend your scheduled clinic visits?

iii. Can you describe a time since your baby was born when you felt shame or embarrassment about your HIV status and how has this affected your ability to take your ART, attend clinic visits or give your baby HIV prevention medicine?

iv. Can you describe a time since your baby was born when someone made it more difficult for you to take your ART and/or keep your scheduled clinic visits?
   a. **Probe**: What did they do and how did it make you feel?

v. Can you describe a time since your baby was born when someone helped you take your ART and/or keep your scheduled clinic visits?
   a. **Probe**: What did they do and how did it make you feel?

Conclusion: This is the end of our interview today. Thank you very much for your time. Do you have any questions for me [*answer any questions*]? If you have additional thoughts or questions, please feel free to contact me or a member of our study team.

Curriculum Vitae

Adi Noiman

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615 N. Wolfe Street, W5031
Baltimore, MD 21205
Email: anoiman@jhsph.edu

EDUCATION

April 2017 — **Doctor of Philosophy (Ph.D.),** Department of International Health, Program in Global Disease Epidemiology and Control (GDEC), Johns Hopkins Bloomberg School of Public Health (JHSPH), Baltimore, MD
Dissertation: Changes in adherence and program retention and the factors affecting adherence and program retention for HIV-infected pregnant women and mothers receiving Option B+ for PMTCT in Kampala, Uganda: A mixed methods approach (Dr. Andrea Ruff)

May 2010 — **Master of Health Sciences (M.H.S.),** Department of International Health, GDEC, JHSPH, Baltimore, MD

May 2007 — **Bachelor of Arts (B.A.),** Romance Languages and Literatures (French), Washington University in St. Louis, St. Louis, MO

PROFESSIONAL TRAINING

November 2015 — Good Clinical Practice (GCP) for Clinical Trials Involving Drugs and Devices, JHSPH, Department of International Health, Baltimore, MD

February 2012 — Basic Human Subjects Research Course, JHSPH, Department of International Health, Baltimore, MD

RESEARCH EXPERIENCE

May 2015-Present — **Student Investigator,** Makerere University-Johns Hopkins University Research Collaboration (MUJHU), Kampala, Uganda

- Led study coordination, protocol development, staff training, data management, analysis and drafting of manuscripts for publication of longitudinal in-depth interviews nested in a large NIH-funded randomized controlled trial to understand changing experiences of HIV+ pregnant women and mothers with Option B+ over time; Collaborated with data management and PMTCT team and supervised medical chart data abstraction efforts to create a longitudinal cohort study measuring rates of adherence and factors affecting adherence to Option B+ from pregnancy to 6 months postpartum;

Collected data from X-rays and ultrasounds to study novel techniques for diagnosis of pediatric tuberculosis; Assisted with data analysis and drafting of additional materials related to preventing vertical HIV transmission for publication and presentation. (Professor Philippa Musoke, Dr. Monica Nolan, Dr. Mary Glenn Fowler)

- Conducted a systematic review of the Option B+ adherence and program retention literature to compare and contrast findings from the Mulago Hospital Option B+ program to those in different countries and health care settings. (Dr. Andrea Ruff)

November 2011-December 2012

Research Assistant, International Injury Research Unit, Department of International Health, JHSPH, Baltimore, MD

- Assisted country managers of the Road Safety-10 project with data analyses and manuscript preparations. (Dr. Abdulgafoor M. Bachani)

December 2010-June 2011

Research Assistant, Department of International Health, JHSPH, Baltimore, MD

- Contributed to a systematic review by screening abstracts and articles for inclusion, abstracting relevant data from the literature, contacting corresponding authors and assessing data quality to study the relationship between maternal folate status and neonatal health outcomes. (Dr. Anne Palaia)

November 2009-November 2010

Research Assistant, Child Health Epidemiology Reference Group (CHERG), Department of International Health, JHSPH, Baltimore, MD

- Collaborated on the systematic review, double data abstraction and manuscript preparation for a meta-analysis assessing effects of breastfeeding practices on diarrheal morbidity and mortality and measures of diarrhea incidence, prevalence, mortality and hospitalization with respect to breastfeeding practices. (Dr. Christa Fischer-Walker)

July 2009-November 2009

Advanced Clinical Monitoring Intern, Johns Hopkins Technical Support for the Ethiopian HIV/AIDS Initiative (TSEHAI), Addis Ababa, Ethiopia

- Prepared for study enrollment by assessing site readiness, completed literature reviews to determine categorical variables for analysis, analyzed programmatic data, randomized potential participants and assessed selection bias, created screening, informed consent and data collection forms, developed job aides to assist study staff with screening and enrollment and assisted with trainings for the Advanced Clinical Monitoring Project consisting of a large, multi-site, PEPFAR-funded study assessing longitudinal effectiveness of ART. (Dr. William Weiss, Dr. Elham Hassen)

October 2007-August 2008

Clinical Trials Associate, Global Development, Bristol-Myers Squibb Company, Princeton, NJ

- Performed study management tasks for large, global, double-blind placebo-controlled, randomized immunology trials studying the efficacy of different biologics and protein kinase inhibitors; Authored monthly newsletter to study sites; presented professional development seminars to improve team understanding of study drugs. (Ms. Amy Coryell)

TEACHING EXPERIENCE

August 2014-Present

Instructor, Department of Public Health, Johns Hopkins University School of Arts and Sciences, Baltimore, MD
Course title: Fundamentals of Epidemiology

- Created new lab materials for confounding, effect modification and critical analysis of public health papers, updated lab materials to reflect current and relevant public health issues, led and prepared weekly lab sessions with 25-30 undergraduate students, held weekly office hours, proctored midterm and final exams, graded homework and examinations. 4 terms. (Dr. Darcy Phelan-Emrick and Dr. Ian Saldanha)

December 2009-March 2011

Teaching Assistant, Department of International Health, JHSPH, Baltimore, MD
Course title: Infectious Diseases and Child Survival

- Scheduled guest lecturers, communicated with students, maintained course website and graded exams and assignments; 2 terms. (Dr. Andrea Ruff and Dr. Ruth Karron)

Course title: Global Disease Epidemiology and Control Seminar

- Scheduled guest speakers and coordinated the creation of a skills-based lecture series and discussion panels on various public health topics, mentored first-year M.H.S. students and maintained course website; 1 term. (Ms. Karen R. Charron)

VOLUNTEER EXPERIENCE

October 2016-December 2016

Instructor, Community Adolescent Sexuality Education (CASE), Johns Hopkins School of Medicine, Baltimore, MD

- Educated a class of 25 8th grade males about sexual health and sexuality through an 8-week course intended to increase self-esteem, improve relationships and decrease incidence of teen pregnancies and sexually transmitted infections.

September 2008- Present

Director of Parent Engagement, Thread, Baltimore, MD

- Designed, implemented and analyzed surveys to identify barriers to engagement of parents/families of Thread students with the organization, utilized data from surveys to plan and execute inaugural Thread Resource Fair, coordinated with Thread staff and community partners to provide resources and services at the fair, created a mechanism for future

communications and drafted a proposal for parent/family engagement to be implemented in the following academic year.

Lead Mentor, Thread, Baltimore, MD

- Provided ongoing intensive academic and social support for 3 Baltimore City high school students at risk for failing out of high school in their freshmen years during and post-high school, managed teams of 3-6 volunteers and communicated with Thread Staff to address emergent or unmet needs of students.

Director of Summer Programs, Thread, Baltimore, MD

- Identified summer employment and successfully placed 72 at-risk high school students at Johns Hopkins Schools, hospitals and affiliated centers as well as companies and organizations in Baltimore, facilitated partnerships between Thread, Johns Hopkins and new community partners, ensured compensation for students through coordination with Baltimore City YouthWorks Program, provided students with free lunch daily through work with Baltimore City Free Lunch Program, developed professional development curriculum for students, supervised 2 undergraduate interns assisting with day-to-day implementation of the 6-week summer program and planned and executed a summer symposium for students, employers and parents to share work and reflect on experiences.

AWARDS

2017 Tong Zhang Innovation Fellow
2015 Thread Hall of Fame Award for "Endless Hope"
2014-2015 Johns Hopkins Martin Luther King Jr. Award for Community Service
2012 Student Outreach Resource Center (SOURCE) Community Service Award

PUBLICATIONS & PRESENTATIONS

Namara-Lugolobi E., Namukwaya Z., Kakande A., **Noiman A.,** Akasiima AS., Bangisibaano I., Kamya S., Josaphat B., Musoke P., Nolan M. "Prevalence of abnormal baseline laboratory tests among HIV infected pregnant women initiation on 'Option B plus' between October 2012 and October 2015 at Mulago Hospital in Kampala, Uganda." Presented at the *21st International AIDS Conference*, Durbin, South Africa, 2016.

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