

Faculty of Medicine and Health Sciences

Implementation of lifelong ART (Option B+) for Prevention of Mother-to-Child Transmission (PMTCT) of HIV in Uganda

Thesis submitted for the degree of

Doctor of Medical Sciences

at the University of Antwerp

to be defended by

Aggrey David Mukose

Supervisors:

Prof. Jean-Pierre Van geertruyden

Prof. Hilde Bastiaens

Prof. Rhoda Wanyenze

Antwerp, 2024

Faculty of Medicine and Health Sciences

Implementation of lifelong ART (Option B+) for Prevention of Mother-to-Child Transmission (PMTCT) of HIV in Uganda

**Implementatie van levenslange ART (Optie B+) voor de preventie
van overdracht van moeder op kind (PMTCT) van HIV in Oeganda**

Thesis submitted for the degree of

Doctor of Medical Sciences

Doctor in de medische wetenschappen

at the University of Antwerp

to be defended by

Aggrey David Mukose

Supervisors:

Prof. Jean-Pierre Van geertruyden

Prof. Hilde Bastiaens

Prof. Rhoda Wanyenze

Antwerp, 2024

Declaration

I, Aggrey David Mukose, declare that this thesis is my original work. It is being submitted for the degree of Doctor of Medical Sciences at the University of Antwerp, Belgium. It has not been submitted before for any degree or examination at this or any other University, and all the sources used or quoted have been acknowledged by references.

Table of Contents

Declaration	iii
List of Tables.....	vii
List of Figures	viii
Dedication.....	ix
Acknowledgements.....	x
List of Abbreviations.....	xii
List of Papers.....	xiii
Thesis structure.....	xv
Samenvatting.....	xvi
Summary	xxi
CHAPTER 1:	1
INTRODUCTION	1
1.1 Burden of HIV.....	1
1.1.1 HIV among the general population.....	1
1.1.2 HIV among women and girls	1
1.2 Mother-to-child transmission of HIV	2
1.3 Prevention of Mother-to-child transmission of HIV	2
1.4 Evolution of PMTCT interventions and guidelines.....	3
CHAPTER 2:	13
Study Background, Rationale and Objectives	13
2.1 Study Background	13
2.2 Rationale	15
2.3 Objectives.....	16
CHAPTER 3:	18
Study Methods	18
3.1 Summary of the sub-studies	18
3.2 Study context and sites	18
3.3 Study design.....	19
3.4 Study population.....	20
3.4.1 Key informant participants	20
3.4.2 In-depth interview participants	20
3.4.3 Prospective cohort	21
3.5: Data collection, management and analysis	22

3.5.1 Data collection	22
3.5.2 Data management and analysis	23
3.5.3 Investigator and Author contribution	24
3.6 Ethical considerations	24
References	25
CHAPTER 4:	33
Health Provider Perspectives of Health Facility Preparedness and Organization in Implementation of Option B+ among Pregnant and Lactating Women in Central Uganda: A Qualitative Study	33
4.1 Abstract	34
4.2 Introduction	36
4.3 Methods	37
4.4 Results	44
4.5 Discussion	52
4.6 Strengths and Limitations	55
4.7 Conclusions and Recommendations	55
References	57
CHAPTER 5:	62
What influences uptake and early adherence to Option B+ (lifelong antiretroviral therapy among HIV-positive pregnant and breastfeeding women) in Central Uganda? A mixed method study	62
5.1 Abstract	63
5.2 Introduction	64
5.3 Methods	65
5.4 Results	72
5.5 Discussion	90
5.6 Strengths and limitations	92
5.7 Conclusions	93
References	95
CHAPTER 6:	101
Suboptimal Adherence to Lifelong ART, and its predictors among HIV- positive pregnant and breastfeeding women in three districts of Central Uganda: a repeated measures analysis	101
6.1 Abstract	102
6.2 Introduction	103
6.3 Methods	105

6.4 Results	108
6.5 Discussion.....	115
6.6 Study strengths and limitations	118
6.7 Conclusions and recommendations.....	118
References	121
CHAPTER 7:	125
Challenges and commonly used countermeasures in the implementation of lifelong antiretroviral therapy for PMTCT in Central Uganda: A health providers' perspective	125
7.1 Abstract	126
7.2 Introduction	127
7.3 Methods.....	129
7.4 Results	134
7.5 Discussion.....	148
7.6 Strengths and limitations.....	154
7.7 Conclusions and Recommendations	155
References	158
CHAPTER 8:	165
GENERAL DISCUSSION	165
8.1 Conclusions and recommendations.....	172
8.2 Recommendation for further research.....	174
References	175
Curriculum Vitae	181

List of Tables

Table 1.1: Antiretroviral treatment options recommended for HIV-positive pregnant women who are eligible for treatment and infant prophylaxis.....	6
Table 1.2: ARV-prophylaxis options recommended for HIV-positive pregnant women who didn't need treatment for their own health	7
Table 4. 1: Characteristics of study participants ^a	41
Table 4. 2: Summary of Identified Themes.....	43
Table 5. 1: Baseline characteristics of HIV-positive pregnant women recruited into the study (N=507).....	73
Table 5. 2: Baseline characteristics of HIV-positive pregnant women who declined to participated in the study (N=41) by Health Facility.....	75
Table 5. 3: Comparison of baseline characteristics of HIV-positive pregnant women recruited into the study (N=507) and those who declined (N=41).....	76
Table 5. 4: Predetermined themes and subthemes	77
Table 5. 5: Enrolment into the study (N=507), ART prescription (n=463) and uptake of Option B+ (n=432) by health facility	80
Table 5. 6: Reasons for not being ready to start ART at the time of prescription (n=64)	81
Table 5. 7: Reasons for non-adherence to Option B+ ART (n=95)	85
Table 5. 8: Factors associated with early adherence to Option B+ ART (n= 410).....	87
Table 6. 1: Baseline sample characteristics	109
Table 6. 2: Comparison of baseline characteristics of study participants included in the repeated measures analysis and those who were excluded.....	111
Table 6. 3: Predictors of suboptimal adherence to lifelong ART among pregnant and breastfeeding women in Central Uganda	113
Table 7. 1: Topics, questions and probes that were included in the study tool	132
Table 7. 2: Characteristics of study participants (n= 54).....	135

List of Figures

Figure 3.1: Map of Uganda showing study districts and Health facilities.....	19
Figure 3.2: Samples for the different sub-studies	22
Figure 4.1: Structure of the public health care system in Uganda.....	38
Figure 5.1: Flow chart for enrolment and two- month follow-up of the study participants	72
Figure 6.1: Suboptimal adherence levels during the follow-up period.....	112
Figure 7.1: Illustrates the themes, categories, sub-themes, and countermeasures in implementation of lifelong ART services for PMTCT in three districts of Central Uganda ..	136

Dedication

This thesis is dedicated to God the Father, God the Son, and God the Holy Spirit for the golden opportunity, wisdom, favour and preservation to pursue the Doctor of Philosophy (PhD) [Deuteronomy 8:18, Philippians 1:6]. Additionally, to my lovely children (Ruth Tendo, Jireh Treasure, and Abigail Triumph), who supported and encouraged me in my academic pursuits. Their prayers, support, and love were a constant source of strength, and inspiration; and instrumental in helping me to persevere through the challenges of the PhD journey.

Acknowledgements

Supervisors:

I would like to express my unwavering gratitude and appreciation to my supervisors, Professor Jean-Pierre Van geertruyden, Professor Hilde Bastiaens, and Professor Rhoda Wanyenze for their support and guidance throughout my PhD journey. I am fortunate to have had you as supervisors. Your expertise, knowledge, patience, support, and encouragement helped me to refine, improve, and complete this thesis.

I would like to thank Professor Rhoda Wanyenze who unveiled the PhD opportunity to me and subsequently introduced me to Professor Jean-Pierre Van geertruyden. Thank you so much Professor Rhoda Wanyenze for always having confidence in me. You gave me invaluable guidance and support throughout my research including the acquisition of the research funding. I am also grateful for the constant encouragement, motivation, counsel, and financial support which have kept me going even during the most challenging times. I am forever grateful. May the Almighty God always bless you abundantly.

Professor Jean-Pierre Van geertruyden, thank you for accepting to be my promoter and linking me to Professor Hilde Bastiaens. I am very grateful for your incredible inspiration, support, critical feedback, and constructive criticism that helped me to improve my research methodology and to produce quality research findings. Beyond the supervision role, you secured for me funding to support my PhD journey.

Finally, I acknowledge Professor Hilde Bastiaens for being an invaluable mentor, providing me with insightful feedback and suggestions on my research at every stage. Your extensive knowledge and expertise in the field of qualitative methodology helped me to develop a deeper understanding of the subject and to identify, and address potential issues in my research. You constantly followed and supported me to progress and not to give up. Your counsel, motivational messages and guidance through my PhD journey are invaluable. Thank you for securing me funds that enabled me to have protected time to write my PhD thesis. I am extremely grateful.

Study team:

I would like to express my deep appreciation to the study team that I worked with on this research project. Their support and hard work have been instrumental in helping me to complete this PhD thesis.

I am particularly grateful to Dr. Fredrick Makumbi, his extensive knowledge and proficiency in the field of biostatistics which enhanced my skills in data interpretation. He helped me to understand the nuances of statistical analyses. His contributions were instrumental in producing the meaningful results presented in this thesis.

Colleagues:

I would like to express my heartfelt gratitude to my colleagues who supported me throughout my PhD journey. Their encouragement, feedback, and insights were priceless in helping me to complete this thesis.

I am particularly grateful to Dr. Geoffrey Musinguzi, who provided me with valuable support and feedback on my entire PhD journey. His comments, insights, feedback, and suggestions helped me to refine my research, strengthen arguments, and produce high quality findings.

Finally, I would like to express my gratitude to Dr. Justine Namwagala, my family and friends for their unwavering support and encouragement. Without their love and support, this achievement would not have been possible.

List of Abbreviations

AGYW	Adolescent girls and young women
AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal Care
ART	Antiretroviral Therapy
ARVs	Antiretroviral drugs
EID	Early Infant Diagnosis
e-MTCT	Elimination of Mother-to-Child HIV Transmission
HIV	Human Immunodeficiency Virus
LMICs	Low- and Middle-Income Countries
MOH	Ministry of Health
MTCT	Mother-to-Child Transmission
PLHIV	People Living with HIV/AIDS
PMTCT	Prevention of Mother-to-Child-Transmission
PNC	Postnatal Care
SRH	Sexual and Reproductive Health
SSA	Sub-Saharan Africa
UAC	Uganda AIDS Commissions
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UNICEF	The United Nations Children's Fund
WHO	World Health Organisation

List of Papers

This thesis is based on the following papers, which are referred to in the text.

- I. **Mukose AD**, Bastiaens H, Buregyeya E, Naigino R, Makumbi F, Musinguzi J, Van geertruyden JP, Wanyenze RK. Health provider perspectives of health facility preparedness and organization in implementation of Option B+ among pregnant and lactating women in Central Uganda: a qualitative study. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2019 Mar 5; 18:2325958219833930.
- II. **Mukose AD**, Bastiaens H, Makumbi F, Buregyeya E, Naigino R, Musinguzi J, Van geertruyden JP, Wanyenze RK. What influences uptake and early adherence to Option B+ (lifelong antiretroviral therapy among HIV-positive pregnant and breastfeeding women) in Central Uganda? A mixed methods study. *Plos one*. 2021 May 5;16(5): e0251181.
- III. **Mukose AD**, Van geertruyden JP, Makumbi F, Buregyeya E, Naigino R, Musinguzi J, Wanyenze RK. Suboptimal adherence to lifelong ART, and its predictors among HIV- positive pregnant and breastfeeding women in three districts of Central Uganda: A repeated measures analysis. Under Review.
- IV. **Mukose AD**, Bastiaens H, Makumbi F, Buregyeya E, Naigino R, Musinguzi J, Van geertruyden JP, Wanyenze RK. Challenges and commonly used countermeasures in the implementation of lifelong antiretroviral therapy for PMTCT in Central Uganda: Health providers' perspective. *PloS one*. 2023 Jan 20;18(1):e0280893.

The papers listed below were published within the same project as the thesis. They do not make direct contribution. However, they are related and relevant to the thesis.

- I. Buregyeya E, Naigino R, **Mukose A**, Makumbi F, Esiru G, Arinaitwe J, Musinguzi J, Wanyenze RK. Facilitators and barriers to uptake and adherence to lifelong antiretroviral therapy among HIV infected pregnant women in Uganda: a qualitative study. BMC pregnancy and childbirth. 2017 Dec;17(1):1-9.
- II. Naigino R, Makumbi F, **Mukose A**, Buregyeya E, Arinaitwe J, Musinguzi J, Wanyenze RK. HIV status disclosure and associated outcomes among pregnant women enrolled in antiretroviral therapy in Uganda: a mixed methods study. Reproductive health. 2017 Dec; 14:1-1.
- III. Naigino R, Makumbi F, **Mukose A**, Buregyeya E, Arinaitwe J, Musinguzi J, Kiene SM, Wanyenze RK. Resumption of Sexual Intercourse Among Postnatal Women Enrolled on Lifelong Antiretroviral Therapy in Uganda. AIDS and Behavior. 2021 Feb 19:1-1.

Thesis structure

This thesis presents studies that were conducted to understand the implementation of lifelong antiretroviral therapy (ART) for prevention of mother-to-child transmission (PMTCT) of human immunodeficiency virus (HIV) among pregnant and breastfeeding women living with HIV in Central Uganda. The thesis has 8 chapters. Chapter 1 provides a general introduction, with specific focus on the burden of HIV, mother-to-child transmission (MTCT) of HIV, PMTCT of HIV, and the evolution of the PMTCT interventions and guidelines. Chapter 2 gives the study background, rationale, and objectives. The summary of the methods is presented in chapter 3. Chapter 4 presents health facility preparedness and organization in implementation of lifelong ART services for PMTCT from the health provider perspectives (Paper I). Uptake of, adherence to lifelong ART for PMTCT of HIV and its predictors (Papers II and III) are presented in chapter 5 and 6 respectively. In chapter 7, challenges and commonly used countermeasures in implementation of lifelong ART for PMTCT of HIV (Paper IV) are presented. The final chapter (8) focuses on the general discussion, conclusions and recommendations.

Samenvatting

Achtergrond: Wereldwijd blijft de epidemie van het humaan immunodeficiëntie virus (HIV) een uitdaging. Uit gegevens van het HIV/AIDS-programma van de Verenigde Naties (UNAIDS) blijkt dat 54% van alle mensen met hiv vrouwen en meisjes zijn, terwijl 49% van alle nieuwe HIV-besmettingen in 2021 wereldwijd bij deze groep voorkomen. In hetzelfde jaar vonden 160.000 nieuwe HIV infecties plaats onder kinderen. De belangrijkste bron van nieuwe HIV-besmettingen bij kinderen is de overdracht van een HIV-positieve moeder op haar kind (verticale overdracht).

Eén op de vijf nieuwe hiv-infecties vindt plaats door verticale overdracht tijdens de zwangerschap, intrapartum of borstvoeding. Dit kan worden voorkomen door effectieve preventie van moeder op kind-overdracht (PMTCT: Prevention of Mother-to-Child Transmission) van hiv-interventies. Eén van die interventies is het gebruik van levenslange ART bij alle zwangere en zogende vrouwen die leven met HIV, ongeacht hun clusters van differentiatie 4 (CD4) cel aantal (een maat voor het immuunsysteem) of het klinische stadium van de Wereldgezondheidsorganisatie (WHO) (Optie B+). Deze aanpak, bekend als optie B+, heeft bijgedragen aan aanzienlijke verminderingen in het aantal hiv-infecties bij kinderen.

Oeganda begon in september 2012 met de uitvoering van levenslange ART voor alle zwangere en borstvoedende vrouwen die leven met HIV, wat goede resultaten opleverde. Ondanks deze enorme stappen en successen in het PMTCT-programma, wijzen recente gegevens erop dat er nog heel wat uitdagingen en kennislacunes zijn met betrekking tot de voorbereiding, organisatie van PMTCT diensten, acceptatie en naleving van levenslange ART, evenals de retentie in de zorg. Deze factoren hebben de inspanningen om de overdracht van moeder op kind van HIV bijna te elimineren (e-MTCT), vertraagd. Informatie over de implementatie van levenslange ART voor PMTCT van HIV is van groot belang voor gezondheidswerkers, beleidsmakers en andere betrokkenen op lokaal, nationaal en internationaal niveau.

Doelstellingen: Het doel van dit proefschrift is om deze kenniskloof te dichten en zo de implementatie, het opschalen en verduurzamen van levenslange antiretrovirale therapie (ART) voor het voorkomen van moeder-op-kind-transmissie van HIV (PMTCT) in lage-inkomenslanden, te ondersteunen. Bedoeling is om zo bij te dragen

aan het verwezenlijken van de doelstellingen van UNICEF, UNAIDS en de WHO om de HIV-epidemie bij kinderen te beëindigen en hun moeders gezond te houden. Dit onderzoek heeft de volgende specifieke doelstellingen: 1. Het exploreren van de perspectieven van zorgverleners met betrekking tot de paraatheid en organisatie van het gezondheidszorgsysteem voor de implementatie van levenslange ART voor in Centraal Oeganda (Deelstudie/Paper I); 2. Het beoordelen van de praktijken met betrekking tot het voorschrijven en slikken van ART (inname), vroege therapietrouw en de bijbehorende factoren onder zwangere en borst voedende vrouwen die leven met HIV die levenslange ART gebruiken voor PMTCT in Centraal Oeganda (Deelstudie/Paper II); 3. Het bepalen van suboptimale therapietrouw aan levenslange ART en de voorspellers daarvan bij zwangere en borst voedende vrouwen die leven met HIV in drie districten van Centraal-Oeganda (deelstudie/Paper III); en 4. Onderzoeken van de perspectieven van zorgverleners in verband met uitdagingen en mogelijke ondersteunende factoren bij de implementatie van levenslange ART onder HIV-positieve zwangere vrouwen en vrouwen die borstvoeding geven in Centraal Oeganda (Deelstudie/Paper IV).

Methoden: Deze studie werd uitgevoerd in Centraal Oeganda in de districten Masaka, Mityana en Luwero. Het onderzoek werd tussen oktober 2013 en maart 2016 uitgevoerd in zes doelbewust geselecteerde openbare gezondheidsinstellingen, waarbij gebruik werd gemaakt van een gemengde aanpak. Deelstudies I en IV zijn uitgevoerd met behulp van een kwalitatieve beschrijvende methode en omvatten interviews met sleutelinformanten. In totaal werden 54 zorgverleners uit alle zes zorginstellingen geïnterviewd. Deelstudie I peilde naar ervaringen van zorgverleners, hun meningen en suggesties over paraatheid en organisatie van diensten tijdens de implementatie van levenslange ART voor PMTCT, terwijl deelstudie IV uitdagingen en en mogelijke ondersteunende factoren onderzocht rond de implementatie en opschaling van levenslange ART bij zwangere vrouwen en vrouwen die borstvoeding geven vanuit het perspectief van de zorgverleners.

Deelstudie II volgde een mixed methods benadering met een cross-sectioneel convergent parallel studieopzet, ingebed in een prospectieve cohort-study van 507 zwangere en borst voedende vrouwen die leven met HIV van drie verschillende gezondheidszorginstellingen. De vrouwen waren ART-naïef of hadden levenslange ART gebruikt gedurende maximaal vier weken op het moment dat ze werden

ingeschreven voor de studie. De kwantitatieve gegevens werden verzameld via gestructureerde interviews, afgenomen door interviewers, met behulp van vragenlijsten. De kwalitatieve component van het onderzoek omvatte interviews met 54 zorgverleners en 57 zwangere of post-partum vrouwen die leven met HIV uit de zes betrokken zorginstellingen. Kwalitatieve gegevens van de vrouwen die leven met HIV werden verzameld door middel van diepte-interviews. Deelstudie II onderzocht de belangrijkste problemen rond het voorschrijven en slikken van ART (opname), vroege therapietrouw en geassocieerde factoren onder zwangere en borst voedende moeders die leven met HIV en die onder levenslange ART stonden.

Tot slot werden in deelstudie III gegevens gebruikt van 385 zwangere en borst voedende vrouwen die leven met HIV die ten minste drie follow-up bezoeken hadden na inschrijving voor de studie. Deze gegevens waren afkomstig van de 507 zwangere vrouwen die leven met HIV die waren ingeschreven voor het prospectieve cohort. Het cohort werd gedurende 18 maanden gevolgd (gedurende de hele zwangerschap, de bevalling en de periode van borstvoeding). Het onderzoek richtte zich vooral op het onderzoeken van suboptimale therapietrouw aan levenslange antiretrovirale therapie (ART) en de factoren die daarop van invloed waren. Dit werd gedaan door middel van herhaalde metingen om veranderingen in de tijd te kunnen identificeren en begrijpen.

Resultaten: In deelstudie II en III vonden we dat eenennegentig procent van de vrouwen (463/507) een levenslange ART voorgeschreven kreeg. Van hen begon 93,3% (432/463) met het slikken van hun medicijnen. De belangrijkste motiverende factoren om ART te slikken waren de persoonlijke wens van vrouwen om gezond te zijn (92,3%) en de wens om hun baby's te beschermen (90,6%). Het niveau van suboptimale therapietrouw gedurende 30 dagen was het hoogst in maand 2 (23,2%), maar varieerde tussen 12%-13,9% in de maanden 4, 6, 10, 14 en 18 na de bezoeken voor inschrijving voor het onderzoek. In de aangepaste analyse werden bepaalde factoren geassocieerd met een verminderde kans op suboptimale therapietrouw, namelijk het openlijk delen van de hiv-positieve status met iemand anders, AOR = 0,50 (0,30 - 0,84), de steun van de partner, AOR = 0,43, (0,28 - 0,67), en de motivatie van zorgverleners om te helpen bij het starten van levenslange ART, AOR = 0,19 (0,07 - 0,51). Aan de andere kant werden factoren geïdentificeerd die de kans op suboptimale therapietrouw vergroten, waaronder onwil om met ART te beginnen, AOR

= 2,38 (1,26 - 4,50), hiv-gerelateerd stigma, AOR = 1,70 (1,05 - 2,75), en het ontvangen van HIV-zorg van Luwero Gezondheidscentrum IV (HC IV), AOR = 5,36 (2,62 - 10,98).

Uit de kwalitatieve bevindingen bleek dat adequate counseling, de bereidheid om te beginnen en het kennen van de voordelen van ART, de opname van ART bevorderden. Redenen om te weigeren met ART te beginnen waren onder andere: niet klaar zijn om met ART te beginnen, angst om levenslang ART te nemen, twijfel over hiv-positieve resultaten en voorkeur voor lokale kruiden. Redenen om zich niet aan de ART te houden waren: wonen op een grote afstand van de zorgfaciliteiten, angst voor bijwerkingen, de HIV positieve status met niemand delen en de perceptie dat de baby na de bevalling veilig is voor besmetting met HIV.

In deelstudie I en IV met betrekking tot paraatheid, organisatie, uitdagingen en mogelijke ondersteunende factoren, stelden we vast dat: training, supervisie en mentorschap van eerstelijnsgezondheidswerkers essentieel waren voor de paraatheid om levenslange ART aan te bieden aan zwangere vrouwen en vrouwen die borstvoeding geven, terwijl counseling en ondersteuningsmechanismen voor patiënten cruciaal waren voor de organisatie van PMTCT-diensten met levenslange ART. De belangrijkste uitdagingen waren 1) ontoereikende hiv-dienstverlening; 2) niet-gebruik van hiv-diensten; en 3) suboptimale therapietrouw. Mogelijke ondersteunende factoren waren training op de werkplek, mentorschap, taakverschuiving, herverdeling van hiv-medicate over faciliteiten, begeleiding van vrouwen naar zorgpunten, voortdurende counseling van vrouwen, peer-ondersteuning, steungroepen voor gezinnen en outreach werken in de gemeenschap.

Conclusies: De opname van levenslange ART voor PMTCT was zeer hoog. Suboptimale therapietrouw was echter een groot probleem in deze studie. De suboptimale therapietrouw gedurende 30 dagen was slecht en volgende groepen hadden de slechtste therapietrouw: vrouwen die niet bereid waren om onmiddellijk te beginnen met levenslange ART, vrouwen die aangaven ooit HIV-gerelateerde stigmatisering te hebben ervaren en vrouwen die zorg zochten bij Luwero HC IV. Het onderzoek toont aan dat het bekendmaken van de hiv-positieve status, steun van de partner en motivatie van de zorgverleners om te beginnen met levenslange ART, het risico op suboptimale therapietrouw verminderden. Ondanks het zeer hoge gebruik

van levenslange ART voor PMTCT, blijven verschillende uitdagingen de implementatie van levenslange ART voor PMTCT-diensten belemmeren. Contextspecifieke, innovatieve en systeeminterventies op meerdere niveaus zijn nodig om de opschaling en duurzaamheid van de levenslange ART-strategie voor zwangere vrouwen en vrouwen die borstvoeding geven te verbeteren om uiteindelijk te komen tot de eliminatie van moeder op kind overdracht van HIV (e-MTCT).

Summary

Background: Globally, the human immunodeficiency virus (HIV) epidemic remains a challenge. Data from The Joint United Nations Programme on HIV/AIDS (UNAIDS), indicates that 54% of all people living with HIV (PLHIV) were women and girls while 49% of all new HIV infections occurred in the same population globally in 2021. In the same year, 160, 000 new HIV infections occurred among children. The major source of new HIV infections in children is through transmission from an HIV-positive mother to her child (vertical transmission).

One in five new HIV infections is through vertical transmission during pregnancy, intrapartum, or breastfeeding which can be avoided through use of effective prevention of mother-to-child transmission (PMTCT) of HIV interventions. One such intervention is the use of lifelong ART among all pregnant and breastfeeding women living with HIV regardless of their clusters of differentiation 4 (CD4) cell count or World Health Organization (WHO) clinical stage (Option B+). Use and scale up of this intervention has resulted in the number of HIV infections among children falling significantly.

Uganda started implementing use of lifelong ART for PMTCT among positive pregnant and breastfeeding women living with HIV in September 2012 with commendable results. However, despite tremendous progress and successes noted in the PMTCT program, recent data show that several challenges and information gaps in preparedness, organization of PMTCT services, uptake, and adherence to lifelong ART, and retention in care, still exist which have stagnated the progress to virtual elimination of mother-to-child transmission (e-MTCT) of HIV. Information on implementation of lifelong ART for PMTCT of HIV is important to practitioners, decision & policymakers, and other stakeholders at the local, national, and international levels.

Objectives: The purpose of this thesis is to fill this information gap in order to inform implementation, scale up, and sustainability of lifelong ART for PMTCT of HIV in low income setting and contribute to the achievement of the United Nations Children's Fund (UNICEF), UNAIDS and WHO goal of ending the HIV epidemic in children and keeping their mothers healthy. The specific objectives of the thesis are: 1. To explore perspectives of health providers on health facility preparedness and organization in the implementation of lifelong ART for PMTCT of HIV among pregnant and

breastfeeding women living with HIV in Central Uganda (Sub-study/Paper I); 2. To assess practices around ART prescription and swallowing (uptake), early adherence and associated factors among expectant and lactating mothers living with HIV on lifelong ART for PMTCT of HIV in Central Uganda (Sub-study/Paper II); 3. To determine suboptimal adherence to lifelong ART, and its predictors among pregnant and breastfeeding women living with HIV in three districts of Central Uganda (Sub-study/Paper III); and 4. To explore health providers' perspectives of challenges and corresponding countermeasures in implementation of lifelong ART among pregnant and breastfeeding women living with HIV in Central Uganda (Sub-study/Paper IV).

Methods: This study was conducted in Central Uganda in the districts of Masaka, Mityana, and Luwero. The study was carried out in six purposively selected public health facilities from October 2013 to March 2016 using a mixed methods approach. Sub-studies I and IV employed a qualitative descriptive approach and were conducted among 54 health providers from all the six health facilities using key informant interviews. Sub-study I elicited experiences of health providers, their opinions, and suggestions on preparedness and organization of services during implementation of lifelong ART for PMTCT, while sub-study IV explored challenges and countermeasures around the implementation and scale-up of lifelong ART among pregnant and breastfeeding women from the health providers' perspectives.

Sub-study II used a mixed methods cross-sectional convergent parallel study design nested in a prospective cohort of 507 pregnant women living with HIV from three health facilities. The women were ART naïve or had been on lifelong ART for ≤ 4 weeks at the time of study enrolment. Quantitative data were collected using interviewer administered questionnaires. The qualitative component was among the 54 health providers and 57 pregnant or post-partum women living with HIV from the six health facilities. Qualitative data from the women living with HIV were collected using in-depth interviews. Sub-study II, assessed key issues around ART prescription and swallowing (uptake), early adherence and associated factors among HIV-positive expectant and lactating women on lifelong ART.

Finally, sub-study III used data from 385 pregnant and breastfeeding women living with HIV who had at least three follow-up visits after study enrolment. This data was accrued from the 507 pregnant women living with HIV who were enrolled for the

prospective cohort. The cohort was followed up for 18 months (throughout pregnancy, childbirth and breastfeeding period) focusing on suboptimal adherence to lifelong ART and its predictors among pregnant and breastfeeding women living with HIV using repeated measures analysis.

Results: In sub-study II and III, we found that 91.3% of the women (463/507) received a prescription of lifelong ART. Of these, 93.3% (432/463) started swallowing their medicines. Main motivating factors to swallow ART were women's personal desire to be healthy (92.3%), and desire to protect their babies (90.6%). The 30-day suboptimal adherence level was highest at month 2 (23.2%) but varied between 12%-13.9% at month 4, 6, 10, 14, and 18 post study enrolment visits. In the adjusted analysis, disclosure of HIV-positive status to anyone, AOR = 0.50 (0.30 – 0.84), spousal support, AOR = 0.43 (0.28 – 0.67), and motivation from health providers to start lifelong ART, AOR = 0.19 (0.07 – 0.51) were associated with lower odds of suboptimal adherence. Unreadiness to start ART, AOR = 2.38 (1.26 – 4.50), HIV-related stigma, AOR = 1.70 (1.05 – 2.75), and receipt of HIV care from Luwero Health Centre IV (HC IV), AOR = 5.36 (2.62 – 10.98) were associated with higher odds of suboptimal adherence. Facilitators of ART uptake from qualitative findings included adequate counseling, willingness to start, and knowing the benefits of ART. Reasons for refusal to start ART included being unready to start taking ART, fear to take ART for life, doubt of HIV- positive results, and preference for local herbs. Reasons for nonadherence were having travelled far away from the health facilities, fear of side effects, non-disclosure of HIV-positive results to anyone, and perception that the baby is safe from HIV infection post-delivery.

In sub-study I and IV regarding preparedness, organization, challenges, and countermeasures, we observed that: training, supervision, and mentorship of frontline health providers were key for preparedness to offer lifelong ART among pregnant and breastfeeding women living with HIV while counseling and support mechanisms for patients were crucial under organization of lifelong ART PMTCT services. The main challenges included 1) inadequacy of HIV service delivery; 2) Non-utilization of HIV services; and 3) Suboptimal treatment adherence. Countermeasures were on-job training, mentorship, task shifting, redistribution of HIV commodities across facilities, accompanying women to care points, ongoing counseling of women, peer support, family support groups, and community outreaches.

Conclusions: Uptake of lifelong ART for PMTCT was very high. However, suboptimal adherence was a major concern in this study. The 30-day suboptimal adherence level was high, higher among women who were not ready to start taking lifelong ART immediately, those who reported having ever experienced HIV -related stigma, and those who sought care from Luwero HC IV. Disclosure of HIV- positive status, spousal support, and receiving motivation from health providers to start lifelong ART reduced the risk of suboptimal adherence. Despite the very high uptake of lifelong ART for PMTCT, several challenges continue to impede the implementation of lifelong ART for PMTCT services. Context-specific, innovative, and multilevel system interventions are needed to enhance scale up, and sustainability of the lifelong ART strategy for pregnant and breastfeeding women living with HIV so as to ultimately achieve e-MTCT of HIV.

CHAPTER 1:

INTRODUCTION

1.1 Burden of HIV

1.1.1 HIV among the general population

Globally, the HIV epidemic remains a challenge [1, 2]. At the end of 2021, nearly 84.2 million people were infected with HIV since the start of the epidemic, and 38.4 million people were living with HIV globally. Of these, around 1.5 million accounted for new infections [3,4]. In 2021, nearly 650,000 deaths from AIDS-related illnesses were reported worldwide, compared to 2.0 million individuals in 2004 and 1.4 million people in 2010 [3,4]. The sub-Saharan African (SSA) region remains most severely affected, with nearly 1 in every 25 adults living with HIV and accounting for more than two-thirds of the PLHIV worldwide [5-8]. It was reported that this situation was exacerbated further by the coronavirus disease 2019 (COVID-19) disruptions [9, 10].

Although AIDS-related deaths in Uganda declined by 67% from 51,000 in 2010 to 17,000 in 2021 and new HIV infections decreased by 39% from 88,000 in 2010 to 54,000 by the end of 2021[11, 12], the country still faces a generalized HIV epidemic. The national HIV prevalence is estimated at 5.5% among persons aged 15-49 years, higher among females (7.2%) compared to males (4.3%). An estimated 1.4 million people were living with HIV at the end of 2021 compared to 1.2 million in 2010, arise largely attributed to increased access to and use of HIV care services [11, 13].

1.1.2 HIV among women and girls

Women and girls are disproportionately affected by HIV because of vulnerabilities created by unequal cultural, social and economic status [6]. According to the 2021 data from UNAIDS, 54% of all PLHIV were women and girls with 49% of all new HIV infections occurring in the same population globally [3, 11]. During the same year, almost 4900 young women aged 15–24 years became HIV infected every week. The same data show that girls and young women aged 15–24 years are twice as likely to be living with HIV compared to young men in SSA. Worse still, women and girls accounted for 63% of all new HIV infections while six in seven new HIV infections among adolescents aged 15–19 years were among girls in SSA [3, 7, 14].

In Uganda, nearly two-thirds (65%) of new HIV infections among adults occurred in women in 2021. Meanwhile, among young people, adolescent girls and young women (AGYW) are even more susceptible to HIV infection, with four in five (79%) of new HIV infections in young people occurring in AGYW aged 10-24 years [11, 13].

1.2 Mother-to-child transmission of HIV

HIV can be transmitted from an HIV-positive mother to her child during pregnancy, labour, childbirth or breastfeeding [15]. Mother-to-child transmission of HIV, which is also known as 'vertical transmission' accounts for most infections in children (0-14 years). One in five new HIV infections occurs via vertical transmission from the mother to the infant during pregnancy, intrapartum or breastfeeding [16-19]. Without any intervention, HIV transmission rates range from 15% to 45%. However, this rate can be reduced to less than 5% with effective PMTCT interventions such as use of lifelong ART [20, 21]. Hence, fewer children are acquiring HIV than a decade ago. For instance, there were approximately 160,000 new HIV infections among children (aged ≤14 years) in 2021 compared to 320,000 in 2010 globally [3, 22].

In Uganda, MTCT of HIV is the main source of new HIV infections among children and the second major mode of HIV transmission after sexual transmission. Mother-to-child transmission accounts for approximately 14% of all new HIV infections in Uganda. New infections among children ages 0-14 years reduced by 77%, from 23,000 in 2010 to 5,300 in 2020 [23]. This was attributed to better PMTCT interventions [24-27]. However, the number of new infections increased to 6,000 new infections in 2021. Similarly, the estimated MTCT rate increased from 5.8% in 2020 to 6.8% in 2021[11]. The surge could have been due to the COVID-19 interruptions [9, 10].

1.3 Prevention of Mother-to-child transmission of HIV

PMTCT has been at the fore front of global HIV prevention activities among pregnant and breastfeeding women since 1998. This followed the success of short-course Azidothymidine (AZT) and single-dose Nevirapine (sd-NVP) in preventing MTCT of HIV [8]. PMTCT has tremendously reduced the number of children being infected with HIV. Globally, 1.3 million pregnant women were approximated to be living with HIV in 2021, of which approximately 81% [63–97%] received ART to prevent MTCT of HIV [28].

Use of lifelong ART among expectant and lactating women has resulted in a significant reduction of the number of HIV infections among children due to the scaling up of effective PMTCT interventions. The number of new infections among children reduced by 52% from 310,000 in 2010 to 150,000 in 2019 [5]. Regrettably, progress in preventing MTCT slowed, with only a 22% reduction in new pediatric infections from 2016 to 2021. About 160,000 children were newly infected with HIV globally and almost 85% of new vertical infections occurred in SSA in 2021[3]. The global HIV response including the drive towards e-MTCT of HIV slowed in the period 2015–2021. This was largely due to the colliding AIDS and COVID-19 pandemics—along with economic and humanitarian emergencies. Unfortunately, low- and middle-income countries (LMICs) have been affected most [22].

In Uganda, the PMTCT program has registered tremendous progress. Lifelong ART coverage for PMTCT is over 95%, and consequently, 21, 000 new pediatric infections were averted in 2021 [11, 12, 13].

1.4 Evolution of PMTCT interventions and guidelines

Over the past ten years, incredible advances have been made in the PMTCT of HIV, principally due to gallant policies, including the latest universal lifelong ART for pregnant and breastfeeding women (Option B+) [29].

The first PMTCT intervention was translated into policy by The Centers for Disease Control and Prevention (CDC) in 1985. It recommended that postpartum women living with HIV should use formula feeding instead of breastfeeding [30].

Following the Pediatric AIDS Clinical Trials Group 076 (PACTG 076) study in 1994, that showed a 67% reduction in MTCT of HIV with the administration of a combination of prenatal, intrapartum and neonatal AZT [31], this regimen was quickly included in the United States (US) PMTCT Public Health Service Guidelines and used in the entire US [32]. In 1999, a European mode of delivery trial demonstrated that the MTCT of HIV rate further declined to 1.8% if women who received AZT prophylaxis were also randomized to deliver by elective cesarean section compared to women who had vaginal delivery (10.5%) [33]. As a result of this European trial and a large meta-analysis [34], the American College of Obstetricians and Gynecologists in 2000, recommended that all women with HIV viral loads higher than 1000 copies per milliliter be counseled on the benefit of elective caesarean delivery in addition to AZT prophylaxis to further lower the risk of perinatal HIV transmission [35].

Despite the clear benefits these interventions in reducing MTCT of HIV, implementation in LMICs was not possible due to cost and feasibility. Accordingly, studies were done to find a shorter, more feasible, and less expensive antiretroviral (ARV) treatment for PMTCT of HIV in LMICs [36-43].

The WHO PMTCT guidelines have been revised several times based on several studies, feasibility and cost implications [44-48]. The first WHO PMTCT of HIV recommendations were issued in 2000, they were informed by different studies including the HIVNET 012 trial that was conducted in Uganda which compared sd-NVP to the mother at the time of labor and to the infants within 72 hours of birth versus AZT given to the mother during labor and to infants for seven days after birth. The HIVNET 012 study established that Nevirapine (NVP) lowered the risk of HIV-1 transmission during the first 14–16 weeks of life by almost 50% in a breastfeeding population. At that time, WHO endorsed regimens that included AZT alone or in combination with lamivudine (3TC) and NVP. The simplest regimen entailed of sd-NVP at the onset of labour plus a single dose for the infant soon after birth [41, 49, 50]. In 2001, a technical consultation on the PMTCT of HIV was assembled by WHO in Geneva from 11-13 October 2000 on behalf of the United Nations Interagency Task Team on MTCT of HIV infection and gave guidance on the use of NVP in PMTCT programmes. The guidance provided basic information on: the design of a comprehensive PMTCT-prevention programme; the choice of antiretroviral regimens for preventing MTCT; the efficacy and safety of NVP for preventing MTCT; the efficacy and safety of NVP for the prevention and treatment of HIV/AIDS; and the management of NVP donations [41, 44, 50]. In 2002, the United Nations approved a comprehensive strategic approach for PMTCT. It addresses a broad range of HIV-related prevention, care, and treatment and support needs of pregnant women, mothers, their children and families [51, 52].

The strategy comprises the following four prongs/components:

- a. Primary prevention of HIV infection among women of childbearing age;
- b. Preventing unintended pregnancies among women living with HIV;
- c. Preventing HIV transmission from a woman living with HIV to her infant; and
- d. Providing appropriate treatment, care and support to mothers living with HIV and their children and families.

In 2004, the WHO revised the previous recommendations in the context of rapidly expanding ART programs using simplified and standardized regimens. Endorsements on the choice of regimens in the context of escalating access to ART to diverse clinical circumstances were made [48]. The main endorsements in the guidelines were;

1. Pregnant women who needed ART for their own health should receive it in accordance with the WHO guidelines since its use when indicated, during pregnancy substantially benefited the health of the woman and decreased the risk of MTCT of HIV.
2. HIV-positive pregnant women who did not have indications for ART, or didn't have access to it were offered ARV prophylaxis for PMTCT using one of the recommended ART regimens that were safe and effective:
 - a. AZT from 28 weeks of pregnancy plus sd-NVP during labour and sd-NVP and one-week AZT for the infant.
 - b. Alternative regimens based on AZT alone, short-course AZT + 3TC or sd-NVP alone were also recommended.
3. Countries that were in position to offer more complex ARV regimens were recommended to do so.

The WHO made further revisions in the PMTCT guidelines in 2006. This was aimed at supporting the public health approach where PMTCT programs use standardized regimens, and simplified strategies suitable for the majority of women. ART was used for PMTCT in line with, and aim to support, the "Call to Action Towards an HIV free and AIDS-free Generation". The guidelines gave direction to support national ministries of health in the provision of ART for pregnant women who needed treatment, and in the selection of ARV prophylaxis regimens for inclusion in PMTCT programs, taking into account the health systems needs and constraints in the different settings. The recommended first-line ART for treating pregnant women during pregnancy, labour and post-delivery was AZT+3TC and NVP while the infant received AZT for seven days. However, if the expectant women received less than four weeks of ART during pregnancy, then four weeks, instead of one week, of infant AZT was recommended. The endorsed prophylactic ARV regimens for expectant mothers who were not yet eligible for ART was: AZT starting at 28 weeks of gestation or as soon as feasible thereafter, then sd-NVP + AZT/3TC during labour and AZT/3TC for seven days post-delivery. The infant received sd-NVP within 72 hours of delivery + AZT for seven days [45, 53].

In 2010, the WHO revised the 2006 PMTCT guidelines. The reviewed guidelines were on two fundamental approaches:

1. Lifelong ART for HIV-positive women in need of treatment for their own health, which is also safe and effective in reducing MTCT of HIV.
2. ARV prophylaxis for PMTCT of HIV during antepartum, intrapartum and breastfeeding for HIV-positive women not in need of ART.

The endorsements emphasized the need to have a cohesive approach to preventing MTCT throughout pregnancy, labour and delivery, postpartum, and the lactating period. This was the first time when evidence allowed new recommendations on ARV prophylaxis to either the mother or infant during lactation, in areas where breastfeeding was judged to be the best choice of infant feeding for mothers living with HIV. These guidelines were geared towards e-MTCT of HIV. This followed a modeling study which showed that e-MTCT of HIV would be attainable if PMTCT programs accomplish high (>90%) coverage of highly effective ARV interventions [54]. Precisely, HIV-positive pregnant women were initiated on lifelong ART for their own health and PMTCT if they had CD4 cell counts of ≤ 350 cells/mm³, irrespective of WHO clinical staging, and those in WHO clinical stage 3 or 4, irrespective of the CD4 cell count. This group of women used ART options shown in table 1.1 starting as soon as possible irrespective of gestational age, and continued during pregnancy, delivery and thereafter daily. In the first trimester, Efavirenz (EFV) was to be avoided and instead use NVP.

Table 1.1: Antiretroviral treatment options recommended for HIV-positive pregnant women who are eligible for treatment and infant prophylaxis

Mother	Infant
AZT + 3TC + NVP or	Daily NVP or twice-daily AZT from birth until 4 to 6 weeks of age (irrespective of the mode of infant feeding)
AZT + 3TC + EFV or	
TDF* + 3TC (or FTC**) + NVP or	
TDF + 3TC (or FTC) + EFV	

*TDF - Tenofovir Disoproxil Fumarate, **FTC – Emtricitabine

HIV-positive pregnant women who did not qualify to start ART for their own health were recommended ARV prophylaxis for PMTCT of HIV during pregnancy, intrapartum, postpartum and during the breastfeeding period. Two ARV regimens

(Option A or B) were recommended for this category of women as shown in table 1.2. Prophylaxis would start as early as 14 weeks of gestation or instantly thereafter if women present later [46].

Table 1.2: ARV-prophylaxis options recommended for HIV-positive pregnant women who didn't need treatment for their own health

Option A: (Maternal AZT+3TC & Infant prophylaxis)	Option B: (Maternal triple ARV & Infant prophylaxis)
Mother	Mother
Antepartum: AZT twice daily from 14 weeks of gestation and continued during pregnancy	Triple ARV prophylaxis beginning 14 weeks of gestation and continued until delivery, or, if breastfeeding, continued until 1 week after all infant exposure to breast milk has ended. Endorsed regimens included: AZT + 3TC + Lopinavir boosted with ritonavir or AZT + 3TC + Abacavir (ABC) or AZT + 3TC + EFV or TDF + 3TC (or FTC) + EFV
Intrapartum and postpartum: sd-NVP and AZT + 3TC twice daily for 7 days postpartum	
<i>(If maternal AZT was given for more than 4 weeks during antenatal care (ANC), sd-NVP and AZT + 3TC could be disregarded; maternal AZT was continued during labour and stopped at delivery)</i>	
Infant	Infant
If breastfeeding: Daily NVP from birth for a minimum of 4 to 6 weeks, and until 1 week after all exposure to breast milk has ceased.	Daily NVP or twice-daily AZT from birth until 4 to 6 weeks of age (irrespective of the mode of infant feeding)
Receiving replacement feeding only: Daily NVP or sd-NVP + twice-daily AZT from birth until 4 to 6 weeks of age	

In 2011, Malawi revised its policies for PMTCT of HIV and for ART in response to WHO's 2010 guidelines. In the revision, Malawi started implementing a new approach of lifelong ART for all pregnant and breastfeeding women with HIV irrespective of CD4 count or WHO clinical stage, commonly referred to as "Option B+" [55-57]. This innovative approach had a huge impact on the PMTCT program in Malawi. There was

a seven-fold increase in the number of pregnant and breastfeeding women started on ART per quarter during the first year of Option B+ which had multiple potential benefits to mothers, their partners, and their children [55]. Subsequently, the WHO revised its 2010 guidelines and issued a programmatic update on use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants in April 2012. A third option (Option B+) was incorporated into the PMTCT of HIV WHO guidelines. Option B+ entailed use of triple ARVs starting as soon as diagnosed and continued for life for the HIV-positive woman while the infant received Daily NVP or AZT from birth through age 4–6 weeks regardless of infant feeding method [29]. The clinical and programmatic advantages of Option B+ included: no need for CD4 testing to determine ART eligibility (as required in Option A) or whether ART should be stopped or continued after the risk of mother-to-child transmission has ceased (as in Option B); simple message of ART for all, and once started, it's taken for life; protection against MTCT of HIV in forthcoming pregnancies; benefit to the woman's health of earlier ART initiation; protection of HIV-negative partners in sero-discordant relationships and avoiding stopping and starting treatment repeatedly, particularly in countries of high fertility. The preferred regime for Option B+ for the women consisted of TDF + 3TC (or FTC) + EFV [40]. In 2018, WHO interim guidelines recommended dolutegravir (DTG)-containing regimens as the preferred first- and second-line antiretroviral therapy (ART) regimens for PLHIV with a note of caution about women of childbearing potential using DTG due to fears of possible development of neural tube defects in the baby. However, these guidelines were updated in 2019 and recommended use of DTG-based regimens as preferred first line for all eligible PLHIV including pregnant and breastfeeding adolescent girls and women [58].

In Uganda, the PMTCT program started in 2000. The program started with five sites in three districts as a pilot project following the HIVNET 012 study which demonstrated that Nevirapine (NVP) reduced the risk of HIV-1 transmission during the first 14–16 weeks of life by nearly 50% in a breastfeeding population. The five sites were Mulago, Nsambya and Mengo Hospitals in Kampala district; Arua Hospital in Arua district and Lacor hospital in Lira district. The PMTCT guidance at that time recommended sd-NVP tablet to be taken by the mother at labor on set and an oral dose of NVP syrup (2mg/kg) to be given to the infant within 72 hours of birth. The postpartum mothers had to practice replacement feeding [41, 44]. However, subsequent evidence showed

that combining sd-NVP with AZT was effective in reducing nonnucleoside reverse-transcriptase inhibitor mutations in mothers and infants [42, 59]. Centered on this research evidence and guidance from WHO, the Uganda ministry of health (MOH) revised the national PMTCT guidelines of 2002. The guidelines were also informed by feasibility, efficacy, acceptability, and cost of the chosen regimen [44]. In 2006, the MOH revised the PMTCT guidelines in line with the WHO policy recommendations and a more efficacious combination regimen was recommended. In the revised guidelines pregnant women living with HIV were offered AZT from 28 weeks of gestation, or AZT and 3TC from 32 weeks of gestation and sd-NVP during labour. HIV exposed infants received sd-NVP within 72 hours of birth and AZT syrup for 7 days. Combination ART was recommended if the mother had CD4 <350 or WHO clinical stage III and IV. The guidelines for exclusive breastfeeding were also changed to recommend it for 3-6 months with abrupt weaning. The revised guidelines were scaled up and by June 2009, 77% of all health facilities in Uganda, were offering PMTCT services [60]. A major landmark was arrived at when Uganda revised her PMTCT guidelines and started implementing lifelong ART for all HIV-positive pregnant and breastfeeding women regardless of their CD4 cell count or WHO clinical stage (Option B+) in September 2012 [61].

In addition to the guidelines, there was need to ensure that 90% of HIV pregnant women access care and are retained in the PMTCT cascade (ANC, attending counselling, initiation, and adherence to ART during pregnancy, labour, delivery, and after delivery). Uganda uses the United Nations recommended four- pronged approach to increase coverage and scale up uptake of e-MTCT services [62].

Prong 1: Primary prevention of HIV infection which targets women and men of reproductive age including adolescents.

Prong 2: Prevention of unintended pregnancies among women living with HIV focusing on women including adolescents living with HIV and their partners.

Prong 3: Prevention of HIV transmission from women living with HIV to their infants by centering on pregnant and breastfeeding women including adolescents living with HIV. Lifelong ART (Option B+) for all pregnant and breastfeeding women living with HIV regardless of their CD4 cell count or WHO clinical stage which is the focus of this study is one of the efforts of this prong.

Prong 4: Provision of treatment, care, and support to women living with HIV, their children, and their families. This targets HIV-positive women and their families.

The focus of PMTCT of HIV has also evolved over time. In the early stages, the PMTCT programs aimed at reducing the transmission of HIV from HIV-positive mothers to their infants during pregnancy, childbirth, or breastfeeding. However, in 2011, the UNAIDS through a consultative process, developed the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive [63]. The plan served as a basis for country-led initiatives towards the elimination of new HIV infections among children and keeping their mothers alive. It mainly focused on the 22 low- and middle-income countries (Uganda inclusive) with the highest estimated burden of pregnant women living with HIV at that time. At end of 2014, the global plan had helped to reduce the number of new HIV infections among children by 48%, 8 out of 10 pregnant women living with HIV started on ART for PMTCT of HIV, and the final MTCT rate had declined to 14% from 28% in 2009 (the baseline year) averting 89% of HIV infections among children in Global Plan priority countries [64].

In 2016, the achievements of the Global Plan were taken forward by the Start Free, Stay Free, AIDS Free initiative [65]. This campaign was led by the UNAIDS and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). It provides a roadmap for urgently elevating and amplifying key initiatives that are already accelerating progress for children, adolescents and young women. The focus was on enhancing actions in 23 countries with high numbers of children, adolescents and young women living with HIV. The targets of the Start Free, Stay Free, AIDS Free campaign were quite ambitious but reaching them was envisaged as essential to ending the AIDS epidemic among children, adolescents and young women by 2020. Despite the tremendous global achievements and progress none of the campaign targets set out for 2018 or 2020 were attained [66]. For instance, a target was set to eliminate new HIV infections among children (aged 0–14 years) by reducing the number of children newly infected annually to less than 40,000 by 2018 and 20,000 by 2020. However, approximately 130,000 new HIV infections occurred among children in 2022 globally. Another target was to reach and sustain 95% of pregnant women living with HIV with lifelong HIV treatment by 2018 but, 82% of pregnant women living with HIV had access to ART to prevent transmission of HIV to their child in 2022 [67].

Furthermore, in 2020, the UNICEF and partners including the Start Free working group, the UNAIDS and the WHO developed a document titled "Key Considerations

for programming and prioritization going the ‘Last mile’ to EMTCT: A road map for ending the HIV epidemic in children” [68]. This document provides guidelines for coordinated action so that national programmes address local priority areas to achieve e-MTCT in an effective, people-centred, efficient, and directed manner. Some of the key guidelines include early and sustained ANC to ensure HIV testing and early ART initiation among pregnant women to test HIV-positive. The other key considerations include support to ensure retention in care, adherence to lifelong ART, and early services for infants at risk of HIV acquisition [68].

In a bid to achieve elimination of vertical transmission, the WHO has been issuing global guidance on criteria and processes for validation of e-MTCT as a public health priority. The first guidance on e-MTCT of HIV and syphilis was in 2014 [69]. In 2015 the Global Validation Advisory Committee was established to assess if countries had achieved e-MTCT [70] and in the same year Cuba became the first country to be validated for having achieved e-MTCT of HIV and Syphilis [71]. The second edition of the guidance on validation was released in 2017 and it incorporated a section on criteria for the recognition of progress in high HIV or syphilis burden countries [72]. In 2021, WHO released the third version which incorporates guidance for validation of e-MTCT of hepatitis B virus (HBV), within the triple elimination initiative (e-MTCT of HIV, syphilis and HBV) [73].

The third version of global guidance on criteria and processes for validation of e-MTCT of HIV, syphilis and HBV proposes a package of interventions and metrics to support the integrated management and monitoring of vertical transmission of the three major communicable diseases across a wide range of epidemiological and programmatic contexts.

At the of 2022, only 16 countries or territories had been validated for e-MTCT of HIV and/or syphilis globally, these were (in chronological order): Cuba, Thailand, and Belarus (HIV & Syphilis), Armenia (HIV only), Republic of Moldova (syphilis only), Anguilla, Montserrat, Cayman Islands, Bermuda, Antigua and Barbuda, St Christopher and Nevis, Malaysia, Maldives, Sri Lanka, Dominica, and Oman (HIV & Syphilis) [74]. As of 2021, Botswana was the first high-burden country to be certified by WHO for achieving an important milestone on the path to eliminating vertical transmission of HIV [75,76]. With such a slow progress towards e-MTCT of HIV, syphilis and HBV, the WHO has set new impact and programmatic coverage indicators and targets, and

policy milestones. For instance, some of the targets set for HIV include; reducing the number of children 0-14 years of age newly infected with HIV per year from 150,000 in 2020 to 20,000 in 2025 and 15,000 in 2030. The other targeted is to increase the number of countries validated for the e-MTCT of either HIV, hepatitis B, or syphilis from 15 in 2020, to 50 in 2025, and 100 in 2030 [77].

Subsequently, more strategic guidance and calls have been made for renewed global efforts in order to meet these new targets [78,79].

CHAPTER 2:

Study Background, Rationale and Objectives

2.1 Study Background

Uganda started implementation of lifelong ART for HIV-positive pregnant and breast-feeding women (Option B+) in September 2012 [80, 81]. Implementation started in districts with the highest HIV prevalence and by the end of 2013 all the districts in Uganda were offering Option B+ [61]. Option B+ was preferred because it offers a lot of advantages which include; radical simplification of PMTCT program, health benefit of earlier treatment and avoiding the risks of interrupting ARTs, protection from MTCT in future pregnancies, protection for negative partners in sero-discordant couples and reduction in HIV related maternal mortality [29]. In addition, Uganda was among countries with characteristics relevant for provision of Option B+. These characteristics include: a generalized HIV epidemic; high fertility rates and low family planning coverage; low partner testing rates; inadequate access to CD4 testing; low existing coverage of ART for pregnant women who meet the treatment eligibility criteria for non-pregnant individuals; and long duration of breastfeeding by women living with HIV [40]. At the time of the current study, evidence from the evaluation of the lifelong ART on elimination of MTCT of HIV and on maternal and infant health outcomes, found that only 1,240 (57.2%) infants could be identified as having been in care and linked to their mothers. Of these, 1,089 (87.8%) had a 1st PCR test with 4.6% identified as HIV-positive, while only 29% had a final antibody test. Poor adherence to antiretroviral (ARV) drugs by the mothers and an infant receiving no ARV drugs were associated with increased risk of MTCT of HIV. Furthermore, the proportion of HIV-positive mothers who were retained in care post ART initiation at 6, 12 and 18 months was 74%, 67% and 62%, respectively [82, 83]. However, this study was retrospective using records review. Given the weaknesses of records review, particularly in Uganda where they are usually inaccurate and incomplete, there was need for a more objective measurement of PMTCT key indicators i.e., uptake, and adherence to lifelong ART among pregnant and lactating women by conducting a prospective study.

PMTCT indicators for uptake of services in Uganda had improved but were still below the expected standards for the achievement of the e-MTCT goals. For example, of the two thirds (65%) of pregnant women who attended ANC in 2010 and were tested

for HIV, just about half (52%) accessed ARVs for PMTCT while only 41% delivered under skilled care and 30% of exposed infants were tested for HIV [84]. The national policy recognized the need to increase coverage and targeted to reach at least 95% of all pregnant women who attend ANC with PMTCT services by 2015 [84].

Introduction of lifelong ART for HIV-positive pregnant women could increase uptake of services at various levels of the PMTCT cascade, by keeping women within the health care system right from initiation of ART during pregnancy, labour, delivery, and throughout breastfeeding. That was envisaged to improve adherence since simpler drug regimens like the ones used in general HIV patients. Additionally, it could increase facility-based deliveries, HIV testing for exposed infants as well as uptake of other services such as post-delivery family planning, and child immunisations. Conversely, lifelong ART could also have potential challenges. Acceptance of ART by women who do not yet need it for their own health has not been evaluated in the Ugandan setting and it is possible that women who do not yet need ART may be less likely to accept it. In addition, pregnancy, and the first months of motherhood are associated with stressors in a women's life, including unique challenges associated with pregnancy, childbirth, and caring for the young child [85], which could compromise ART adherence. Barriers to ART adherence during this period included family obligation and stressful life due to childbirth, failure to disclose HIV-positive status, feeling healthy and thus no need for ART and HIV related stigma. During postpartum period, women have been found to miss more scheduled clinic visits, and adherence to ART tends to be lower than during pregnancy [86-89]. Studies have also shown that up to 50% of the women stop their ART after childbirth, some of them on their own without health workers' knowledge or approval [87, 88, 90]. To ensure smooth transition from PMTCT to HIV chronic care, the health systems and programs need to be evaluated and strengthened as women transition from ART during pregnancy to post-delivery care.

Previously conducted cohort studies among pregnant women receiving PMTCT, were of short follow up periods, and mainly stopped at the postnatal period. Consequently, a number of unanswered questions remain in PMTCT programming especially in under-resourced settings. Among these include; What are the health facility successes (preparedness and organization of PMTCT services), challenges (constraints) and countermeasures in the implementation of Option B+? What is the level of uptake,

barriers and facilitators of lifelong ART uptake among HIV-positive pregnant and breastfeeding women? What is the level of adherence to lifelong ART and its predictors among pregnant and breastfeeding women on Option B+? Only a paucity of studies has attempted to answer these questions. For example, a study conducted at lower-level health care facilities in Kampala City and rural mid-western Uganda found that only 37% of HIV-positive expectant mothers identified in ANC, were linked to HIV chronic care while a mere 16% mother-baby pairs were linked to HIV care and early infant diagnosis [91]. Given the limited information about lifelong ART for PMTCT, preparedness, organization, health system challenges, and the need to generate information and contribute to efforts to attainment of WHO, UNAIDS, and the Uganda Ministry of Health targets of achieving e-MTCT of HIV, our study set out to determine the uptake, and adherence to lifelong ART in a cohort of pregnant women followed for 18 months in a rural setting in Central Uganda. A cohort of HIV-positive pregnant women at three health facilities in Central Uganda was followed through pregnancy, labour, delivery and breastfeeding to assess early uptake of lifelong ART, adherence to lifelong ART and the associated factors. Health providers and women living with HIV participated in qualitative interviews to provide information on health facility preparedness, organization, challenges and countermeasures in the implementation of lifelong ART for PMTCT of HIV.

2.2 Rationale

Effective use of lifelong ART among pregnant and breastfeeding mothers living with HIV is beneficial to the mother, exposed infant and male HIV-negative spouse in sero-discordant relationships. Notably, lifelong ART among pregnant and postpartum mothers is an impactful intervention to achieve UNAIDS's and Uganda's 95–95–95 targets (to diagnose 95% of all HIV-positive individuals, ART for 95% of those diagnosed and achieve viral suppression for 95% of those treated) by 2025 for all population age [92,93] and subsequently the UNICEF, UNAIDS and WHO goal of ending the HIV epidemic in children (GOING the 'LAST MILE' to EMTCT) [68]. Elimination of MTCT of HIV is in line with Uganda Vision 2040 [94], the East African Vision 2050 [95], the Africa Agenda 2063 [96] and the sustainable development goals (SDGs) [97,98]. E-MTCT directly contributes to SDGs 3 and 5 and indirectly towards other SDGs. SDG 3 focuses on ensuring healthy lives and promoting well-being for all

at all ages including people living with or at risk of HIV. Whereas SDG 5 emphasizes to achieve gender equality and empower all women and girls both SDGs are vital to sustainable development. Although tremendous progress has been made by the PMTCT program in Uganda, several gaps persist and these should be addressed to reduce the number of new paediatric HIV infections by 95% by 2025, achieve e-MTCT, and thus contribute towards ending AIDS as a public health and socio-economic threat by 2030 [93]. For example, although, Uganda has sustained PMTCT ART coverage (access) of > 95% for over 5 years [12], it is intriguing to understand why MTCT of HIV still contributes to about 14% of all HIV infections. New annual HIV infections among children increased from 5,300 in 2020, to nearly 6,000 in 2021[13]. This has been attributed to challenges in retention of women in care, adherence to lifelong ART, linkage to care challenges, HIV related stigma and discrimination, failure to re-test early mothers who seroconvert to HIV-positive later in pregnancy and breastfeeding, and limited access to health facilities that provide ART [13, 22] which can all be addressed. In Uganda, data shows that almost 20% of HIV-positive mothers stop ART by 12 months in care and 44% of new paediatric MTCT HIV infections are from mothers who are nonadherent to ART during pregnancy and breastfeeding [13]. It is worrisome that these challenges have continued to cripple the e-MTCT of HIV efforts.

Evidence-based innovative interventions to address such challenges have to be designed, scaled up and the achievements sustained so as to achieve e-MTCT of HIV. Therefore, the research in this PhD thesis focuses on health system preparedness, uptake of, and adherence to lifelong ART, challenges, and countermeasures in implementation of lifelong ART for PMTCT of HIV. This information is important to practitioners, decision and policymakers at local, national and international levels to inform further scale up, learning, and sustainability of novel interventions. The findings of this study may also form the basis for future studies that will impact on the PMTCT program in Uganda, and other LMICs in the era of universal HIV test and treat.

2.3 Objectives

2.3.1 General objective:

The general objective of the study was to examine the preparedness, organization, uptake, adherence to lifelong ART, challenges, and countermeasures during the

implementation of lifelong ART for PMTCT of HIV among pregnant and breastfeeding women living with HIV (Option B+), in Uganda. .

2.3.2 Specific objectives

The specific objectives of this study were:

1. To explore health provider perspectives of health facility preparedness and organization in implementation of Option B+ among pregnant and lactating women living with HIV in Central Uganda. (Sub-study/Paper I).
2. To assess practices around ART prescription and swallowing (uptake), early adherence and associated factors among HIV- positive expectant women and lactating mothers on Option B+ in Central Uganda (Sub-study/Paper II).
3. To determine suboptimal adherence to lifelong ART, and its predictors among pregnant and breastfeeding women living with HIV in three districts of Central Uganda (Sub-study/Paper III).
4. To explore health providers' perspectives of challenges and corresponding countermeasures in the implementation of lifelong ART for PMTCT in Central Uganda (Sub-study/Paper IV).

CHAPTER 3:

Study Methods

3.1 Summary of the sub-studies

This study consisted of four sub-studies each providing aspects related to the implementation of lifelong ART for PMTCT of HIV in Central Uganda from October 2013 to March 2016. Sub-study I used a descriptive qualitative approach to elicit experiences and perspectives of health providers on preparedness and organization of health services during implementation of lifelong ART for PMTCT of HIV in Central Uganda (Paper I/Chapter 4). In sub-study II, key issues around ART prescription and swallowing (uptake), early adherence and associated factors among HIV-positive expectant women and lactating mothers on lifelong ART in Central Uganda were assessed. A mixed methods cross-sectional convergent parallel design nested in a prospective cohort was used for this sub-study (Paper II/Chapter 5). Sub-study III was a prospective health facility - based cohort study to determine suboptimal adherence to lifelong ART and its predictors among pregnant and breastfeeding women living with HIV using repeated measures analysis in Central Uganda (Paper III/Chapter 6). In sub-study IV, challenges and countermeasures around the implementation of lifelong ART among pregnant and breastfeeding women living with HIV in Central Uganda were explored from the health providers' perspectives using a qualitative descriptive inquiry (Paper IV/Chapter 7).

3.2 Study context and sites

This study was conducted in Central Uganda in the districts of Masaka, Mityana and Luwero as shown in Figure 3.1. Masaka is approximately 130 km, while Mityana is 70 km and Luwero is 61.3 km from Kampala, the country's capital city. These districts were purposively selected because they were among the 'Central 1 and 2' districts with the highest HIV prevalence (10.6% and 9.0% respectively) at the time of the study [99], and were prioritized for the phase 1 scale-up of life-long ART among pregnant and post-partum HIV-positive women in 2012. 'Central 1' districts (South Buganda region) still have the highest HIV prevalence (8.1%) in Uganda [11]. Six public health facilities were purposively included in the study. In Masaka district, the following health facilities were included: Masaka Regional Referral Hospital (RRH), Kyanamukaka HC IV, and Ssunga HC III. Mityana Hospital was chosen in Mityana district, while the

facilities in Luwero district included Luwero HC IV, currently the general hospital, and Katikamu HC III. The selected facilities were the first to implement lifelong ART for PMTCT in the districts and had fully operational lifelong ART programs.

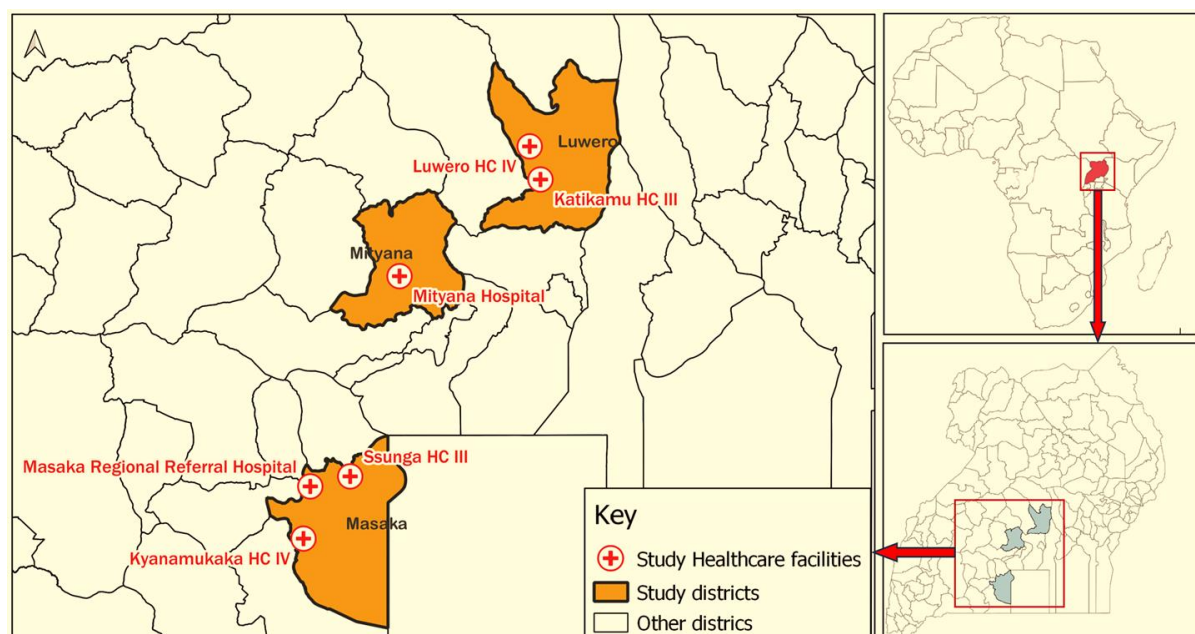


Figure 3.1: Map of Uganda showing study districts and Health facilities

3.3 Study design

The sub studies employed different study designs. Sub-studies I and IV employed a qualitative descriptive approach and were conducted among 54 health providers from the six health facilities. Key informant interviews were used to collect data from the health providers.

Sub-study II was a mixed methods cross-sectional convergent parallel study design nested in a prospective cohort of 507 HIV-positive women. Mixed methods guaranteed complementarity and facilitation of greater understanding of uptake and early adherence to lifelong ART among pregnant and breastfeeding women. The qualitative component was among the 54 health providers and 57 HIV-positive women from the six health facilities. Qualitative data from the women living with HIV was collected using in-depth interviews.

Finally, sub-study III used a health facility-based prospective cohort that enrolled 507 HIV-positive pregnant women from three health facilities namely Masaka RRH, Mityana GH and Luwero HC IV. These were ART naïve or had been on ART for ≤ 4 weeks. They were followed up for 18 months (throughout pregnancy, child birth and breastfeeding period). The women who had at least three follow-up visits after study enrolment (385) were included in the repeated measures analysis of predictors of suboptimal adherence to lifelong ART for sub-study III.

3.4 Study population

3.4.1 Key informant participants

Fifty-four health providers from all the six health facilities (Masaka RRH, Kyanamukaka HC IV, Ssunga HC III, Mityana Hospital, Luwero HC IV, and Katikamu HC III) participated as key informants. Participants (health providers) were purposively selected based on their roles, work station, and experience. The aim was to select participants from a broad and diverse sample of providers and clinics to get a comprehensive view on experiences and the organization of services concerning implementing lifelong ART for PMTCT of HIV. They were grouped into formal and informal health providers. Formal providers were health workers who had received recognized training with a defined curriculum. They comprised midwives, nurses, counselors, nursing assistants, store assistants (Assistant inventory management officer), dispensers, laboratory assistants, clinical officers, and medical doctors. Informal health providers were health workers who had not received formally recognized training and typically not mandated by any formal institution. Instead, they had some level of training through apprenticeships, seminars, and workshops [100]. Informal providers enrolled in the study were expert clients. Expert clients are people living with HIV who have disclosed their HIV status and are willing to support other HIV clients voluntarily [101]. We included participants who had been involved in lifelong ART services provision to pregnant or breastfeeding women for at least one year. Eligible participants who were too sick or unavailable at the time of the interviews to participate in the study were excluded from the study.

3.4.2 In-depth interview participants

In-depth interviews were conducted among purposively selected pregnant or post-partum women living with HIV who had been on lifelong ART longer than six months in order to provide longer experiences pre- and post-delivery. The participants were

from Masaka RRH, Kyanamukaka HC IV, Ssunga HC III, Mityana Hospital, Luwero HC IV, and Katikamu HC III. They were categorized into three groups: good ART adherers, poor ART adherers and delayed ART acceptors. In total 57 IDIs were conducted with 18 pregnant and 37 lactating women and one woman who had a miscarriage and the other lost the baby.

3.4.3 Prospective cohort

A cohort study of HIV+ pregnant women were enrolled from three (Masaka RRH, Mityana GH and Luwero HC IV) of the six health facilities. Enrolment started in October 2013 and was completed in August 2014. The study participants were followed up until March 2016. Serial quantitative surveys, at baseline/enrollment; every two months during follow up until month six post-enrolment into the study (three interviews); and then every four months up to month 18 (additional three interviews) were conducted. In total, seven interviews at 0, 2, 4, 6, 10, 14, and 18 months were conducted. This enabled us to understand the implementation of lifelong ART during pregnancy, labour, and the post-natal period. The sample size used was estimated using uptake of lifelong ART by all diagnosed HIV+ women during ANC as the outcome (Sub-study II). The Kish-Leslie formula for proportion was used for the sample size calculation. An assumption that $p=80\%$ of the women would be enrolled on lifelong ART [102] was used. Other assumptions were a two-sided $\alpha=0.05$ and a 5% level of precision, yielding a sample size of 246. This was adjusted for design effect by a factor of 2 due clustering at two levels (district and health facility level) yielding an overall sample size of 496 (~500). Since enrolment was done consecutively at the three study sites, 507 study participants were included in the study. Figure 3.2 summarizes the samples used for the different sub-studies. Sub-study 1(Paper 1) is on preparedness and organization in the implementation of lifelong ART for PMTCT of HIV in Central Uganda, sub-study 2 (Paper 2) is on uptake of and early adherence to lifelong ART for PMTCT of HIV in Central Uganda, sub-study 3 (Paper 3) is on suboptimal adherence to lifelong ART for PMTCT of HIV and its predictors in Central Uganda, and sub-study 4 (Paper 4) is on challenges and commonly used countermeasures in the implementation of lifelong ART for PMTCT in Central Uganda. The main cohort was the quantitative sample of 507 pregnant women living with HIV who were enrolled at baseline. This sample size was used to describe the characteristics of the study participants in sub-study 2. The second sample was 463 study participants which was

used to calculate the uptake of lifelong ART in sub-study 2 (44 participants were excluded because they had not yet been prescribed lifelong ART). Four hundred and ten participants had data on adherence and were used for sub-studies 2 and 3 to measure early adherence and suboptimal adherence respectively. The 53 participants who were excluded had missing data on adherence. The final quantitative sample of 385 participants who had at least three follow-up visits was used to determine predictors of suboptimal adherence using repeated measures analysis in sub-study 3. The 54 health providers who participated in the key informant interviews provided the data used in sub-studies 1, 2, and 4. Lastly, 57 women living with HIV participated in in-depth interviews to get data that informed part of sub-study 2. All the sub-studies enabled us to achieve the general objective of the study.

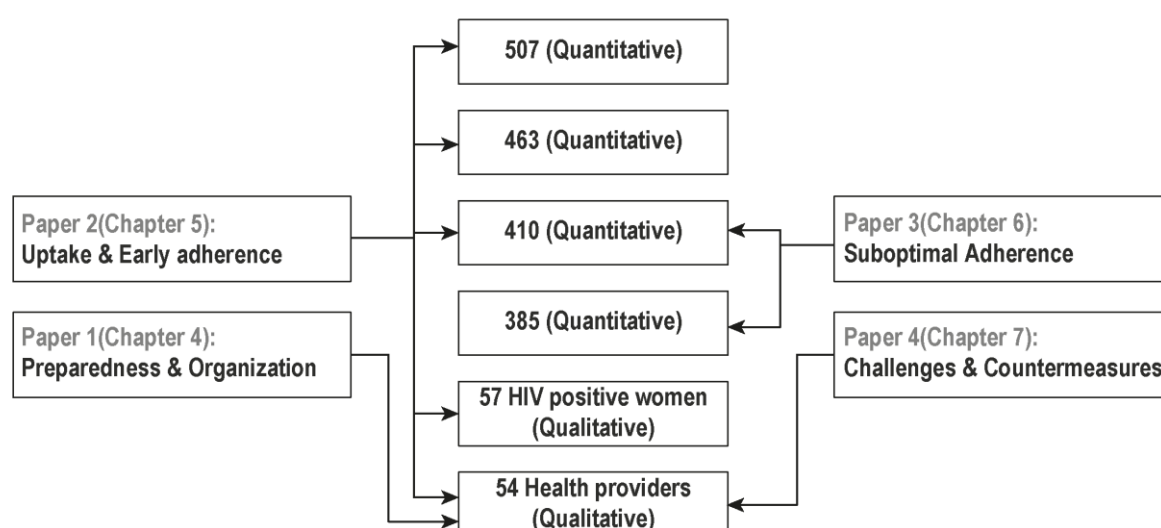


Figure 3.2: Samples for the different sub-studies

3.5: Data collection, management and analysis

3.5.1 Data collection

Three data sets comprising key informant interviews (KIIs), In-depth Interviews (IDIs), and surveys were collected. Data collection for the qualitative component took place from February to May 2014, while that for the quantitative part was done from October 2013 to March 2016. KIIs were conducted with healthcare providers and data were collected by four investigators using pre-tested KII guides. The majority of interviews were conducted in English and a few interviews with expert clients were conducted in

their local language (Luganda) which they were more comfortable using. In-depth interviews with pregnant or post-partum women living with HIV were conducted by trained research assistants using pre-tested semi-structured IDI guides. IDIs were conducted in Luganda. The quantitative structured interviews with pregnant and post-partum women living with HIV enrolled in the cohort were conducted by well-trained research assistants and conducted in Luganda. Research assistants were females, each stationed at each of the three study health facilities (Masaka RRH, Mityana GH, and Luwero HC IV) to conduct the face-to-face structured interviews using a tool with both pre-coded and open-ended questions.

3.5.2 Data management and analysis

All the qualitative data from the KIs and IDIs were transcribed verbatim; data in Luganda were concurrently translated and transcribed into English. Final transcripts were exported to Atlas software (Atlas.ti, Version 7 software, Berlin, Germany) for analysis. A thematic analysis approach was taken. We used the interview scripts as initial guidance for the analysis. Relevant features of data related to the study aim were coded using descriptive and interpretive approaches. Coding was discussed and adapted. Codes were collated into themes. We reviewed and discussed identified themes to support reflexivity on analysis process and the interpretation of data. Finally, defining and naming of themes were agreed upon by all researchers. Typical quotes were identified and used to emphasize identified themes.

Regarding the quantitative data, (study II and III), exploratory data analysis was conducted on the independent and dependent variables using STATA version 14. Descriptive statistics were generated providing percentages for categorical variables, while means (standard deviation) and median (inter-quartile range) for continuous variables. Frequencies and percentages were computed and presented for categorical variables. In sub-study II, bivariate and multivariable analyses were conducted to generate prevalence ratios as a measure of association, using log-binomial regression to establish factors associated with optimal adherence. For sub-study III, the mixed effects logistic model was used to assess the predictors of suboptimal adherence to lifelong ART using the backward elimination method.

3.5.3 Investigator and Author contribution

Conceptualization of the PhD study: Aggrey David Mukose. **Methodology:** Aggrey David Mukose, Jean-Pierre Van geertruyden, Fredrick Makumbi, Hilde Bastiaens, Rhoda K. Wanyenze. **PhD study supervision:** Hilde Bastiaens, Jean-Pierre Van geertruyden, Rhoda K. Wanyenze. **Study implementation:** Aggrey David Mukose, Fredrick Makumbi, Rhoda K. Wanyenze. **Data analysis: (1) Quantitative;** Aggrey David Mukose, Jean-Pierre Van geertruyden, Fredrick Makumbi, Rhoda K. Wanyenze; **(2) Qualitative;** Aggrey David Mukose, Hilde Bastiaens, Rhoda K. Wanyenze. **Drafting papers and PhD monograph:** Aggrey David Mukose. **Writing, reviewing and editing:** Aggrey David Mukose, Hilde Bastiaens, Jean-Pierre Van geertruyden, Fredrick Makumbi, Rhoda K. Wanyenze.

3.6 Ethical considerations

Ethical approval was gotten from Makerere University School of Public Health Higher Degrees, Research and Ethics Committee, and Uganda National Council for Science and Technology (UNCST). Furthermore, permission to conduct the study was obtained from each of the study districts and health facilities. Written informed consent was attained from every study participant prior to conducting interviews.

References

1. He, H., et al., Spatial and temporal trends in HIV/AIDS burden among worldwide regions from 1990 to 2019: a secondary analysis of the global burden of disease study 2019. *Frontiers in Medicine*, 2022. **9**: p. 808318.
2. Mahy, M.I., et al., Progress towards 2020 global HIV impact and treatment targets. *Journal of the International AIDS Society*, 2021. **24**: p. e25779.
3. UNAIDS. UNAIDS Fact Sheet 2022. 2022 [cited 2022 20th September 2022]; Available from: https://www.unaids.org/en/resources/documents/2022/UNAIDS_FactSheet.
4. WHO. Latest HIV estimates and updates on HIV policies uptake, July 2022. 2022 [cited 2022 2022]; Available from: https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/2022_global_summary_web_v12.pdf.
5. UNAIDS, Fact sheet— World AIDS day 2020. 2020, UNAIDS Geneva, Switzerland.
6. UNAIDS, Seizing the moment: tackling entrenched inequalities to end epidemics. 2020.
7. UNAIDS, UNAIDS Data 2022. 2022, Joint United Nations Programme on HIV/AIDS; 2022: Geneva.
8. WHO, Estimates and updates on HIV policies uptake, in World Health Organization. 2020.
9. Chanda-Kapata, P., et al., Tuberculosis, HIV/AIDS and malaria health services in sub-Saharan Africa—a situation analysis of the disruptions and impact of the COVID-19 pandemic. *International Journal of Infectious Diseases*, 2022. **124**: p. S41-S46.
10. Uwishema, O., et al., The syndemic burden of HIV/AIDS in Africa amidst the COVID-19 pandemic. *Immunity, inflammation and disease*, 2022. **10**(1): p. 26-32.
11. UAC, Uganda HIV and AIDS Factsheet 2022. 2022, UAC: Kampala.
12. UAC, Annual Joint AIDS Review Report 2022. 2022, UAC: Kampala.
13. Dirlikov, E., et al., Scale-up of HIV antiretroviral therapy and estimation of averted infections and HIV-related deaths—Uganda, 2004–2022. *Morbidity and Mortality Weekly Report*, 2023. **72**(4): p. 90.
14. Murewanhema, G., et al., HIV and adolescent girls and young women in sub-Saharan Africa: A call for expedited action to reduce new infections. *IJID Regions*, 2022. **5**: p. 30-32.
15. WHO, Prevention of Mother-To-Child Transmission (PMTCT) Briefing Note. 2007: Geneva, Switzerland.

16. WHO, HIV transmission through breastfeeding: a review of available evidence, in HIV transmission through breastfeeding: a review of available evidence. 2004, World Health Organization: Geneva, Switzerland. p. 25-25.
17. Coutoudis, A., L. Kwaan, and M. Thomson, Prevention of vertical transmission of HIV-1 in resource-limited settings. *Expert review of anti-infective therapy*, 2010. **8**(10): p. 1163-1175.
18. McGowan, J.P. and S.S. Shah, Prevention of perinatal HIV transmission during pregnancy. *Journal of Antimicrobial Chemotherapy*, 2000. **46**(5): p. 657-668.
19. Kourtis, A.P., et al., Mother-to-child transmission of HIV-1: timing and implications for prevention. *The Lancet infectious diseases*, 2006. **6**(11): p. 726-732.
20. Govender, T. and H. Coovadia, Eliminating mother to child transmission of HIV-1 and keeping mothers alive: recent progress. *Journal of Infection*, 2014. **68**: p. S57-S62.
21. WHO, PMTCT strategic vision 2010-2015: Preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals: moving towards the elimination of paediatric HIV, December 2009. 2010, World Health Organization: Geneva, Switzerland. p. World Health Organization.
22. UNAIDS, IN DANGER: UNAIDS Global AIDS Update 2022. 2022, Joint United Nations Programme on HIV/AIDS; 2022: Geneva.
23. UAC, Uganda HIV and AIDS Factsheet 2021. 2021, UAC: Kampala, Uganda.
24. Muyunda, B., et al., Effectiveness of lifelong ART (Option B+) in the prevention of mother-to-child transmission of HIV programme in Zambia: observations based on routinely collected health data. *Frontiers in public health*, 2020. **7**: p. 401.
25. VanDeusen, A., et al., Cost effectiveness of option B plus for prevention of mother-to-child transmission of HIV in resource-limited countries: evidence from Kumasi, Ghana. *BMC infectious diseases*, 2015. **15**(1): p. 1-10.
26. Wang, X., et al., Cost-effectiveness of option B+ in prevention of mother-to-child transmission of HIV in Yunnan Province, China. *BMC infectious diseases*, 2019. **19**(1): p. 1-12.
27. Tweya, H., et al., Comparative cost-effectiveness of Option B+ for prevention of mother to child transmission of HIV in Malawi: Mathematical modelling study. *AIDS (London, England)*, 2016. **30**(6): p. 953.
28. WHO. Estimated percentage of pregnant women living with HIV who received antiretrovirals for preventing mother-to-child transmission 2021 [cited 2021 28th August 2021]; Available from: <https://www.who.int/data/gho/data/indicators/indicator-details/GHO/estimated-percentage-of-pregnant-women-living-with-hiv-who-received-antiretrovirals-for-preventing-mother-to-child-transmission>.

29. WHO, Programmatic Update: Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants, in Geneva: WHO. 2012: Geneva, Switzerland.
30. CDC, Recommendations for assisting in the prevention of perinatal transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus and acquired immunodeficiency syndrome, in MMWR Morb Mortal Wkly Rep. 1985. p. 721-6, 731-2.
31. Connor, E.M., et al., Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. New England Journal of Medicine, 1994. **331**(18): p. 1173-1180.
32. Minkoff, H.L., et al., Recommendations of the US Public Health Service Task Force on the Use of Zidovudine to Reduce Perinatal Transmission of Human Immunodeficiency Virus. Atlanta: Center For Disease Control, 1994.
33. Collaboration, E.M.o.D., Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. The Lancet, 1999. **353**(9158): p. 1035-1039.
34. Group, I.P.H., The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1—a meta-analysis of 15 prospective cohort studies. New England Journal of Medicine, 1999. **340**(13): p. 977-987.
35. Practice, C.o.O., ACOG committee opinion scheduled Cesarean delivery and the prevention of vertical transmission of HIV infection. Number 234, May 2000 (replaces number 219, August 1999). International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics, 2001. **73**(3): p. 279-281.
36. Dabis, F., et al., 6-month efficacy, tolerance, and acceptability of a short regimen of oral zidovudine to reduce vertical transmission of HIV in breastfed children in Côte d'Ivoire and Burkina Faso: a double-blind placebo-controlled multicentre trial. The Lancet, 1999. **353**(9155): p. 786-792.
37. Shaffer, N., et al., Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. The Lancet, 1999. **353**(9155): p. 773-780.
38. Wiktor, S.Z., et al., Short-course oral zidovudine for prevention of mother-to-child transmission of HIV-1 in Abidjan, Cote d'Ivoire: a randomised trial. The Lancet, 1999. **353**(9155): p. 781-785.
39. Dabis, F., et al. Effectiveness of a short course of zidovudine+ nevirapine to prevent mother-to-child transmission (PMTCT) of HIV-1: The Ditrane Plus ANRS 1201 Project in Abidjan, Cote d'Ivoire. in 14th International AIDS Conference. 2002.

40. Fowler, M.G., et al., Reducing the risk of mother-to-child human immunodeficiency virus transmission: past successes, current progress and challenges, and future directions. *American journal of obstetrics and gynecology*, 2007. **197**(3): p. S3-S9.
41. Guay, L.A., et al., Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *The Lancet*, 1999. **354**(9181): p. 795-802.
42. Lallémand, M., et al., Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *New England Journal of Medicine*, 2004. **351**(3): p. 217-228.
43. Team, P.S., Efficacy of three short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother to child in Tanzania, South Africa, and Uganda (Petra study): a randomised, double-blind, placebo-controlled trial. *The Lancet*, 2002. **359**(9313): p. 1178-1186.
44. WHO, Prevention of mother-to-child transmission of HIV: selection and use of nevirapine: technical notes. 2001, World Health Organization.
45. WHO, Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants in resource-limited settings: towards universal access: recommendations for a public health approach. 2006, WHO: Geneva, Switzerland.
46. WHO, Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: recommendations for a public health approach-2010 version. 2010: World Health Organization.
47. WHO, Consolidated guidelines on general HIV care and the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach, in Geneva: World Health Organization. 2013, WHO: Geneva, Switzerland. p. 269.
48. WHO, Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: guidelines on care, treatment and support for women living with HIV/AIDS and their children in resource-constrained settings. 2004: Geneva, Switzerland.
49. WHO, New data on the prevention of mother-to-child transmission of HIV and their policy implications: conclusions and recommendations: WHO Technical consultation on behalf of the UNFPA/UNICEF/WHO/UNAIDS Inter-Agency Task Team on Mother-to-Child Transmission of HIV, Geneva, 11-13 October 2000. 2001, World Health Organization: Geneva, Switzerland.
50. Jackson, J.B., et al., Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: 18-month follow-up of the HIVNET 012 randomised trial. *The Lancet*, 2003. **362**(9387): p. 859-868.

51. WHO, Guidance on global scale-up of the prevention of mother to child transmission of HIV: towards universal access for women, infants and young children and eliminating HIV and AIDS among children. 2007, WHO: Geneva, Switzerland.
52. Hairston, A.F., E.A. Bobrow, and C.S. Pitter, Towards the elimination of pediatric HIV: Enhancing maternal, sexual, and reproductive health services. *International Journal of MCH and AIDS*, 2012. **1**(1): p. 6.
53. WHO, Antiretroviral therapy for HIV infection in adults and adolescents in resource-limited settings: towards universal access. 2006 revision. 2006: Geneva, World Health Organization.
54. Mahy, M., et al., What will it take to achieve virtual elimination of mother-to-child transmission of HIV? An assessment of current progress and future needs. *Sexually transmitted infections*, 2010. **86**(Suppl 2): p. ii48-ii55.
55. CDC and Prevention, Impact of an innovative approach to prevent mother-to-child transmission of HIV--Malawi, July 2011-September 2012, in *MMWR. Morbidity and mortality weekly report*. 2013. p. 148-151.
56. Malawi, H., National 2012 global AIDS response progress report: Malawi country report. Malawi, HIV National Commission, 2012.
57. Schouten, E.J., et al., Prevention of mother-to-child transmission of HIV and the health-related Millennium Development Goals: time for a public health approach. *The Lancet*, 2011. **378**(9787): p. 282-284.
58. WHO, Update on First and Second line Antiretroviral Regimes. 2019, World Health Organization; 2019 (WHO/CDS/HIV/19.15): Geneva, Switzerland. p. 16.
59. Shapiro, R.L., et al., Maternal single-dose nevirapine versus placebo as part of an antiretroviral strategy to prevent mother-to-child HIV transmission in Botswana. *Aids*, 2006. **20**(9): p. 1281-8.
60. UAC, UNGASS country progress report Uganda, January 2008-December 2009, in Retrieved November. 2010. p. 2011.
61. UAC, HIV and AIDS Uganda country progress report 2013, in Kampala: Uganda AIDS Commission. 2014, Uganda AIDS Commission (UAC).
62. UAC, Annual Joint AIDS Review Report 2019/2020. 2020: Kampala, Uganda. p. 183.
63. UNAIDS, U., Countdown to ZERO: global plan towards the elimination of new HIV infections among children by 2015 and keeping their mother alive. 2011: UNAIDS.
64. UNAIDS, 2015 Progress report on the global plan towards the elimination of new HIV infections among children and keeping their mothers alive. 2015, UNAIDS: Geneva, Switzerland.
65. UNAIDS, P. Start Free, Stay Free, AIDS Free 2016 [cited 2023 27 November 2023]; Available from: <https://free.unaids.org/>.

66. UNAIDS, Progress towards the Start Free, Stay Free, AIDS Free targets; 2020 Report. 2020, Joint United Nations Programme on HIV/AIDS.
67. UNAIDS, UNAIDS Global HIV Statistics Fact sheet 2023. 2023, UNAIDS: Geneva, Switzerland.
68. UNICEF, U.a.W., Key considerations for programming and prioritization. Going the 'Last Mile' to EMTCT: A road map for ending the HIV epidemic in children. 2020, UNICEF: New York, USA.
69. WHO, Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV and syphilis. 2014, Geneva: WHO.
70. WHO. Validation Process and Tools. 2015 [cited 2023 27 November 2023].
71. WHO. WHO validates elimination of mother-to-child transmission of HIV and syphilis in Cuba. 2015 [cited 2023 27 November 2023]; Available from: <https://www.who.int/news/item/30-06-2015-who-validates-elimination-of-mother-to-child-transmission-of-hiv-and-syphilis-in-cuba#:~:text=Cuba%20today%20became%20the%20first,Chan%2C%20WHO%20Director%2DGeneral.>
72. WHO, Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV and syphilis. 2017, WHO: Geneva.
73. WHO, Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV, syphilis and hepatitis B virus. 2021.
74. WHO. Countries which have received WHO validation. 2022 2023 [cited 2023 25/11/2023]; Available from: <https://www.who.int/initiatives/triple-elimination-initiative-of-mother-to-child-transmission-of-hiv-syphilis-and-hepatitis-b/validation>.
75. UNAIDS. Botswana is first country with severe HIV epidemic to reach key milestone in the elimination of mother-to-child HIV transmission. 2021 2023 [cited 2023 25 November 2023]; Available from: https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2021/december/emtct_botswana.
76. WHO. Botswana is first country with severe HIV epidemic to reach key milestone in the elimination of mother-to-child HIV transmission. 2021 [cited 2023 25 November 2023]; Available from: <https://www.afro.who.int/countries/botswana/news/botswana-first-country-severe-hiv-epidemic-reach-key-milestone-elimination-mother-child-hiv>.
77. WHO, Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. 2022.
78. UNAIDS, The path that ends AIDS: UNAIDS Global AIDS Update 2023, in Licence: CC BY-NC-SA 3.0 IGO. 2023, Joint United Nations Programme on HIV/AIDS; 2023. : Geneva.

79. Elgalib, A., et al., Elimination of mother-to-child transmission of HIV, syphilis and viral hepatitis B: A call for renewed global focus. *International Journal of Infectious Diseases*, 2023. 127: p. 33-35.
80. Doherty, T., et al., "If donors woke up tomorrow and said we can't fund you, what would we do?" A health system dynamics analysis of implementation of PMTCT option B+ in Uganda. *Globalization and Health*, 2017. **13**(1): p. 51.
81. Reliefweb. Government adopts new PMTCT strategy. 2023 [cited 2023 25th April 2023]; Available from: <https://reliefweb.int/report/uganda/government-adopts-new-pmtct-strategy>.
82. Muhumuza, S., et al., Retention in care among HIV-infected pregnant and breastfeeding women on lifelong antiretroviral therapy in Uganda: A retrospective cohort study. *PLOS ONE*, 2017. **12**(12): p. e0187605.
83. UCSF, M.a., Effectiveness of Lifelong ART for Pregnant and Lactating Mothers on Elimination of Mother to Child Transmission of HIV and on Maternal and Child Health Outcomes:Uganda 2013-2015. 2015, Makerere University & University of California, San Francisco: Kampala, Uganda.
84. UAC, National Strategic Plan for HIV&AIDS 2011/12 -2014/15. 2011, Uganda AIDS Commission (UAC): Kampala, Uganda.
85. Yali, A.M. and M. Lobel, Coping and distress in pregnancy: an investigation of medically high risk women. *Journal of Psychosomatic Obstetrics & Gynecology*, 1999. **20**(1): p. 39-52.
86. Kreitchmann, R., et al., Antiretroviral adherence during pregnancy and postpartum in Latin America. *AIDS patient care and STDs*, 2012. **26**(8): p. 486-495.
87. Mellins, C., et al., Adherence to antiretroviral treatment among pregnant and postpartum HIV-infected women. *AIDS care*, 2008. **20**(8): p. 958-968.
88. Nachega, J.B., et al., Adherence to antiretroviral therapy during and after pregnancy in low-, middle and high income countries: a systematic review and meta-analysis. *AIDS (London, England)*, 2012. **26**(16): p. 2039.
89. Nassali, M., et al., Access to HIV/AIDS care for mothers and children in sub-Saharan Africa: adherence to the postnatal PMTCT program. *AIDS care*, 2009. **21**(9): p. 1124-1131.
90. Ickovics, J.R., et al., Prenatal and postpartum zidovudine adherence among pregnant women with HIV: results of a MEMS substudy from the Perinatal Guidelines Evaluation Project. *Journal of acquired immune deficiency syndromes (1999)*, 2002. **30**(3): p. 311-315.

91. Mugasha, C., et al., Intra-facility linkage of HIV-positive mothers and HIV-exposed babies into HIV chronic care: rural and urban experience in a resource limited setting. *PLoS One*, 2014. **9**(12): p. e115171.
92. MOH, Annual Health Sector Performance Report Financial Year 2019/20. 2020, Ministry of Health: Kampala, Uganda. p. 222.
93. UAC, National HIV and AIDS Strategic Plan 2020/21–2024/25: Ending the HIV and AIDS epidemic: Communities at the forefront. 2020, Uganda AIDS Commission (UAC): Kampala, Uganda. p. 108.
- .
94. UNPA, Uganda Vision 2040. 2013, Uganda National Planning Authority: Kampala, Uganda. p. 136.
95. EAC, East African Community Vision 2050. 2015: Arusha, Tanzania. p. 141.
96. AUC, The African Union Commission Agenda 2063: The Africa We Want. 2014: Addis Ababa, Ethiopia.
97. UNDP. What are the Sustainable Development Goals? 2015 2021 [cited 2021 23rd September]; Available from: https://www.undp.org/sustainable-development-goals?utm_source=EN&utm_medium=GSR&utm_content=US_UNDP_PaidSearch_Brand_English&utm_campaign=CENTRAL&c_src=CENTRAL&c_src2=GSR&gclid=EAlaIQobChMlvc2vvOmU8wIvRuztCh3P7QvcEAAYASAAEgKZ2vD_BwE.
98. UNDP, From the MDGs to Sustainable Development for All. 2016: New York, NY, 10017 USA.
99. Ministry of Health/Uganda and ICF International, Uganda AIDS Indicator Survey (UAIS) 2011. 2012, Ministry of Health/Uganda and ICF International: Calverton, Maryland, USA.
100. Sudhinaraset, M., et al., What is the role of informal healthcare providers in developing countries? A systematic review. *PloS one*, 2013. **8**(2): p. e54978.
101. Kyakuwa, M., A. Hardon, and Z. Goldstein, "The adopted children of ART": expert clients and role tensions in ART provision in Uganda. *Medical anthropology*, 2012. **31**(2): p. 149-161.
102. Barigye, H., et al., Operational evaluation of a service for prevention of mother-to-child transmission of HIV in rural Uganda: barriers to uptake of single-dose nevirapine and the role of birth reporting. *Tropical medicine & international health*, 2010. **15**(10): p. 1163-1171.

CHAPTER 4:

Health Provider Perspectives of Health Facility Preparedness and Organization in Implementation of Option B+ among Pregnant and Lactating Women in Central Uganda: A Qualitative Study

Aggrey David Mukose, MBChB, MS^{1,2*}, Hilde Bastiaens, MD, PhD³, Esther Buregyeya, MBChB, MPhil, PhD⁴, Rose Naigino, BST/B, MHSR⁵, Fredrick Makumbi, MS, MHS, PhD¹, Joshua Musinguzi, MBChB, MPH⁶, Jean-Pierre Van geertruyden, MD, PhD², and Rhoda K. Wanyenze, MBChB, MPH, PhD⁴.

¹ Department of Epidemiology and Biostatistics, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda.

² Global Health Institute, Department of Epidemiology and Social Medicine, University of Antwerp, Antwerp, Belgium.

³ Department of Primary and Interdisciplinary Care, University of Antwerp, Antwerp, Belgium.

⁴ Department of Disease Control and Environmental Health, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda.

⁵ School of Public Health, College of Health Sciences, Makerere University Kampala, Uganda.

⁶ Ministry of Health, STD/AIDS Control Program, Kampala, Uganda.

Journal of the International Association of Providers of AIDS Care Volume 18: 1-11© The Author(s) 2019.

Date received: 19 March 2018; revised: 18 September 2018; accepted: | February 2019

DOI: 10.1177/2325958219833930 journals.sagepub.com/home/jia

4.1 Abstract

Introduction: Uganda adopted Option B+ for prevention of mother-to-child transmission (PMTCT) of HIV in 2012. However, there is limited data on preparedness and organization of Option B+ services. These data are critical in informing PMTCT programs and provision of universal antiretroviral therapy (ART) for all populations. This study explored health providers' experiences of preparedness and organization of Option B+ services in Central Uganda.

Methods: Key informant interviews with 54 health providers from 6 health facilities in 3 districts were conducted. A thematic approach was employed to analyze data.

Results: Themes identified on preparedness were training of frontline health providers and provision of Option B+ guidelines, supervision and mentorship, and provision of essential medicines and medical health supplies, whereas those concerning organization were HIV counseling and testing, ART initiation, follow-up, and patient support mechanisms. Innovations like use of expert clients, assessing women's readiness to start Option B+, and retaining women in antenatal care clinic depending on the need are important in provision of Option B+.

Conclusion: This study provides insights into preparedness and organization of Option B+ services which are important in provision of Option B+ and universal ART for all populations. Research around models of follow-up is recommended.

1. What do we already know about this Topic?

Effectiveness of Option B+ strategy in prevention of mother-to-child transmission (PMTCT) is well established; however, data on preparedness and organization of services is not well-documented, yet organization of services has implications for the quality of services and treatment outcomes (e.g., retention and viral suppression) for the women and HIV transmission to their infants.

2. How does your research contribute to the field?

This study provides vital data on preparedness and organization of Option B+ services in Uganda through description of innovative approaches used by health providers to offer services and informs programs and future research in the field particularly on health system approaches and interventions to enhance PMTCT outcomes.

3. What are your research's implications toward Theory, Practice, or Policy?

Regular training, support and mentorship of midwives, informal health providers, and use of context-specific models of follow-up are critical in improving implementation of Option B+ services.

4.2 Introduction

In 2012 and 2013, World Health Organization issued new guidelines towards virtual elimination of mother-to-child transmission (e-MTCT) of HIV including Option B+, where HIV-positive pregnant and breastfeeding women are initiated on lifelong antiretroviral therapy (ART) irrespective of their CD4 or clinical staging.^{1,2} Option B+ offers many advantages: health benefits of early treatment for the mother, avoiding risks of interrupting ART, protection against MTCT in future pregnancies, and protects HIV-negative partners in discordant couples.^{3,4} Option B+ was recommended for high HIV burden and high fertility countries.⁵

Uganda started implementing Option B+ in September 2012 and rapidly scaled it up to all the 112 districts by the end of 2013.^{3,6} The number of health facilities offering Option B+ increased to 2,130 in September 2013.⁷ In an evaluation focusing on lessons learned from early implementation of Option B+ among 11 African countries, the number of HIV- positive women accessing ART during antenatal care (ANC) increased tremendously.⁸ Drawing from this study, increase in number of women who seek prevention of mother-to-child transmission (PMTCT) of HIV services could overwhelm the staff in health facilities and subsequently affect quality of Option B+ services if adequate preparations and organization are lacking.⁸⁻¹¹

In Malawi, a number of key steps were undertaken before and during implementation of Option B+. Some of the steps taken were national consultations, review of PMTCT policies and guidelines, mobilization of funds, procurement of essential commodities, and capacity building for health workers. In addition, continuous program evaluations and reviews were done to ensure successful implementation of Option B+ strategy.¹²⁻

14

Pregnant and breastfeeding women have unique challenges which require special interventions to ensure that they utilize Option B+ services. For example, previous studies show that pregnancy, childbirth, and postpartum-related obligations and stress have a negative impact on ART adherence and retention in HIV care.^{15,16} Furthermore, challenges faced during implementation of Option B+ such as stigma, non-disclosure of HIV status, nonadherence and nonretention in HIV care, are anticipated to occur in the implementation of universal ART for all populations and may slow achievement of the Joint United Nations Programme on HIV and AIDS 90-90-90 targets. Lessons

learned from Option B+ experience in Malawi have been used by countries that are adopting the universal ART strategy for all populations.¹³

In Uganda, data on preparedness and organization of Option B+ services are scarce. Current studies have focused on effectiveness of the Option B+ strategy.¹⁷⁻¹⁹ Preparedness and organization are crucial in ensuring uptake of Option B+ services, retention in care and adherence to ART. To address the research gap, we conducted this study to explore perspectives of health providers on facility preparedness and organization of services in implementation of Option B+ in Central Uganda. Findings from this study will inform provision of HIV services for Option B+ and universal ART for all populations.⁹

4.3 Methods

The research described in this article is part of a larger mixed methods study titled “Implementation of Option B+ for PMTCT in Uganda: Service Uptake and Retention of Mothers and their Infants into PMTCT Services.” The main goals of the whole study were to determine the uptake of ART and other PMTCT-related services by HIV-positive pregnant women and their infants and to assess retention in care and adherence to ART. The study also qualitatively explored factors affecting the health-care system, perceptions, and experiences in delivery of Option B+ for pregnant women. This article focuses on preparedness and organization of Option B+ services from the health providers’ perspective. Preparedness in this study meant all activities that were undertaken to ensure readiness of health providers and health facilities to deliver Option B+ services. Organization referred to how Option B+ services were offered. Organization entailed the following: cadre of health providers who offered the services, where and how services were provided, linkages, and patient support as well as follow-up mechanisms.

Study design

A descriptive qualitative study approach was adopted so as to elicit experiences of providers, their opinions, and suggestions on preparedness and organization of services during implementation of Option B+ strategy. Use of key informant interviews (KIIs) enabled health providers to give honest descriptions²⁰ of what was done before and during the implementation of Option B+ strategy.

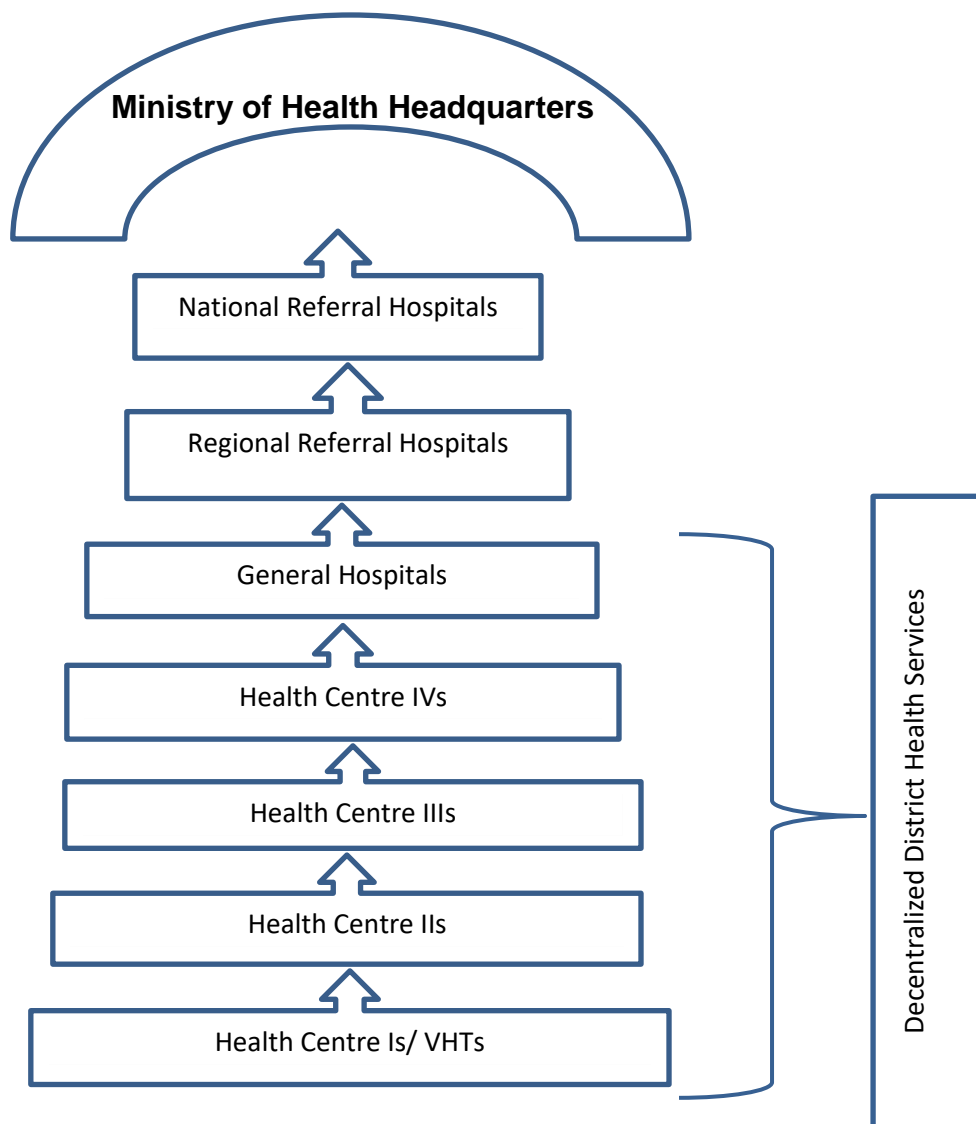


Figure 4.1: Structure of the public health care system in Uganda

Study context

Health services in Uganda are provided by public and private sectors in a decentralized referral system. Ministry of Health (MOH) provides leadership for the health sector to ensure provision of all health services in Uganda.²¹

Figure 4.1 illustrates the structure of the Uganda public health-care system. There are seven levels of healthcare in the public health sector in Uganda, organized from

lower to higher levels in a hierarchy. Village Health Team (VHT)/Health Centre (HC) I is the first contact for health services. This level has no physical structure. Village Health Team members work voluntarily to advise, educate, and distribute essential medicines and refer patients to the next level, HC II. Health Centre IIs serve a few thousand people at parish level, run an out-patient clinic, treat common diseases and offer ANC services. Next in hierarchy is a HC III. This is located at the sub-county level and runs a general outpatient clinic and a maternity ward. A HC III provides support and supervision to the community and HC IIs. The next level is a HC IV which serves a county or a parliamentary constituency (Health sub-district). In addition to offering services that HC IIIs give, HC IVs provide in-patient health services, surgery, blood transfusion, laboratory and medical imaging services. Health Centre IVs also supervise and support community-based health-care programs and HC IIIs. At the district level, General Hospitals (GHs) offer services given at HC IVs in addition to providing in-service training, consultation and operational research in support of community-based health-care programs. Regional Referral Hospitals (RRHs) serve several districts (subregion), with general, consultant, and specialist clinical services. They are also involved in teaching and research, in addition to offering services provided by GHs. The district health structure is responsible for service delivery in the district except for the RRHs where they exist. National Referral Hospitals are at the national level, offer comprehensive specialist services, conduct health research, and teach. Option B+ services are mainly offered at HC IIIs and higher-level health facilities.²²

Study site

The study was conducted in three predominantly rural districts of Luwero, Mityana, and Masaka. The districts and health facilities were purposively selected because they were among the first to implement Option B+ in Uganda and were the most experienced at the time. Health facilities were Katikamu and Ssunga HC IIIs, Luwero and Kyanamukaka HC IVs, Mityana GH, and Masaka RRH.

The U.S. President's Emergency Plan for AIDS Relief works through several organizations, often referred to as “implementing partners,” to implement various HIV services and provide technical assistance to the MOH and public health facilities.^{23,24} At the time of implementing this study, the Uganda MOH predominantly worked in collaboration with two PMTCT implementing partners within the Central region

including Protecting Families Against HIV/AIDS (PREFA) - Uganda and Mildmay Uganda to support district service delivery.

Study Participants

The participants were grouped into formal and informal health providers. Formal providers are health workers who have received recognized training with a defined curriculum. Formal health providers included in this study were midwives, nurses, counsellors, nursing assistants, store assistants, dispensers, laboratory assistants, clinical officers, and medical doctors. Some of the services provided by this category of health workers include HIV testing, post-test counseling, assess eligibility for antiretroviral (ARV) medications, prescription of drugs, dispense drugs, carry out laboratory tests, monitor, counsel, and support mothers who are on Option B+.

Informal health providers are health workers who have not received formally recognized training and are typically not mandated by any formal institution. Instead, they have some level of training through apprenticeships, seminars, and workshops.²⁵

Informal participants enrolled in the study were expert clients (peer mothers and fathers) and VHTs. Expert clients are people living with HIV who have disclosed their HIV status and are willing to support other HIV clients on a voluntary basis. Informal health providers offer services such as health education, registering, tracking, and escorting women who are on Option B+ within the health facilities and giving support during family support groups (FSGs). Family Support Groups are psychosocial groups that offer peer support to HIV-positive, pregnant, or lactating mothers in care. Use of FSGs was one of the interventions used to support women on Option B+, their children, and partners. The purpose of FSGs is to create a structured support group for the mother and enhance access to and uptake of PMTCT services, retention, adherence, and follow-up of mother-baby pairs. Each health facility holds FSG meetings once a month.

Selection of participants

Participants were purposively selected based on their roles, workstation/department, and experience. The aim was to select a broad and varied sample of health providers and departments in order to get a comprehensive perspective on experiences of preparedness and organization of services in implementation of Option B+. To adhere to our proposed varied sample, a total of fifty-four participants were identified and enrolled across the study sites. Table 4.1 shows the details of study participants.

Table 4. 1: Characteristics of study participants ^a

Characteristic	Number
Health Facility	
Masaka RRH	12
Mityana GH	10
Luwero HC IV	10
Kyanamukaka HC IV	10
Katikamu HC III	7
Ssunga HC III	5
Sex	
Male	13
Female	41
Category	
Facility manager	20
Clinic staff	34
Cadre	
Midwife	22
Nursing assistant	8
Expert client	7
Doctor	4
Store assistant	4
Clinical officer	3
Nurse	3
Counsellor	1
Dispenser	1
Laboratory assistant	1
Received training in provision of Option B+	
Yes	27
No	27
Number of years working in HIV care	Median (IQR) = 5 (1-8); Mean (SD) = 5.4 (4.5)

Abbreviations: GH, general hospital; IQR, inter quartile range; RRH, regional referral hospital; SD standard deviation.

^a n = 54.

Data Collection, Management and Analysis

Based on our research question of preparedness and organization of Option B+ services, we developed an interview guide. The research team discussed the issues/topics to be explored based on the gaps in the literature. The topics included; roles of the health providers in provision of Option B+, preparedness of health providers who offer PMTCT services, health providers' experience of preparing women to initiate Option B+ (counseling), when and how provision of ART started, organization of Option B+ services, and support provided to women receiving Option B+. From the topics that the investigators identified, the team developed an interview guide which spelt out how the interviews were to be conducted. We developed a list of questions or issues in a semi-structured format to be explored during the interview and the sequence to be followed. In addition, follow-on questions or probes were included where necessary. The initial tool was pretested by all key investigators and subsequently discussed. Concurrences and discrepancies were noted and resolved through consensus to ensure consistency in administration of the interview guide and interpretation of the questions. Interviews were conducted by five of the lead investigators (A.M., R.W., E.B., R.N., and F.M.) between April and May 2014. On average, each interview lasted 1.5 hours and was audio recorded. Majority of interviews were conducted in English. A few KIIs with expert clients were conducted in their local language (Luganda) which they were more comfortable to use.

All data were transcribed verbatim; data in Luganda were concurrently translated and transcribed into English. On average, transcription of each interview took 2-3 days. Each transcript was reviewed by A.M. and one other co-investigator for content and completeness. Additional reviews of selected transcripts were done by R.W. for quality control and to ensure reflexivity. Final transcripts were exported to Atlas software (Atlas.ti, Version 7 software, Berlin, Germany) for analysis. Thematic analysis approach as described by King and Horrocks²⁶ was taken. We used the interview scripts as an initial guidance to the analysis. A.M. read through all transcripts several times and marked relevant information so as to be familiar with the data. Relevant features of data related to the study aim were coded using descriptive and interpretive approaches. H.B. and R.W. co-coded the first interviews that were analyzed. Coding was discussed and adapted. A.M. analyzed the remaining transcripts using the adapted codes. Codes were collated into themes. A.M., H.B., and R.W., reviewed and discussed identified themes to support reflexivity on analysis process and the

interpretation of data. Finally, defining and naming of themes was agreed upon by all researchers. Typical quotes were identified and used to emphasize identified themes. An overview of themes is available in Table 4.2.

Table 4. 2: Summary of Identified Themes

Focus	Theme
Preparedness to offer Option B+	i) Training of frontline health providers and provision of Option B+ guidelines ii) Supervision and mentorship of health providers iii) Provision of essential medicines and medical health supplies
Organization of Option B+ services	i) HCT ii) ART initiation iii) Follow-up/linkage of mothers on Option B+ iv) Support mechanisms for women to remain in care and adhere to ART (family support groups, expert clients, midwives, nurses, VHTs, and some counsellors)
Abbreviations: ART, antiretroviral therapy; HC, Health Centre; HCT, HIV counseling and testing; VHT, Village Health Team.	

Ethical considerations

This study was approved by Makerere University School of Public Health Higher Degrees, Research and Ethics Committee (approval number: IRB00011353) and Uganda National Council for Science and Technology (Registration Number: SS3153). Permission was also obtained from districts and health facilities involved in the study. Participants were assured of anonymity and confidentiality. Written informed consent was obtained from each study participant. Interviews were conducted in a private environment and transcripts did not bear participant names. Each participant received compensation of 10,000 Uganda Shillings (equivalent to US\$4 at the time of the study) for their time. Final transcripts were stored securely on password-protected laptops and external drives.

4.4 Results

Characteristics of study participants (Health Providers)

A total of 54 interviews were conducted: 34 with clinic staff category (solely provided patient care) and 20 with facility managers (largely played a supervisory role and provided minimal patient care in their respective health facilities). Twenty-three midwives, eight nursing assistants, seven expert clients, four medical doctors, four store assistants, and other cadres were interviewed as shown in table 4.1. Half (27) of the overall participants had received training in Option B+. More than a third (20) were working at HC IVs. The minimum experience in providing HIV care was half a year with a maximum of 17 years. All health facilities reportedly started implementing Option B+ between October and December 2012.

Preparedness and Organization of Health Providers and Facilities for the Implementation of Option B+

The results on health providers' perspectives are presented in 2 foci: preparedness and organization of services for Option B+. Three themes were identified regarding preparedness: training of frontline health providers and provision of Option B+ guidelines, supervision and mentorship, and provision of essential medicines and medical health supplies. Meanwhile, 4 themes were identified concerning organization of services for Option B+: HIV counseling and testing, ART initiation, follow-up, and

support mechanisms. A summary of themes that were identified is presented in Table 4.2.

Preparedness to Offer Option B+

Training of Frontline Service Health Providers and Provision of Option B+ Guidelines.

Participants reported that key PMTCT health providers were trained prior to their involvement in provision Option B+. Participants reported that the training was offered by MOH in collaboration with two implementing partners: PREFA - Uganda and Mildmay Uganda. Training was conducted at one central place that had been identified by MOH and implementing partners. The 6-day-long training was reported to have comprised both practical and theoretical sessions on definition of and rationale for Option B+, HIV counseling and testing (HCT), introduction to e-MTCT, care for HIV-positive pregnant and breastfeeding women, assessment and ART initiation, management of HIV-exposed infants, ART adherence, quality improvement, community support for Option B+, and communication skills.

Participants described the training as very informative and enriching basing on the topics that were taught and the vast experience of the trainers. The practical aspect of training involved use of role-plays and sharing experiences. Participants recommended that training should be offered to all health providers involved in giving care to pregnant and breastfeeding women. Participants echoed that they were able to offer option B+ services comfortably compared to their colleagues who had not received the training.

They acknowledged that after being trained, they were able to give health education, counsel, initiate ART, use different PMTCT registers, and monitor women without difficulty. One of the participants shared her experience as follows:

“We had to go for training somewhere in Mukono (a central place where training took place) for a week; we were trained on all the details of Option B+. That is why we find it easier to give Option B+ services.” (Health Provider, HC IV)

Most participants felt that the training they had received was adequate, but noted that they had received the training more than one and a half years ago, and needed refresher courses to keep up-to-date with current trends. Most of those trained were midwives because of their forefront role of offering maternal, neonatal, and child health services. Most study participants stated that they had Option B+ guidelines in their health facilities. Health providers who had not received training on Option B+ read the guidelines to enable them provide PMTCT services. All participants who had used

guidelines said that they were easy to understand and use to explain to clients. Besides, they used internal consultations to aid management of HIV-positive women whenever necessary.

“We were given quite a number of guidelines on how to prescribe the drugs, and we use the guidelines now and then. Of course, one thing I believe [in is that] with medicine, consultation is inevitable; you can’t avoid consulting a colleague.” (Health Provider, HC IV)

Supervision and Mentorship of Health Providers.

There was a general agreement among all participants that supervisory and mentorship mechanisms were in place to enhance their performance. Supervision was mainly received from MOH, PREFA, Mildmay Uganda and district health team. Mentorship was reported to be done by the implementing partners. Participants noted that supervision and mentorship took place on different dates, and it was done by different teams. Both activities were done once every three months throughout the implementation of all HIV programs. However, most participants indicated that supervisory support was sometimes characterized by accusation and fault finding which they described as discouraging. On the other hand, majority of participants reported that they received mentorship which they expressed as beneficial –because they were conducted in a nonaccusatory manner and they acquired practical skills in providing Option B+ services.

“Supervisors look for faults only and don’t see the good things that we do; but mentors, tell us both the good and bad practices. Mentors do it very well. They [mentors] tell us what we should do; we actually spend almost the whole day here with them and they don’t abuse us. That is one thing that I like about the mentors, they don’t abuse us like those people who do supervision. I would suggest that it replaces supervision.” (Health Provider, HC III)

Provision of Essential Medicines and Medical Supplies.

In all study sites, MOH through National Medical Stores (NMS) and implementing partners provided essential medicines and medical supplies including ARV medications, Cotrimoxazole, HIV and early infant diagnosis (EID) testing kits, PMTCT registers, referral books, maternal and child ART cards. Study participants specifically noted that mothers were very happy to take a single ARV tablet daily in comparison to other HIV-positive patients who took more than one pill daily. Participants noted that

this reduced the pill burden. All participants pointed out that their health facilities had never run out of ARV medications for women.

“For Option B+ medicines and supplies, NMS has been supplying them and we didn’t get stock outs of ARVs for the women.” (Health Provider, Hospital)

Organization of Option B+ services

Participants’ experiences with the organization of offering ART services could be grouped into four themes:

i) HIV counseling and testing, ii) ART initiation, iii) Follow-up/linkage, and iv) Support mechanisms for women.

i) HIV counseling and testing

Across all study sites, women were prepared for Option B+ through health education and counseling. This was done before starting ART through group and individual sessions. Interviews revealed that group counseling entailed providing Option B+ information to women during group sessions. Participants pointed out that, counseling covered various topics such as importance of HIV testing, benefits of Option B+, duration of treatment, when and who to start ART and adherence. Other topics mentioned were HIV disclosure and stigma, what happens during pregnancy, birth and breastfeeding, family planning, EID, infant feeding and immunization, cervical cancer screening, and HIV partner testing. Women who had never tested for HIV received individual HCT after group sessions. However, those who required retesting were not taken through the detailed counseling processes. Thereafter, both HIV- positive and negative women received individual or couple post HIV test counseling.

“We give group counseling; after getting [receiving] the results, we do individual or couple counselling.” (Health Provider, HC IV)

Both facility managers and clinic staff noted that mostly midwives and expert clients did counseling. Participants reported that both midwives and expert clients had been trained to counsel women in preparation for and during the implementation of Option B+. However, in some health facilities where trained counsellors were available, they supported the midwives and expert clients to carry out counseling.

HIV testing was done mostly by midwives in ANC clinics, labor wards and postnatal (PNC) clinics as opposed to being done in facility laboratories. This was intended to reduce movements of mothers within facilities, and waiting time for HIV test results.

The mothers received HIV results on the same day of testing. Participants also indicated that using actual perinatal care facilities for testing of HIV could reduce stigma.

“HIV testing is done in ANC clinic and labor suit. Initially, we used to do it in the laboratory, but we realized that there was need to minimize patients’ movements and also avoid HIV stigma related challenges.” (Health Provider, HC IV)

ii) ART initiation

Most women were started on ART in the ANC clinics. A few women were initiated on ART in the labor ward or PNC clinic after they tested HIV- positive. Participants observed that at the start of the Option B+ strategy, HIV-positive pregnant women were counseled to start ART on the same day they were diagnosed. They noted that this was accepted by most women. However, some women refused to start same day ART initiation because of refusal to accept HIV-positive results or denial, feeling healthy, fear of ART side effects, and to first disclose to their partners. Indeed, some participants acknowledged that it was the woman’s right to refuse to start ART that same day bearing in mind that the treatment was lifelong.

“When a mother tests HIV-positive, she is given the results by the counsellor; she undergoes post-test counseling. Once she accepts the results – [because she has the right to refuse them – we have these mothers that reject the results] the mother is initiated on Option B+. There is no time lag.” (Health Provider, HC IV)

Study participants also stated that some health facilities devised strategies such as assessing for readiness of mothers before ART initiation because they noticed that some mothers who were started on Option B+, did not come back for follow-up. Some health providers felt that women who tested HIV-positive in ANC for the first time needed more time to fully comprehend the positive results and Option B+.

“Comparing today and the time we had just started this Option B+, in November 2012, we had a lot of mothers we started on ARVs. At that moment, you could start a woman on drugs whether she was ready or not. [In the past], mothers would start on these drugs but they would not come back for refills [while] others would provide wrong telephone numbers because they were not ready to start treatment. So, we had many women being lost to follow-up. We changed and started giving mothers time to become ready.” (Health Provider, Hospital)

iii) Follow-up of women on Option B+

Health facilities used different models to follow-up women on Option B+. Interviews revealed that the models of follow-up were agreed upon by the health providers and implementing partners. The models were chosen depending on what worked best for each health facility and these did not necessarily fully align with the guidelines. Participants noted that follow-up was done either in the ANC or general HIV clinic. The general clinics provided only HIV services, which raised concerns about stigma and subsequently loss-to- follow-up. On the other hand, some women preferred the ANC clinics which provide services to both HIV-positive and negative pregnant women and could thus mask their HIV status.

At 2 of the 6 health facilities, newly identified HIV-positive pregnant mothers were started on Option B+ during ANC and were followed up during PNC at the same location for one and a half years. Thereafter, they were transferred (linked) to the general HIV clinic for follow-up. This model of follow-up was adopted after health providers and implementing partners realized that many women were lost to follow-up if they were transferred to the general HIV clinic early. This model worked well for the 2 health facilities to reduce the number of women lost to follow-up. Participants attributed the loss to follow-up to HIV- related stigma. Women on Option B+ feared being seen by other patients and especially relatives and friends who attended the general HIV clinic.

“We realized that we enroll so many mothers, yet many are lost to follow-up. So, together with the implementing partners, we came up with another model where mothers and their babies continue to receive care in the ANC clinic up-to when the baby is one and a half years old; mothers had been dropping out of care because of fear to go and get drugs from the general HIV (chronic care) clinic due to stigma.”

(Health Provider, Hospital)

At another facility, newly identified HIV-positive pregnant mothers were started on Option B+ during ANC and followed-up during PNC at the same location. They were later on transferred to the general HIV clinic, after the infant had made the age of 1 year.

“We let the mothers and their babies to continue receiving care from the ANC clinic up-to when the baby under goes a second PCR HIV test on dried blood spot (DBS), then we transfer them to the general ART (HIV) clinic.” (Health Provider, HC III)

At 2 health facilities, newly identified HIV-positive pregnant mothers were initiated on ART and followed-up at the ANC clinic until they gave birth. The mothers were followed-up in the general HIV clinic from the time they came back for PNC when the baby was 6 weeks old. These 2 facilities had large volumes of women on Option B+ and chose the model of transferring women who had delivered to the general HIV clinic as soon as possible to avoid congestion in the ANC clinics.

One health facility reportedly registered fewer women on ART. On average they initiated 2 women on Option B + every month and 16 women were followed-up every week. Participants also noted that there was no need for a general HIV clinic. All women were initiated on Option B+ and followed-up in the ANC clinic.

“... the mothers continue getting treatment from here, we don’t transfer [link] them. The babies [exposed babies] also remain here because after the mother has delivered, the baby is given Nevirapine and has to be followed up to ensure that child services are given. So, they just continue coming to the ANC clinic, we don’t transfer them.” (Health Provider, HC III)

iv) Support mechanisms for women on Option B+

All 6 health facilities had mechanisms to support women on ART both at facility and community levels. The support was given by midwives, nurses, expert clients, and VHTs during routine clinical care and FSGs. This support is meant to ensure that women take up Option B+, remain in care, and are adherent to ART.

Family Support Groups. Five of the 6 health facilities had FSGs for HIV-positive pregnant and breastfeeding mothers at the time of the study, which were supported by health providers and implementing partners.

“They (women) get familiar to everything in regards to Option B+ through the family support group; they have a specific day in a month when they are supposed to come to meet so as to be supported.” (Health Provider, Hospital)

The facility that did not have FSGs cited delayed funding as the reason for not running them. It was hoped that as soon as money is secured FSGs would be operational.

Expert Clients and VHTs. Expert clients play a key role in giving peer education and HIV counseling to women on Option B+. Participants noted that, expert clients share the lived experience on various HIV-related issues such as benefits of testing for HIV, and of adherence to ART, importance of retention in care, HIV disclosure, and so on,

which are helpful to the women. In addition, together with VHTs, they tracked women who had been initiated on Option B+. Expert clients and VHTs worked together to support the formal health workers, keep a record of attendance lists to community events and refer pregnant and lactating mothers to appropriate health facilities. All health facilities in our study had expert clients and VHTs. Majority of study participants acknowledged the great role played by expert clients and VHTs. They reported that they strengthened follow-up and retention of mother-baby pairs. Expert clients did this through recruiting peer mothers and fathers, following-up pregnant and lactating mothers who missed appointments. They also counseled women on adherence, family planning, and nutrition and made reports to health facilities on adherence of pregnant and lactating mothers.

“Expert clients have helped us a lot, they talk very well to the mothers and encourage them to start and adhere to ARVs. They share their experiences on HIV testing, treatment, care, and positive living. When you are faced with a patient who is in HIV denial, experiencing side effects or HIV disclosure challenges; it’s the expert client to help out because, surely, it sometimes gets too hard for you as a health worker to put yourself into the shoes of an HIV-positive patient. So, the expert clients assist in counseling. Some expert clients come from the same villages where mothers on Option B+ reside. Expert clients therefore, remind those mothers to come back to the facility for follow-up.” (Health Provider, HC IV)

Midwives, Nurses and Counsellors. Participants emphasized the pivotal role of midwives and nurses in implementation of Option B+. In addition to managing pregnant and lactating mothers at health facilities, they supported HIV-positive women through a number of ways: organizing other actors (VHT, FSG, expert clients, peer mothers and fathers), calling mothers to remind them of their appointments or following up those who had not honored their appointment, and conducting home visits with peer mothers/fathers and expert clients. In some instances, health providers followed up women who had missed clinic appointments via telephone reminders. They also received referrals from communities and made communication plans to encourage mothers to bring their partners to health facilities for ANC.

“Mostly midwives and nurses carry out ANC and that is where PMTCT comes in because we do HIV counseling, testing and when we diagnose one to be HIV-positive, we enroll her, start on treatment, and follow-up.” (Health Provider, HC IV)

4.5 Discussion

This study explored health facility preparedness and organization for the implementation of Option B+ from the health provider perspective in selected health facilities in Central Uganda. The study found that health providers and facilities were reasonably prepared before and during the implementation of Option B+. Health providers were trained, supervised, and mentored. Health facilities were stocked with necessary essential medicines and health supplies such as ARV medications, HIV and EID testing kits, new e-MTCT registers, and drugs for opportunistic infection prophylaxis by MOH and implementing partners. In terms of organization of Option B+ services, HCT and ART initiation for pregnant women was being done in ANC clinic mostly by midwives. There were linkages right from ANC clinic, mother-infant pair care point (EID) clinic up to the general HIV clinic. Mothers were followed up and supported by formal and informal health providers.

Preparing health providers and facilities is very critical to ensure that Option B+ strategy is integrated in the health-care system without distorting already existing programs.^{27,28} Training of forefront personnel who provide Option B+ services was undertaken to ensure readiness for implementation and service delivery standards.⁹ However, despite initial training, regular support, and supervision, mentorship and refresher trainings are required to maintain adequate numbers of skilled and motivated health providers. Supervision should be positive and motivating other than fault finding, to enable open discussion and resolution of challenges faced by health providers and provide feedback on opportunities for improvement. Countries that have adopted Option B+ ensured that health providers were trained to offer this service. Regular trainings should be provided to enable health providers improve skill acquisition. Ongoing training is crucial, especially where the turnover of health providers is high.^{9,13} Indeed previous studies show that repetitive learning interventions, rather than single interventions, were superior for achieving desired learning outcomes.²⁹ In a study by Lipira et al, training at least one health provider in HIV care and support was associated with a lower risk of loss to follow-up from Option B+ services.³⁰ In another study, health worker trainings enabled roll out of Option B+ to more health facilities.¹⁴ Unlike in our study where training was in a residential and central location, the centers for training in other countries were in different geographical locations.^{31,32} Training in a central location enabled the trainees to

remain focused and avoid disruptions from routine service activities. Health facilities had Option B+ clinical guidelines for reference and used internal consultations to aid proper management of HIV-positive pregnant and breastfeeding women and their infants. Clinical guidelines have the potential to improve the quality and process of care and patient outcomes.³³ The guidelines should be available and accessible to health providers.

Initial counseling was done for several women in groups and later individually. This is similar to what was done in Malawi.³⁴ Adequate counseling and support around the time of Option B+ initiation has shown to improve treatment uptake, adherence, and retention in care.⁸ All women who were found to be HIV-positive were encouraged to start on ART that same day as per the national (MOH) policy recommendation. However, health facilities were innovatively flexible. Women who were not ready to start ART were given an opportunity for continual counseling until they were ready. If women are started on ART hurriedly, such challenges as nonuptake, nonadherence, and loss to follow-up are bound to occur. For example, in Malawi, most women on Option B+ who were lost to follow-up started therapy on the day they tested HIV-positive.³⁵ Individual tailored counseling and support is critical in keeping women and their infants on Option B+. Testing for HIV and initiating ART within ANC and PNC clinics, and labor wards enabled women to stay in same clinic which avoided a lot of movements and long waiting time. Women got their HIV results on the same day; this prevented missed opportunities. It is an important finding that health facilities never ran out of ART for women which dispelled fears that had been anticipated at the start of Option B+ strategy. This is similar to what was found in Malawi.^{12,36}

This study identified four models that were being used to follow-up women and their infants. This shows context flexibility in study sites which allowed health facilities to implement a model or combination of models, which best suited their daily operations. Health facilities worked collaboratively with the implementing partners to choose the best model of follow-up depending on what worked best for them based on their context rather than following guidelines. A study done in Malawi found four models of care and three were different from those identified in our study.³⁷ In their study, the model of care chosen influenced uptake of HIV testing in ANC and retention in HIV care. This highlights the importance of understanding models of HIV care that are being used and their impact on uptake of HIV services, adherence to ART, and

retention in care. One particular model of follow-up that our study identified was retaining women in the same clinic without linkage to the general HIV clinic. This is beneficial because it ensures retention; however, with time, it might lead to congestion and overload of women in ANC clinic as the number women on Option B+ increases. Depending on the context such as level of facility, volume of women served, number of health providers, or challenges experienced, there were variations in adaptation of service organization across study sites. Ministry of Health should provide guidance on service organization including models of follow-up as ultimately women cannot be kept in ANC clinic forever. Women preferred to stay in ANC clinic longer due to HIV-related stigma. However, retaining the women longer in ANC facilities creates congestion in large volume clinics and could also raise more suspicion for women who are kept longer than usual in these clinics. This calls for rigorous evaluations of the different models of follow-up and their impact on patient outcomes and the health facilities.

Although midwives provided most of the Option B+ services, informal health providers, especially expert clients, were crucial in providing certain services such as counseling, tracking, registering, escorting women who were on Option B+ within the health facilities, and giving support during FSG meetings. Expert clients have the potential to provide Option B+ services since they share the lived experience on various issues with women on Option B+ such as non-HIV disclosure, HIV-related stigma, and nonadherence to ART.³⁸ This is similar to what other countries have found and adopted.³⁹⁻⁴¹ This cadre of informal health providers should be equipped with standard and well-structured training on provision of Option B+ services. It is also important to ensure that the informal health providers are well integrated in the existing health-care system and receive adequate support and supervision from the formal health providers. The informal providers will subsequently offer quality Option B+ services and reduce the workload on the formal health providers. These informal health providers offer various services and are critical in counseling, follow-up of women, and their infants to ensure retention in care and adherence to ART.⁴² This is even more so in the current era of universal ART for all populations where many patients are being enrolled into HIV care.^{9,13}

4.6 Strengths and Limitations

We used structured interviews to explore experiences of preparedness and organization of Option B+ services from a broad range of health providers working in health facilities that were among the first implementers. Findings from this study are important and could be transferable to other health facilities, regions, and countries in similar contexts since there is a detailed description of how health facilities were prepared and organized to implement Option B+ services.

The limitations with this study are we did not interview staff from MOH, district headquarters, and implementing partners who supervise and mentor health providers to get their views. Secondly, there was potential for social desirability bias in the participants' responses; however, this was minimized through use of probes.

4.7 Conclusions and Recommendations

Health facilities and providers were prepared in various ways for implementation of Option B+ services. Option B+ services were organized to suit health facility settings. In this regard and the current era of universal ART for all populations, we recommend that all health providers offering HIV treatment services should be regularly trained, supervised, and mentored in a nonaccusatory manner. Informal health providers should have standardized training and algorithms that are tailored to their work. In addition, appropriate and effective context-specific models of service delivery and follow-up mechanisms in health facilities offering Option B+ services are recommended. Future research to generate evidence-based implementation strategies is recommended to rigorously assess the models of service delivery that result into higher levels of Option B+ uptake, adherence, and retention in care in a cost-effective manner.

Authors' Note

The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of Global Fund, Ministry of Health or Makerere University School of Public Health.

Acknowledgements

The authors wish to thank all study participants without whom this study wouldn't have been successful. Special thanks also go to the respective heads of facility for Masaka RRH, Mityana General Hospital, Luwero HC IV, Kyanamukaka HC IV, Ssunga, and Katikamu HC IIIs for their continued support rendered to us throughout the data collection process. Authors also acknowledge the tireless efforts of all study interviewers in collecting data at their respective study sites.

Author Abbreviations

A.M.: Aggrey David Mukose
E.B.: Esther Buregyeya
F.M.: Fredrick Makumbi
H.B.: Hilde Bastiaens
J.M.: Joshua Musinguzi
J.P.: Jean-Pierre Van geertruyden
R.N.: Rose Naigino
R.W.: Rhoda K. Wanyenze

Author Contributions

A.M., R.W., E.B., J.M., and F.M. were involved in development of the proposal. A.M., R.N., R.W., E.B., and F.M. carried out field work. A.M., R.W., and H.B. undertook data analysis. A.M. conceptualized the research question and wrote the first draft of the manuscript. R.W., H.B., J.P., J.M., and F.M. revised the draft manuscript to strengthen its intellectual content. A.M., R.W., R.N., E.B., F.M., J.M., J.P., and H.B. approved the final draft.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article. The authors received funding for the research from the Global Fund through the Ministry of Health - Uganda [Grant Number: UGD-708-G07-H].

ORCID iD

Aggrey David Mukose, MBChB, MS <https://orcid.org/0000-0002-0309-8926>

References

1. World Health Organization. Use of Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. Geneva, Switzerland: World Health Organization; 2012.
2. World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. Geneva, Switzerland: World Health Organization; 2013.
3. Godfrey E. PMTCT Implementation in Uganda: Option B Plus Experience. 2013; http://www.vaccineenterprise.org/sites/default/files/02-Esiru_0.pdf. Accessed June 14, 2015.
4. World Health Organization. Programmatic Update on Use of ART for Treating Pregnant Women and Preventing HIV Infection in Infants. Geneva, Switzerland: World Health Organization; 2012.
5. UNAIDS. Global Plan towards the Elimination of New HIV Infections among Children by 2015 and Keeping Their Mothers Alive. Geneva, Switzerland: UNAIDS; 2011.
6. The Interagency Task Team on the Prevention and Treatment of HIV Infection in Pregnant Women MaC. Option B+ Countries and PMTCT Regimen. 2016. <http://www.emtct-iatt.org/b-countries-and-pmtct-regimen/>. Accessed January 10, 2016.
7. Ministry of Health. Consolidated Mid-term review report of the National HIV/AIDS Strategic Plan 2011/12- 2014/15. Kampala, Uganda: Uganda AIDS Commission; 2014.
8. Kieffer MP, Mattingly M, Giphart A, et al. Lessons learned from early implementation of option B+: the Elizabeth Glaser Pediatric AIDS Foundation experience in 11 African countries. *J Acquir Immune Defic Syndr*. 2014;67(suppl 4):S188–S194.
9. Doherty T, Besada D, Goga A, Daviaud E, Rohde S, Raphaely N. “If donors woke up tomorrow and said we can’t fund you, what would we do?” A health system dynamics analysis of implementation of PMTCT option B+ in Uganda. *Global Health*. 2017;13(1):51.

10. Aní'gila'je' EA, Ageda BR, Nweke NO. Barriers to uptake of prevention of mother-to-child transmission of HIV services among mothers of vertically infected HIV-seropositive infants in Makurdi, Nigeria. *Patient Prefer Adherence*. 2016;10:57–72.
11. Lumbantoruan C, Kermode M, Giyai A, Ang A, Kelaher M. Understanding women's uptake and adherence in Option B+ for prevention of mother-to-child HIV transmission in Papua, Indonesia: a qualitative study. *PLoS One*. 2018;13(6):e0198329.
12. World Health Organization. Implementation of Option B+ for Prevention of Mother-To-Child Transmission of HIV: The Malawi Experience WHO Regional Office for Africa. Brazzaville, Republic of Congo: World Health Organization; 2014.
13. Kalua T, Tippet Barr BA, van Oosterhout JJ, et al. Lessons learned from option B+ in the evolution toward "Test and Start" from Malawi, Cameroon, and the United Republic of Tanzania. *J Acquir Immune Defic Syndr*. 2017;75(suppl 1):S43–S50.
14. Herce ME, Mtande T, Chimbwandira F, et al. Supporting Option B+ scale up and strengthening the prevention of mother-to-child transmission cascade in central Malawi: results from a serial cross-sectional study. *BMC Infect Dis*. 2015;15(1):1.
15. Nachega JB, Uthman OA, Anderson J, et al. Adherence to antiretroviral therapy during and after pregnancy in low-, middle and high income countries: a systematic review and meta-analysis. *AIDS (London, England)*. 2012;26(16):2039.
16. Kreitchmann R, Harris DR, Kakehasi F, et al. Antiretroviral adherence during pregnancy and postpartum in Latin America. *AIDS Patient Care STDS*. 2012;26(8):486–495.
17. Baryamutuma R, Kansime E, Nuwagaba CK, Nabitaka L, Muhumuza S, Akello E, Musinguzi J, Bazeyo W, Celentano J, Lindan C. An early assessment of Uganda's roll-out of Option B+: Service capacity and infant outcomes. *East African Journal of Applied Health Monitoring and Evaluation*. 2017 Feb;2017(1):16.
18. Makerere University & University of California, San Francisco. Effectiveness of Lifelong ART for Pregnant and Lactating Mothers on Elimination of Mother to Child Transmission of HIV and on Maternal and Child Health Outcomes: Uganda 2013-2015. Kampala, Uganda: Makerere University & University of California, San Francisco; 2015.
19. Rempis EM, Schnack A, Decker S, et al. Option B+ for prevention of vertical HIV transmission has no influence on adverse birth outcomes in a cross-sectional cohort in Western Uganda. *BMC Pregnancy and Childbirth*. 2017;17(1):82.

20. Sandelowski M. Whatever happened to qualitative description? *Res Nurs Health*. 2000;23(4):334–340.
21. Ministry of Health. Health Sector Strategic Plan III 2010/11-2014/15 Kampala, Uganda. New Delhi, India: Ministry of Health; 2010.
22. Ministry of Health. National HIV AND AIDS Strategic Plan 2015/2016- 2019/2020. Kampala, Uganda: Uganda AIDS Commission; 2015.
23. Institute of Medicine. Evaluation of PEPFAR. Washington, DC: The National Academies Press; 2013.
24. PEPFAR. Glossary of Terms. PEPFAR Dashboards. <https://data.pepfar.net/glossary>. Accessed July 31, 2018.
25. Sudhinaraset M, Ingram M, Lofthouse HK, Montagu D. What is the role of informal healthcare providers in developing countries? A systematic review. *PLoS One*. 2013;8(2):e54978.
26. King N, Horrocks C. Interviews in Qualitative Research. Thousand Oaks, CA: Sage; 2010.
27. Chi BH, Thirumurthy H, Stringer JS. Maximizing benefits of new strategies to prevent mother-to-child HIV transmission without harming existing services. *JAMA*. 2014;312(4):341–342.
28. Pfeiffer J, Montoya P, Baptista AJ, et al. Integration of HIV/AIDS services into African primary health care: lessons learned for health system strengthening in Mozambique—a case study. *J Int AIDS Soc*. 2010;13:3.
29. Bluestone J, Johnson P, Fullerton J, Carr C, Alderman J, Bon-Tempo J. Effective in-service training design and delivery: evidence from an integrative literature review. *Hum Resour Health*. 2013;11:51.
30. Lipira L, Kemp C, Domercant JW, Honore JG, Francois K, Puttkammer N. The role of service readiness and health care facility factors in attrition from Option B+ in Haiti: a joint examination of electronic medical records and service provision assessment survey data. *Int Health*. 2018;10(1):54–62.
31. Elizabeth Glaser Pediatric AIDS Foundation. Gearing Up for Option B+: Health Worker Training in Lesotho. 2013. <http://www.pedaids.org/blog/entry/gearing-up-for-option-b-healthworker-training-in-lesotho>. Accessed November 15, 2017.

32. Elizabeth Glaser Pediatric AIDS Foundation. Option B+ in Malawi: The Origins and Implementation of a Global Health Innovation. 2012; <http://www.msh.org/news-events/stories/option-b-in-malawi-the-origins-and-implementation-of-a-globalhealth-innovation>. Accessed October 15, 2017.
33. Graham ID, Harrison MB. Evaluation and adaptation of clinical practice guidelines. *Evid Based Nurs*. 2005;8(3):68–72.
34. Katirayi L, Namadingo H, Phiri M, et al. HIV-positive pregnant and postpartum women's perspectives about Option B+ in Malawi: a qualitative study. *J Int AIDS Soc*. 2016;19(1): 20919.
35. Tenthani L, Haas AD, Tweya H, et al. Retention in care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women ('Option B+') in Malawi. *AIDS*. 2014; 28(4):589–598.
36. Webb R, Cullel M. Understanding the perspectives and/or experiences of women living with HIV regarding Option B+ in Uganda and Malawi. Final Report. Amsterdam, The Netherlands: Rebekah Webb Consulting. 2013.
37. van Lettow M, Bedell R, Mayuni I, et al. Towards elimination of mother-to-child transmission of HIV: performance of different models of care for initiating lifelong antiretroviral therapy for pregnant women in Malawi (Option B+). *J Int AIDS Soc*. 2014;17:18994.
38. Buregyeya E, Naigino R, Mukose A, et al. Facilitators and barriers to uptake and adherence to lifelong antiretroviral therapy among HIV infected pregnant women in Uganda: a qualitative study. *BMC Pregnancy and Childbirth*. 2017;17(1):94.
39. Samb B, Celletti F, Holloway J, Van Damme W, De Cock KM, Dybul M. Rapid expansion of the health workforce in response to the HIV epidemic. *N Engl J Med*. 2007;357(24):2510–2514.
40. Modi S, Callahan T, Rodrigues J, et al. Overcoming health system challenges for women and children living with HIV through the global plan. *JAIDS J Acquir Immune Defic Syndr*. 2017;75(suppl1):S76–S85.
41. Cataldo F, Sam-Agudu NA, Phiri S, Shumba B, Cornelius LJ, Foster G. The roles of expert mothers engaged in Prevention of Mother-to-Child Transmission (PMTCT) Programs: a commentary on the INSPIRE studies in Malawi, Nigeria, and Zimbabwe. *JAIDS J Acquir Immune Defic Syndr*. 2017;75(suppl 1): S224–S232.

42. Cataldo F, Seeley J, Nkhata MJ, Mupambireyi Z, Tumwesige E, Gibb DM. She knows that she will not come back: tracing patients and new thresholds of collective surveillance in PMTCT Option B. *BMC Health Serv Res.* 2018;18(1):76.

CHAPTER 5:

What influences uptake and early adherence to Option B+ (lifelong antiretroviral therapy among HIV-positive pregnant and breastfeeding women) in Central Uganda? A mixed method study

Aggrey David Mukose^{1,2*}, Hilde Bastiaens^{2,3}, Fredrick Makumbi¹, Esther Buregyeya⁴, Rose Naigino⁵, Joshua Musinguzi⁶, Jean-Pierre Van Geertruyden², and Rhoda K. Wanyenze⁴

¹ Department of Epidemiology and Biostatistics, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda

² Global Health Institute, Department of Epidemiology and Social Medicine, University of Antwerp, Antwerp, Belgium

³ Department of Primary and Interdisciplinary Care, University of Antwerp, Antwerp, Belgium

⁴ Department of Disease Control and Environmental Health, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda

⁵ Makerere University School of Public Health, Kampala, Uganda

⁶ Ministry of Health, Kampala, Uganda

PLoS ONE 16(5): e0251181. <https://doi.org/10.1371/journal.pone.0251181>

Received: July 23, 2020; Accepted: April 21, 2021

DOI: <https://doi.org/10.1371/journal.pone.0251181>

5.1 Abstract

Background: High uptake of, and optimal adherence to Option B+ antiretroviral therapy (ART), increase the effectiveness in averting mother-to-child transmission of HIV. Option B+ ART uptake, early adherence, and associated factors need to be evaluated in Central Uganda.

Methods: A mixed approaches study was carried out in six health facilities in Masaka, Mityana, and Luwero districts from October 2013 to March 2016. Questionnaires were administered to 507 HIV-positive pregnant females seeking antenatal care services. Key informant interviews were conducted with 54 health providers, and in-depth interviews (IDIs) with 57 HIV-positive women on Option B+ ART. Quantitative data were analyzed using log-binomial regression model to determine factors associated with optimal adherence (taking at least 95% of the prescribed ART), while thematic analysis was used on qualitative data.

Results: Ninety one percent of women (463/507) received a prescription of life long ART. Of these, 93.3% (432/463) started swallowing their medicines. Overall, 83% of women who received ART prescriptions (310/374) felt they were ready to initiate ART immediately. Main motivating factors to swallow ART among those who received a prescription were women's personal desire to be healthy (92.3%) and desire to protect their babies (90.6%). Optimal adherence to ART was achieved by 76.8% (315/410). Adherence was higher among females who were ready to start ART (adj. PR= 3.20; 95% CI: 1.15-8.79) and those who had revealed their HIV-positive result to someone (adj. PR= 1.23; 95% CI: 1.04-1.46). Facilitators of ART uptake from qualitative findings included adequate counseling, willingness to start, and knowing the benefits of ART. Reasons for refusal to start ART included being unready to start ART, fear to take ART for life, doubt of HIV-positive results, and preference for local herbs. Reasons for non-adherence were having travelled far away from the health facilities, fear of side effects, non-disclosure of HIV results to anyone, and perception that the baby is safe from HIV infection post-delivery.

Conclusions: Uptake of Option B+ ART was very high. However, failure to start swallowing ART and sub-optimal adherence are a major public health concern. Enhancing women's readiness to start ART and encouraging HIV result revelation could improve ART uptake and adherence.

5.2 Introduction

Mother-to-child transmission (MTCT) of HIV is still a challenge sub-Saharan Africa where HIV prevalence and fertility rates are high [1, 2]. Globally, over 90% of new HIV infections in children occur through MTCT [3]. ART use for prevention of mother-to-child transmission (PMTCT) lessens the HIV MTCT risk to less than 2% and 5% in non- and lactating populations respectively [4, 5]. Since 2000, a decline of 58% in new paediatric HIV infections has been noted as a result of ART use among expectant women living with HIV [1, 6, 7]. To hasten the drop in new HIV infections more, the World Health Organization (WHO) reviewed the PMTCT guidelines in 2012 with the aim of achieving virtual elimination of MTCT (e-MTCT) of HIV. The reviewed guidelines suggested Option B+ (lifelong ART for HIV-positive expecting and lactating mothers irrespective of CD4 or clinical stage) [8].

Implementation of Option B+ in Uganda began in September 2012. Implementation started in districts with the highest HIV prevalence and was scaled up to all districts by the end of 2013 [9]. Women on Option B+ in Uganda received a combination of Tenofovir Disoproxil Fumarate (TDF), Lamivudine (3TC) and Efavirenz (EFV) as a single pill. For e-MTCT of HIV to be realized, ART should be initiated early in pregnancy with adequate adherence in order to achieve viral suppression [10]. However, studies have revealed various gaps in implementation of PMTCT programs. A systematic review and meta-analysis by Huang et al. [11] showed that in China, 71% of HIV-positive women had initiated Option B+ but uptake varied between income levels. Further, a systematic assessment in low and middle-income countries revealed that nearly half of HIV-positive expectant women neither received ART prophylaxis during antenatal care (ANC) nor delivered in health facilities [12]. Other PMTCT studies conducted before adoption of Option B+ revealed varying results. In Malawi, there was low use of ART and single dose Nevirapine, whereas in Kenya high uptake of ART was reported using community-based assessment data [13, 14]. A study using health facility data from 2002 to 2011 in Northern Uganda showed that only 69.4% and 9.6% of HIV-positive gravid women were started on ART for prophylaxis and treatment respectively [15].

Price et al. (2014) specifically evaluated the Option B+ in Malawi using a retrospective cohort where many eligible pregnant women had not taken up an invite to start ART

[16]. Gravidity and the first months of postpartum are associated with significant changes in a woman's life, which might influence ART uptake and adherence. Barriers to ART uptake and adherence during this period among others include family obligations and stress due to pregnancy and child birth, and non-disclosure of HIV-positive status. Postpartum women have been found to miss more medical appointments, and adherence tends to be lower than during pregnancy [17-20]. Studies have shown that between 10% and 50% stopped their ART after delivery, some without health workers' approval [18, 19, 21]. Although critical, issues around prescription, uptake of ART (prescription and starting to swallow ART), and early adherence in the setting of Option B + have scarcely been researched [22, 23]. Though many of the existing studies used prescription and receipt of ART as a measure of uptake, some women who receive the medicines could fail to swallow them for various reasons. If ART non- uptake and non-adherence are identified early, interventions can be instituted to increase uptake, adherence and subsequently effectiveness of Option B+. Early treatment failure and hasty progress to ART drug resistance could also be prevented [24, 25]. Therefore, this study assessed key issues around ART prescription and swallowing (uptake), early adherence and associated factors among HIV-positive expectant women and lactating mothers on Option B+ in Central Uganda. Findings from the study could contribute to achievement of the Joint United Nations Programme on HIV/AIDS (UNAIDS) fast-track targets and subsequently end the HIV/AIDS epidemic as a public health threat by 2030 [26, 27].

5.3 Methods

Study design

A prospective cohort study using mixed methods was conducted at health facilities providing lifelong ART in Masaka, Mityana, and Luwero districts from October 2013 to March 2016. The details of the methodology for the study involving HIV-positive women are already reported elsewhere [28, 29]. In brief, quantitative interviews were conducted in a prospective cohort of 507 HIV-positive women pregnant at baseline and at 2, 4, 6, 10, 14, and 18 months after baseline to establish uptake of ART and other PMTCT linked services for both the HIV-positive mothers and their infants; evaluate retention in care; and measure adherence to ART. Additionally, the study enrolled 54 health providers and 57 HIV-positive women for a qualitative inquiry using

a qualitative descriptive approach. In the current manuscript, a mixed methods cross-sectional convergent parallel study design nested in a prospective cohort was followed. Mixed methods were critical in this study to ensure complementarity and facilitation of greater understanding [30-32] of uptake and early adherence to Option B+ ART. Convergent parallel mixed method design enabled autonomous collection of quantitative and qualitative data which were later integrated at reporting, interpretation, and discussion [30, 33-35]. The quantitative arm aimed to assess issues around ART prescription, uptake, adherence and associated factors. The qualitative arm explored experiences around ART prescription, uptake, and adherence among women on Option B+ and garnered views and perspectives of Option B+ service providers.

Study sites

This study was conducted at six health facilities in Masaka, Mityana, and Luwero districts in Central Uganda. These were among the first districts to implement Option B+ in Uganda following its launch in September 2012. The facilities included three high patient volume facilities (Masaka Regional Referral Hospital (RRH), Mityana General Hospital (GH), and Luwero Health Centre (HC) IV) in accordance with the structure of the Uganda public health-care system [36]. The other three locations were low patient volume facilities (Kyanamukaka HC IV, Ssunga HC III and Katikamu HC III). High patient volume facilities have over 500 individuals in HIV care while low volume facilities have ≤ 500 clients in HIV care [37]. The qualitative study was conducted at all the six facilities whereas the quantitative component was carried out only at the high patient volume facilities.

Study population and data collection

Quantitative component

A total of 507 HIV-positive pregnant females were enrolled and followed-up at Masaka RRH (184), Mityana GH (213), and Luwero HC IV (110) from October 2013 to March 2016. Study eligibility was HIV-positive expectant females seeking ANC services, aged 15-49 years, ART naïve or started on ART for Option B+ within four weeks of enrollment. All women reporting for ANC services at the facilities were assessed for pregnancy either through self-report or pregnancy test and screened for HIV status. The ANC service providers referred all pregnant HIV-positive women to the study

research staff on site. A well-trained female research assistant (RA) was stationed at each study facility to enroll and follow up eligible participants. The RA screened the women for study eligibility, administered written informed consent to the eligible women, and subsequently conducted face-to-face interviews using structured pre-tested and standardized questionnaires. The questionnaire used for data collection was adopted with modifications [38-41]. Pre-testing of the questionnaires was done by administering them to a sample of study eligible participants in a non-study site. Thereafter, the investigators met with the RAs to go through the entire tool to correct any unclear questions. This ensured that all participants were asked the same questions in an identical format and responses recorded in a uniform manner.

Enrolment was done concurrently at all the three sites until the calculated sample size of 500 participants was obtained. This was the sample size for the parent study and was determined as described elsewhere [29]. Due to simultaneous recruitment at all the study sites, a total of 507 were enrolled. Following a baseline interview at enrolment, follow-up visits were scheduled at every two months intervals up to six months, then every four months up to 18 months post enrolment. Study follow-up interviews were aligned to the scheduled ANC/postnatal care (PNC) clinic visits as much as possible to minimize inconvenience to the women. Baseline questionnaires were administered to all 507 women. Analysis on the characteristics of study participants and prescription of ART was done on 507 women. In this article, uptake of and early adherence to Option B+ medicines at two-month follow-up was analysed for 463 and 410 women who had complete data, respectively. Basing on the sample sizes that we used for the two study outcomes (levels of uptake and early adherence), the study had a 5% level of precision. We conducted a power analysis on associated factors such as HIV-positive status disclosure to anyone, and readiness to start ART. We found that our study had sufficient power ($\geq 80\%$) to detect a difference in the study outcome (Early adherence). Quantitative data collection for this study took place between October 2013 and October 2014.

Qualitative component

Participants in the qualitative interviews were purposively selected. We planned to interview 10 HIV-positive women at each health facility (60 women total) for the in-depth interviews. However, 57 interviews were conducted and the participants were

not part of the quantitative component but receiving the same Option B+ services. Use of in-depth interviews enabled the researchers explore women's lived experience in regards to uptake of and early adherence to ART for Option B+. The women were either expectant or post-delivery. They had been on lifelong ART for a minimum of six months so as to provide sufficient experiences before and after delivery. Based on information from health facility staff and records, the women were considered into three groups: good ART adherers, poor ART adherers, and delayed ART acceptors as defined in the articles that were published elsewhere [28, 29]. Qualitative data collection was conducted from February to May 2014 using pre-tested semi-structured interview guides. Three well-skilled research assistants with vast understanding in qualitative research conducted the in-depth interviews.

Fifty-four key informant interviews out of the targeted 60 interviews (10 at each facility) were used to explore health provider perspectives on uptake and early adherence to Option B+ from all the six facilities. The selected health providers were deemed to have the necessary information on uptake of and early adherence to Option B+ ART. Health providers were classified in two categories based on their roles, workstation/department, and experience as described elsewhere [36]. The sample size specification and justification for the qualitative component were predetermined as this was required by the funder, ethics committee, and Ministry of Health (MOH) before the study was implemented [42, 43].

Four of the main investigators (A.M., R.W., E.B., and R.N.) interviewed the key informants. All in-depth interviews and a few key informant interviews with expert clients were conducted in Luganda the commonly spoken local language. All other key informant interviews were carried out in English. On average, each key informant interview lasted 1.5 hours whereas each in-depth interview lasted between 1 and 2 hours. All qualitative interviews were audio-recorded.

Data collection tools and measures

The quantitative data were collected on participants' socio-demographic characteristics, prescription and swallowing of Option B+ ART, reasons for non-prescription and/or refusal to swallow ART, disclosure of HIV status, willingness to start ART, readiness to start taking (initiate) ART, motivation to initiate ART, reasons for delay to initiate ART, understanding of how long the participant was supposed to

be on ART, and self-reported adherence to ART. Uptake of and early adherence to Option B+ ART were the key dependent variables. These were assessed at two months after enrolment into the study). Uptake of Option B+ medicines was defined as having been prescribed and starting to swallow ART. Willingness to start ARTs was assessed among women who had not received a prescription by asking if they were willing to be initiated on ART or not. Reasons for non-willingness to be prescribed ART were also probed. Readiness to take ART was assessed by asking women who had been initiated on ART; how ready they were at the time they started taking ART. The responses were; immediately, later and not at all. Women were also asked to mention what motivated them to start taking ART. Early adherence was measured as a binary outcome and defined as i) optimal if women reported taking at least 95% of the ART doses (≥ 29 doses) in the 30-days before the two-month follow-up interview, or ii) suboptimal if reported taking less than 29 doses in the same period. ART was prescribed to be taken once a day. ART adherence was assessed through self-report by asking for the number of ART doses taken in the past 30 days. A visual analogue scale (0-100%) was used to find the percentage of prescribed ART doses taken at every follow-up study visit. The questionnaires were translated into Luganda, the commonly used local dialect.

Qualitatively, in-depth interview and key informant interview guides were developed by the research team. The topics covered by the interview guides were based on our research question “What influences uptake and early adherence to lifelong ART among HIV-positive pregnant and breastfeeding women in Central Uganda?” Guided by literature gaps, the researchers discussed the issues, listed varied questions and probes in a semi-structured format [28, 36]. This study focused on issues around uptake of, motivation to start and adherence to Option B+ ART. Some of the specific questions to the key informants explored matters around lifelong ART prescription, benefits of lifelong ART, adherence to ART, and retention in HIV care.

The questions to the in-depth interview participants included; experiences round decision and motivation to start Option B+ ART, refusal to start ART, ART adherence and HIV related stigma.

Data analysis

Quantitative data

Exploratory data analysis was conducted on the independent and dependent variables. Descriptive statistics were generated providing percentages for categorical variables, while means (standard deviation) and median (inter-quartile range, IQR) for continuous variables. Percentages were computed for the socio-demographic characteristics, reported Option B+ ART prescription, taking of ART, reasons for non-prescription and/or refusal to take ART, disclosure of HIV status, willingness to take ART, readiness to initiate ART, motivation for initiating ART, reasons for delay in initiating ART, understanding of how long the participant was supposed to be on ART, and adherence to ART. Bivariate and multivariable analyses were conducted to generate prevalence ratio (PR) as a measure of association, using log-binomial regression model to establish factors associated with optimal adherence. Log-binomial regression was preferred to logistic regression because the later technique tends to overestimate the measures of association when the prevalence of the outcome is 10% or higher [44]. We explored for interaction between some of the factors such as: disclosure of HIV status to anyone; readiness to start ART; health facility level; and knowledge on how long ART should be taken and the outcome (early adherence). After testing for collinearity, interaction and confounding, variables that had p-value of ≤ 0.2 at bivariate analysis were included into the final multivariable regression model. STATA version 14 was used for analysis.

Qualitative data

Qualitative data were transcribed verbatim. Data in Luganda were simultaneously translated and transliterated into English. Each transcript was reread by A.M. and one other co-investigator for content and completeness. Additional reviews of selected transcripts were done by R.W. for quality control and to ensure reflexivity. Final transcriptions were transferred to Atlas software (Atlas.ti, Version 7 software, Berlin, Germany) for analysis. Thematic analysis was done using a predetermined frame with the following themes: [45, 46] willingness of HIV-positive pregnant women to start ART, uptake of, readiness and motivation to initiate Option B+ ART, refusal and delay to take Option B+ ART, and early adherence to Option B+ ART as guided by the quantitative and qualitative tools [30]. We identified paragraphs linked to the

predetermined themes and then coded these pieces inductively using thematic analysis. Thereafter, codes were grouped into subthemes within each pre-determined theme. Coding was done by A.M. The codes and subthemes were discussed and reflected on by the co-authors through regular meetings. Distinctive quotes were identified and used to highlight the main issues identified in the interviews. This was done for both the in-depth and key informant interviews.

Ethical considerations

Ethical approval was gotten from Makerere University School of Public Health Higher Degrees, Research and Ethics Committee and Uganda National Council for Science and Technology (UNCST). Authorization to conduct the study was sought from the district health officers and health facility in-charges. Written informed consent was attained from every study participant prior to conducting interviews. HIV-positive pregnant women aged 15-17 years who participated in the quantitative component of the study were considered as emancipated minors as per the UNCST ethics committee guidelines [47].

5.4 Results

Both quantitative and qualitative results are integrated as per the pre-defined themes.

Baseline characteristics

Out of 925 women who were screened for eligibility, 507 HIV-positive expectant females were enrolled into the study. Figure 5.1 shows numbers of women who were screened, recruited in the study and included in the quantitative analyses at the first two-month follow-up visit.

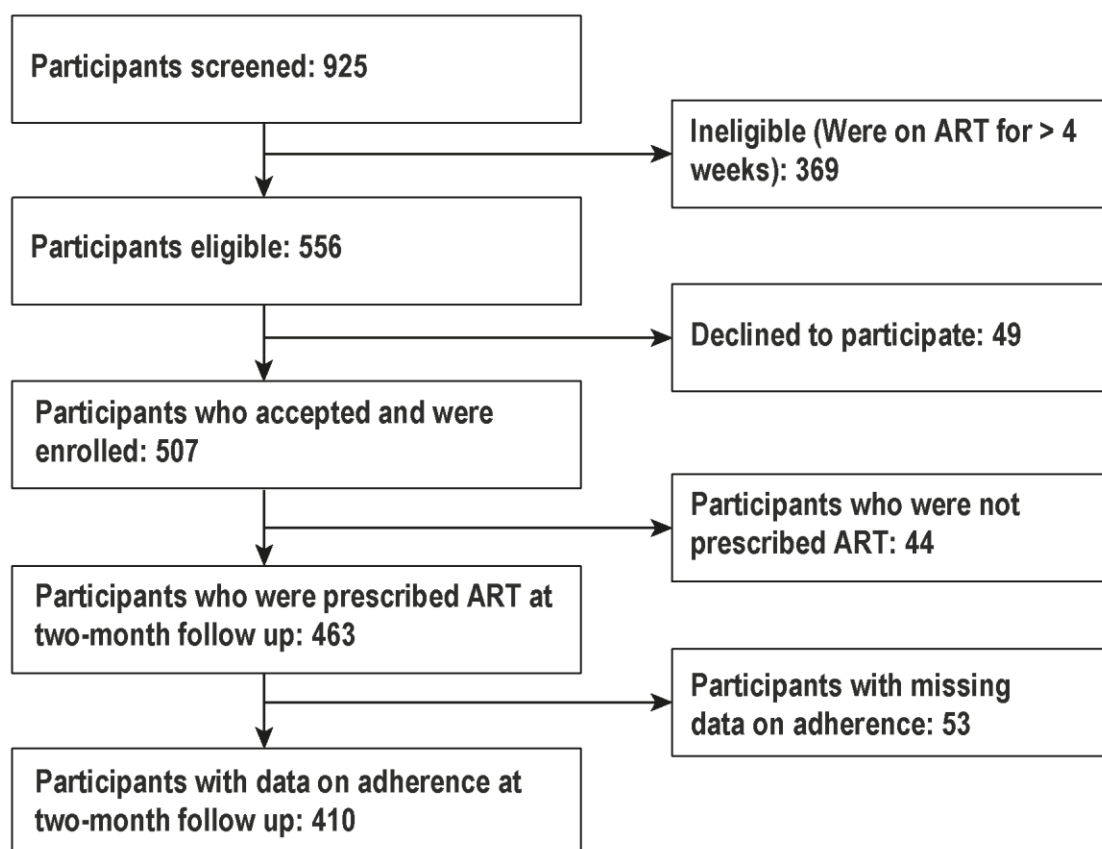


Figure 5.1: Flow chart for enrolment and two-month follow-up of the study participants

Table 5.1 shows baseline characteristics of women who were enrolled in the cohort study (quantitative component). Mityana GH contributed the maximum number of study participants (42.1%, 213), followed by Masaka RRH (36.2%, 184) and Luwero (21.7%, 110).

The median (IQR) age was 24 (21, 28) years. Half (52.1%) were aged 15- 24 years while 28.6% aged 25-29 years. Majority (51.1%) had primary or no education and 48.9% had attained secondary education and above. Four in five (80%) women were married, and Catholic was the most common religion (47.9%). A third (33.7%) of the women were involved in business/commercial activities, 23.1% were home-makers/ housewife, and 18.9% were engaged in subsistence farming. Nearly all study participants (95.5%) indicated that they intended to deliver from the study-enrolling health facility. Just over a quarter (27.2%) had been initiated on Option B+ ART within four weeks prior to enrolment into the study.

Table 5. 1: Baseline characteristics of HIV-positive pregnant women recruited into the study (N=507)

Characteristic	Health Facility			
	Luwero HC IV (n=110, 21.7%)	Mityana GH (n=213, 42.1%)	Masaka RRH (n=184, 36.2%)	Total number (%)
Age (years)				
Median (IQR)	23 (20-28)	25 (21-29)	24 (20.5-28)	24 (21-28)
15-24	63 (57.3)	97 (45.5)	104 (56.5)	264 (52.1)
25-29	29 (26.4)	63 (29.6)	53 (24.8)	145 (28.6)
30-44	18 (16.4)	53 (24.9)	27 (14.7)	98 (19.3)
	Number (%)	Number (%)	Number (%)	
Highest level of education completed				
Primary or below	53 (48.2)	123 (57.7)	83 (45.1)	259 (51.1)
Secondary or above	57 (51.8)	90 (42.3)	101 (54.9)	248 (48.9)
Marital status				
Married	89 (80.9)	172 (80.8)	145 (78.8)	406 (80.1)
Never married	12 (10.9)	19 (8.9)	30 (16.3)	61 (12.0)
Widowed/separated	9 (8.2)	22 (10.3)	9 (4.9)	40 (7.9)
Occupation				

Peasant farmer	18 (9.8)	24 (21.8)	54 (25.4)	96 (18.9)
Salaried	10 (5.4)	6 (5.5)	13 (6.1)	29 (5.7)
Business/commercial	60 (32.6)	24 (21.8)	87 (40.9)	171 (33.7)
Casual worker	1 (0.5)	10 (9.1)	10 (4.7)	21 (4.1)
Not employed	34 (18.5)	9 (8.2)	0 (0.0)	43 (8.5)
Housewife	41 (22.3)	28 (25.5)	28 (22.5)	117 (23.1)
Others	20 (10.9)	9 (8.2)	1 (0.5)	30 (5.9)
Religion				
Catholic	39 (35.5)	99 (46.5)	105 (57.1)	243 (47.9)
Protestant	35 (31.8)	53 (24.9)	20 (10.7)	108 (21.3)
Born again	17 (15.5)	23 (10.8)	15 (8.2)	55 (10.8)
Muslim	15 (13.6)	28 (13.1)	43 (23.4)	86 (17.0)
Other	4 (3.6)	10 (4.7)	1 (0.5)	15 (3.0)
Health Facility where the participant intends to deliver from				
Study site	97 (88.2)	209 (98.1)	178 (96.7)	484 (95.5)
Another facility	13 (11.8)	4 (1.9)	6 (3.3)	23 (4.5)
ART Initiation status				
Within past 4 weeks	37 (33.6)	66 (31.0)	35 (19.0)	138 (27.2)
ART naive	73 (66.4)	147 (69.0)	149 (81.0)	369 (72.8)

Forty-nine women were eligible to participate in the study but declined. Out of these, 41 women had data on their baseline characteristics as shown in Table 5.2. Majority (80.5%) were from Luwero HC IV, and the median (IQR) age was 24 (21, 27) years. More than half (53.7%) were aged 15-24 years while 31.7% aged 25-29 years. Most women (63.4%) had primary or no education and 36.6% had attained secondary education and above. Majority (82.9%) of women were married, and four in five (80.5%) were ART naive.

Women who were enrolled in the study and those who declined had similar baseline characteristics except for the categories of casual worker ($p= 0.019$) and housewife ($p= 0.022$) under the variable “Occupation” (Table 5.3).

Table 5. 2: Baseline characteristics of HIV-positive pregnant women who declined to participated in the study (N=41) by Health Facility

Characteristic	Health Facility			Total number (%)
	Luwero HC IV (n=33, 80.5%) 7.3%)	Mityana GH (n=5, 12.2%)	Masaka RRH (n=3,	
Age (years)				
Median (IQR)	24 (20-27)	27 (22-29)	20 (20-32)	24 (20-27)
15-24	18 (54.5)	2 (40.0)	2 (66.7)	22 (53.7)
25-29	11 (33.3)	2 (40.0)	0 (0.0)	13 (31.7)
30-44	4 (12.1)	1 (20.0)	1 (33.3)	6 (14.6)
	Number (%)	Number (%)	Number (%)	
Highest level of education completed				
Primary or below	22 (66.7)	2 (40.0)	2 (66.7)	26 (63.4)
Secondary or above	11 (33.3)	3 (60.0)	1 (33.3)	15 (36.6)
Marital status				
Married	28 (84.9)	5 (100.0)	1 (33.3)	34 (82.9)
Never married	2 (6.1)	0 (0.00)	2 (66.7)	4 (9.8)
Widowed/separated	3 (9.1)	0 (0.00)	0 (0.00)	3 (7.3)
Occupation				
Peasant farmer	6 (18.2)	1 (20.0)	1 (33.3)	8 (19.5)
Business/commercial	7 (21.2)	0 (0.00)	1 (33.3)	8 (19.5)
Casual worker	5 (15.2)	0 (0.00)	0 (0.00)	5 (12.2)
Not employed	2 (6.1)	0 (0.00)	0 (0.0)	2 (4.9)
Housewife	12 (36.4)	3 (60.0)	1 (33.3)	16 (39.0)
Others	1 (3.03)	1 (20.0)	0 (0.0)	2 (4.9)
ART Initiation status				

Within past 4 weeks	8 (24.2)	0 (0.0)	0 (0.0)	8 (19.5)
ART naive	25 (75.8)	5 (100.0)	3 (100.0)	33 (80.5)

Table 5. 3: Comparison of baseline characteristics of HIV-positive pregnant women recruited into the study (N=507) and those who declined (N=41)

Characteristic	Enrolled	Declined	P- value
	Total number (N=507, %)	Total number (N=41, %)	
Age (years)			
Median (IQR)	24 (21-28)	24 (20-27)	
	Number (%)	Number (%)	
15-24	264 (52.1)	22 (53.7)	0.844
25-29	145 (28.6)	13 (31.7)	0.673
30-44	98 (19.3)	6 (14.6)	0.460
Highest level of education completed			
Primary or below	259 (51.1)	26 (63.4)	0.129
Secondary or above	248 (48.9)	15 (36.6)	0.129
Marital status			
Married	406 (80.1)	34 (82.9)	0.664
Never married	61 (12.0)	4 (9.8)	0.675
Widowed/separated	40 (7.9)	3 (7.3)	0.891
Occupation			
Peasant farmer	96 (18.9)	8 (19.5)	0.925
Salaried	29 (5.7)	0 (0.0)	0.116
Business/commercial	171 (33.7)	8 (19.5)	0.062
Casual worker	21 (4.1)	5 (12.2)	0.019
Not employed	43 (8.5)	2 (4.9)	0.420
Housewife	117 (23.1)	16 (39.0)	0.022
Others	30 (5.9)	2 (4.9)	0.793

ARV Initiation status			
Within past 4 weeks	138 (27.2)	8 (19.5)	0.283
ART naive	369 (72.8)	33 (80.5)	0.283

Fifty-seven participants took part in the in-depth interviews. A total of 54 key informant interviews were conducted with 34 clinic staff category and 20 facility managers. Details of the in-depth and key informant interviews participants were described elsewhere [28, 36].

In the subsequent results, we present the quantitative results under the predetermined themes while qualitative results are under the subthemes shown in Table 5.4.

Table 5. 4: Predetermined themes and subthemes

Predetermined themes	Sub-themes
1. Willingness of HIV-positive pregnant women to start ART	a) Giving HIV-positive women counseling and time to think about starting ART b) Desire to have an HIV-negative baby
2. Uptake of Option B+ ART	a) Adequate counseling
3. Readiness to take Option B+ ART	a) More time and information
4. Motivation to take Option B+ ART	a) Desire to remain healthy and deliver an HIV-negative baby a) Perceived effectiveness of Option B+ ART b) Benefits of Option B+ ART to HIV-negative spouses
5. Refusal and delay to start taking Option B+ ART	a) Doubt of HIV-positive result b) Fear to take ART c) Duration of ART
6. Early adherence to Option B+ ART	a) Disclosure of HIV-positive status b) Participation in health education talks and counseling c) Desire to remain healthy and deliver an HIV-negative baby d) Busy schedule e) ART side effects

Prescription of ART by health providers

At enrolment into the study, 27.2% (138/507) of women had received ART prescription within 4 weeks, increasing to 91.3% (463/507) at the month-2 interview. Prescription of ART by month-2 was significantly lower in Masaka RRH (77.7%, 143/184, $p < 0.001$) than Luwero HC IV (98.2%, 108/110) and Mityana GH (99.5%, 212/213).

Willingness of HIV-positive pregnant women to start ART

Women who had not been prescribed ART at month 2 ($n=44$) were asked if they were willing to be initiated on ART using the quantitative tool. Of these, 39 (88.6%) were willing to be started on ART, four (9.1%) were not willing, and one participant (2.3%) had missing data. Reasons for not having been prescribed ART among those who wished to start included being told by health workers to go and think about it (71.8%, 28/39), not ready to start immediately after the HIV-positive test (20.5%, 8/39), lack of ART at the previous ANC facility (2.6%, 1/39), wanted to come with spouse (2.6%, 1/39), and being uninformed of the presence of Option B+ approach (2.6%, 1/39).

Giving HIV-positive pregnant women counseling and time to think about starting ART

Similar to the quantitative results, many key informant and in-depth interview participants said that most HIV-positive gravid females were counseled and given time to think about starting lifelong ART. Key informants envisioned that counseling and giving HIV-positive expectant females time to think about Option B+ before prescription of ART could enhance acceptability and uptake of, and adherence to, Option B+ ART and retention in HIV care.

“When a woman tests HIV-positive, we ask her to decide basing on the counseling she has received. If she says that she’s not ready to start ART we allow her time to think and come back when ready.” (Health provider, Hospital)

Congruently, many in-depth interview participants indicated that they were willing to initiate ART on the same day they tested HIV-positive but the health providers told them to come back later after internalizing issues around lifelong ART.

“The health workers first found me with the virus (HIV-positive), they told me to come back and get the medicines [ART] on another day. Even though I wanted it to be given to me on

that very day they tested me, I had to come back later after thinking about it well.” (IDI Participant, Mityana GH)

Desire to have an HIV-negative baby

From the in-depth interviews, most participants indicated that they were willing to start on ART the same day they were found to be HIV-positive so as to deliver an HIV-negative baby. Desire for an HIV-negative baby as the main reason for preference of same day ART initiation was also mentioned by key informant interview participants.

“After testing HIV-positive, I was willing to start ART immediately but they [health workers] told me to go and think about it, then come back when ready to start on ART. I did not refuse to start immediately, because I was pregnant and I wanted to deliver a healthy [HIV-negative] baby.” (IDI Participant, Masaka RRH)

“The reason why they [women] are willing to test for HIV and start on Option B+ is because they are pregnant and want to prevent their babies from getting HIV infected.” (Health provider, HC III)

The quantitative results showed that three of the four women who were not willing to start ART were from Masaka RRH while the fourth was from Luwero HC IV. Fear of taking ART, being depressed due to the HIV-positive status, and lack of a place for hiding ART from family members were the key reasons for not willing to start ART.

Uptake of Option B+ ART

At two months follow up, the majority of the women had been prescribed ART and 93.3% (432/463) had started swallowing the medication (Table 5.5). Uptake of ART was higher in Masaka RRH and Mityana GH (95.8%) but lower in Luwero HC IV (85.2%). Most women started swallowing ART on the same day of prescription, (370/432; 85.7%), some started swallowing after 1-7 days, 52/432 (12.0%), and 10 (2.3%) started after one week.

Table 5. 5: Enrolment into the study (N=507), ART prescription (n=463) and uptake of Option B+ (n=432) by health facility

Health Facility	Number enrolled	ART prescription/ initiation (n, %)	Uptake of ART (Prescription and swallowing) [n, %]
Masaka RRH	184	143 (77.7)	137 (95.8)
Mityana GH	213	212 (99.5)	203 (95.8)
Luwero HC IV	110	108 (98.2)	92 (85.2)
Total	507	463 (91.3)	432 (93.3)

Adequate counseling

The qualitative component revealed that most key informants said that if the HIV-positive gravid females were appropriately counselled, they would start swallowing ART on the same prescription day.

“Most of them [women] start swallowing ART on the same day of prescription once they are well counseled. The few who refuse to start on ART do so later after on-going counselling.” (Health provider, HC III)

Consistently, in-depth interviews s indicated that most women began swallowing their ART on the same day it was prescribed after being tested and counseled by health providers.

“They [health providers] gave me medicines [ART] on the very day I tested HIV-positive. I was well counseled and told to choose a particular time when to swallow those medicines at night. I decided to swallow at 9.00pm and I started immediately on that very day.” (IDI Participant, Katikamu HC III)

“I received good [meaning adequate] counseling from the health providers and I accepted to start on the medication [ART] there and then.” (IDI Participant, Mityana GH)

Readiness to take Option B+ ART

Women who started swallowing ART by two months' follow-up (n=432) were requested to state their readiness to initiate ART at the time of prescription. Among women with data on this question, majority (82.9%, 310/374) were ready to

immediately start, but 12.6% (47) wanted to delay while 4.6% (17) were not ready at all. Readiness to start swallowing ART immediately varied by health facility, Mityana GH (88.2%) and Masaka RRH (85.6%), but lower in Luwero HC IV (67.1%). Women were further asked to give reasons for not being ready to start ART at the time it was prescribed. Desire for more time (53.1%, 34/64), lack of sufficient information on Option B+ ART (23.4%, 15/64) and desire to repeat (confirmatory) HIV tests (9.4%, 6/64) were the most commonly mentioned hindrances to start taking ART. Other reasons cited are shown in Table 5.6.

Table 5. 6: Reasons for not being ready to start ART at the time of prescription (n=64)

Reason	n (%)
Needed more time think about starting Option B+	34 (53.1)
Needed more information on Option B+	15 (23.4)
Wanted to do a repeat/confirmatory HIV test	6 (9.4)
Wanted to first acquire a watch to set time for swallowing ART	2 (3.1)
Wanted to first recover from sickness	2 (3.1)
Lacked food	1 (1.6)
Discouraged by a friend	1 (1.6)
Wanted to deliver first	1 (1.6)
Feared the size of the tablets	1 (1.6)
Wanted to start after showing signs of HIV	1 (1.6)

More time and information

Similar to the quantitative findings, in-depth interview participants echoed the need for more time and information before prescription of ART. This was envisioned to enable one to understand how to take ART.

“Health workers should first give us enough time and information before prescribing ART. If one is given the medicines [ART] before he/she has understood well all the necessary dos

and don'ts, one may end up taking it poorly or not taking ART at all." (IDI Participant, Mityana GH)

"That time I wasn't given enough information, because the health worker didn't explain well. I didn't get information on how to swallow the medicines and care for myself." (IDI Participant, Masaka RRH)

Motivation to take Option B+ ART

The quantitative results showed that motivation to start taking Option B+ ART by women at all facilities was majorly for own health (92.3%, 334/362), and to protect their unborn babies (90.6%, 326/362) or spouses (7.5%, 27/362) from HIV infection. Additional reasons that were obtained through the quantitative interviews include; advise from health providers, falling sick frequently, desire to live longer, fear of symptoms of HIV disease to be noticed and encouragement from spouses.

Desire to remain healthy and deliver an HIV-negative baby

Similar to the quantitative results, in-depth interviews revealed the desire to stay healthy and have an HIV-negative baby by women as a motivation to start Option B+ ART. Participants indicated that they needed to be healthy to continue working and look after their families. Most participants felt that when women are given adequate counseling and told the benefits of Option B+ ART, with the majority accepting ART.

"I wanted to save my life, remain healthy so that I can look after my family and deliver a healthy [HIV-negative] child too." (IDI Participant, Masaka RRH)

Key informant interview participants also alluded to desire for an HIV-negative baby as a motivation to take Option B+ ART.

"When these mothers are tested and they are found to be HIV-positive, they are advised to start on the medicines [ART]. Most women accept to take the medicines [ART] because they want to give birth to an HIV-negative child." (Health provider, HC IV)

Perceived effectiveness of Option B+ ART

All in-depth interview participants who were good ART adherers emphasized that if ART is taken well, they make one healthy and the baby is born HIV-negative. This was attributed to the effectiveness of Option B+ ART in comparison to the strategies before the Option B+ era and motivated them to take the ART.

“The good thing I see in this one they brought (meaning Option B+), is that it seems better than the old one which came first [Option A] because most of the time, when women deliver, their children don’t have the sickness (meaning HIV-negative babies), unlike in the past, some could deliver, and when you test, they could find the babies infected with the virus.” (IDI Participant, Mityana GH)

Furthermore, good ART adherers illustrated the experience of women that once on ART, one lives longer than those who were not taking ART. It was noted that this enables HIV-positive women to care for their children for a long time.

“Medicines [meaning ART] help us to live longer and look after our children for a number of years” (IDI Participant, Katikamu HC III)

Benefits of Option B+ ART to HIV-negative spouses

Most in-depth interviews revealed that participants were either not aware of the benefits of the Option B+ ART to their spouses or were only interested in the benefits for the woman’s health and that of her baby.

“They [health providers] told me that if I concentrate on taking the ART, the baby will not be infected with HIV and I will remain health. I was not told anything in regards to the benefits of ART to my spouse.” (IDI Participant, Mityana GH)

Refusal and delay to start taking Option B+ ART

Quantitative results revealed that thirty-one participants who received a prescription and ART had not yet started taking their ART by two months of the study. Reasons cited were; not ready/ prepared (14), fear to take ART for life (9), preference for local herbs due to fear of ART tablets (3), wanting to start taking after giving birth (3), and doubting the HIV-positive result (2) and wanting to have a repeat (confirmatory) HIV test.

Both providers and women alluded to similar reasons during qualitative interviews as per the sub-themes below.

Doubt of HIV-positive results

Some women who delayed to start taking ART indeed said that if they are given a positive HIV result for the first time, they would go to other health facilities to repeat

the test. The women said they would start taking ART after getting a confirmatory HIV-positive test.

“When I got the first pregnancy, I was told that I was HIV-positive. However, I never believed, but took Septrin tablets only. When I got the second pregnancy, I had not yet started on the big tablets [ART]; I tested for HIV again wanting to prove whether I was truly positive. The test gave the same results [HIV-positive]. I had nothing to do but to start taking ART.” (IDI Participant, Masaka RRH)

Likewise, key informant interview participants indicated that some women doubt positive HIV results and request for repeat tests.

“Some women refuse, ‘am not HIV-positive!’ If we test a woman and she doubts the results we have given her, we repeat the test or refer her to another Health facility ‘X’ - they believe in it so much. So, we refer them there and wait for the results.” (Health provider, HC IV)

Fear to take ART

Among women who participated in in-depth interviews, fear to take ART was identified as a barrier to start ART. Women expressed a number of fears like taking ART for life, being seen by the spouse, and possible side effects.

“I delayed to start the ART because I was fearing. I feared to swallow it all the time and I kept thinking of the medicines [ART] all the time! But now am no longer thinking like that.” (IDI Participant, Masaka RRH)

“I did not start immediately because I had fear, I had to think for some time, like a number of days. I first feared, because people scared us that, the tablet is very big and things like that.” (IDI Participant, Masaka RRH)

“At first I feared to start swallowing the ART because I did not want the man [spouse] to see me taking medicines. He had told me that, if they test you and you are found with the HIV virus, we will separate [meaning divorce].” (IDI Participant, Mityana GH)

A few women had a misconception that some people can even die faster if they start swallowing ART. The community was said to be the source of such misinformation.

“People in the village (those who were swallowing ART), told us that there is that new ART (Option B+ ART) which kills people very fast- some people come when they are sick [have advanced HIV] and they are given what kills fast.” (IDI Participant, Ssunga HC III)

Duration of ART

A number of women indicated that they were scared of taking ART for the rest of their lives. They went ahead to compare taking ART to other short course medicines such as anti-malaria medicines, which take only a few days.

“I was worried, because I didn’t know how to swallow the daily medicines [ART] for life. I am used to short treatment: when I am sick of malaria, I swallow two tablets and I know that I am now healed, but I thought of the daily medicines [ART]...will I manage, I was worried!” (IDI Participant, Katikamu HC III)

Early adherence to Option B+ ART

Adherence was assessed on 410 participants who had complete quantitative data at the two- month follow up. Just over three quarters (76.8%, 315/410) of study participants had optimal ART adherence. Optimal adherence was more common among women who were ready to immediately start ART at time of prescription 83.2% (258/310), and lower for women who wished to delay the start of ART 64.1% (25/39), and lowest if a woman did not want to ever start, 17.6% (3/17). Table 5.7 shows the reasons given for non-adherence. Most common reasons from the quantitative interviews included having travelled far away from the health facilities (24.2%, 23/95), side effects of ART (16.8%, 16/95), running out of ART (14.7%, 14/95), and forgetting to take ART (12.6%, 12/95).

Table 5. 7: Reasons for non-adherence to Option B+ ART (n=95)

Reason	n (%)
Travelled far and failed to pick ART	23 (24.2)
Side effects of ART	16 (16.8)
Ran out of ART	14 (14.7)
Forgot to swallow ART	12 (12.6)
Lacked food to eat before swallowing ART	06 (6.3)
Non-disclosure of HIV status to partner	06 (6.3)
Had no money for transport to pick ART	05 (5.3)

Doubt of HIV-positive status	04 (4.2)
Too sick to pick ART	04 (4.2)
Feared the tablets due the big size	03 (3.2)
Lost the bag which contained the ART	01 (1.1)
<u>Was on many other medicines</u>	<u>01 (1.1)</u>

Table 5.8 shows factors associated with optimal early adherence to Option B+ ART. Prevalence ratios are indicated, and no interactions were found among factors analysed. Optimal ART adherence was similar among women at Mityana GH and Masaka RRH, which were significantly higher than at Luwero HC-IV. Other factors associated with optimal adherence were readiness to immediately start and disclosure of HIV status to anyone (Table 5.8).

Table 5. 8: Factors associated with early adherence to Option B+ ART (n= 410)

Factors		Unadjusted PR	95%CI	Adjusted PR**	95%CI
Health facility					
	Masaka RHH	1.66	1.30, 2.12	1.33	1.04, 1.69
	Mityana GH	1.86	1.48, 2.35	1.44	1.14, 1.81
	Luwero HCIV	1	1	1	Referent
Disclosure of HIV status to anyone					
	Yes	1.51	1.22, 1.87	1.24	1.04, 1.48
	No	1	1	1	Referent
Motivation for starting ART: Protect baby					
	Yes	1.58	1.14, 2.19		
	No	1	1		Referent
Motivation for starting ART: Protect self					
	Yes	1.90	1.23, 2.92		
	No	1	1		Referent
Readiness to start ART					
	Immediately	1.67	1.27, 2.17	3.22	1.15, 8.96
	Later/Not at all	14.73	1	1	Referent

Note**: Adjusted for health facility, HIV disclosure status, motivation to start ART and readiness to start ART.

Disclosure of HIV-positive status

In the qualitative interviews, disclosure of HIV-positive status was mentioned both in in-depth and key informant interviews as a facilitator of optimal adherence. Women who disclose their HIV-positive status to their partners or a close relative get reinforced to continue taking their ART. However, those who don't disclose their status end up hiding their ART for fear of being seen by their spouses.

“He [spouse] has helped me a lot, it's very important to disclose. Those who didn't disclose have faced problems; they hide the medicines [ART] so that the spouse cannot see them and they end up missing some doses.” (IDI Participant, Luwero HC IV)

Participation in health education and counseling

In-depth interview participants who were given health education and satisfactory counseling stated that this helped them to start and remain adherent to the ART.

“The health workers first counseled me. I was told to start the medicines [ART] and from then up to today I have never missed. They [health workers] told me to take it [ART] on time without missing, I started swallowing without missing, and even I swallow at the exact hour/time. I have never missed even a single day.” (IDI Participant, Masaka RRH)

On the other hand, lack of health education and counseling were highlighted as barriers to starting and remaining adherent to Option B+ ART. Some of the women who had suboptimal ART adherence attributed it to having not attended the pre-ART health education talks and counseling sessions.

“I used to reach when they had already given health education to other women. Therefore, I was not provided with any pre-ART education and orientation sessions before I started taking ART.” (IDI Participant, Kyanamukaka HC IV)

“Mmhmmh...they just gave me the tin [meaning the tin containing ART] and I took it home to swallow. I almost I did not get any health education at all. I shouldn't lie to you.” (IDI Participant, Mityana GH)

Equally, most key informant interview participants stated that good counseling could result in adherence to clinic appointments and ART.

“For me, I think that if the counseling has been good to the extent that the mother gets to know the benefits of option B+, I believe, she can adhere to her appointments and even take her medicines well for reasons that she wants an HIV-negative child” (Health Provider, Luwero HC IV)

Desire to remain healthy and deliver an HIV-negative baby

Most in-depth interview participants said that they didn’t want to miss any ART doses so as to remain healthy and give birth to HIV-negative babies. They anticipated that being adherent to the ART would result in a rise in their CD4 count and thus remain healthy.

“I can’t miss any of my doses because I want my “asikaris” [meaning CD4 cells] to go higher all the time to remain healthy, so that am able to deliver a healthy child [meaning HIV-negative].” (IDI Participant, Mityana GH)

Busy schedule

During the in-depth interviews, some participants attributed suboptimal adherence to ART to busy schedules. A number of women had many chores to accomplish which resulted in their forgetting to swallow ART

“At times you become too busy with many things like house work and digging. Time passes and that’s when you forget to swallow the medicines [ART].” (IDI Participant, Kyamukaka HC IV)

ART side effects

Side effects due to ART were commonly mentioned as being responsible for suboptimal adherence. In-depth interview participants mentioned varying side effects including dizziness, headache, drowsiness, nausea, vomiting and nightmares.

“At the start, I felt bad whenever I would swallow the ART. I was vomiting, all the time I would feel like vomiting, just like someone suffering from malaria.” (IDI Participant, Katikamu HC III)

5.5 Discussion

This study assessed uptake and early adherence to ART and associated factors among HIV-positive gravid and lactating mothers starting lifelong ART in Central Uganda. Results from this study show that majority (91.3%) of expectant HIV-positive women were prescribed ART immediately after they tested positive, as recommended by the MOH. Our finding is slightly lower than that of Uganda population-based HIV impact assessment (UPHIA)-2016/2017 where 95.3% of HIV-positive mothers who were 12 months post-delivery reported receiving ART. The slight difference might be ascribed to the fact that the UPHIA involved women who were on ART at the time of their first ANC and had delivered 12 months prior to the survey [48].

Most women who had not received a prescription in our study were willing to be started on ART, which indicates a missed opportunity for immediate ART initiation. Uptake of Option B+ ART (prescription and swallowing of ART) was nearly universal by two months of follow-up, which is very encouraging. Importantly, most women started taking their ART on the same day of prescription. However, prescription and uptake of ART varied by health facility which might be attributed to differences in practices such as assessing women for readiness to start ART, giving women time to get ready, providing adequate counseling, and ensuring that women understood the benefits of Option B+ ART. Whereas it is desirable to start ART immediately, women who are not ready to start treatment should be screened and provided with additional follow-up support. Further, the delay to start taking the medicines after prescription highlights the need to carefully track the immediate start and to support women who may encounter challenges in this early phase. This is congruent with recommendations by a trial conducted at 70 research sites in 15 countries within sub-Saharan Africa, Asia, and the Americas where one-third of asymptomatic HIV-positive pregnant and postpartum women did not initiate ART immediately for desire for more time to make a decision [49].

Initiation of Option B+ ART by health providers and actual taking in this study was higher than reported elsewhere [11, 12, 16]. The high level of ART uptake could be due to the wish to have HIV free infants as well as the women's own health status. For the barriers such as preference for local herbs, fear of ART side effects, among others reflect a need

for further education and support including counseling for reassurance and to reduce misinformation.

Early adherence was suboptimal (76.8 %), although uptake was very high and most women were ready to start Option B+ ART immediately and knew the reasons for taking ART. Such a low adherence level soon after ART initiation is worrying since women are expected to be more motivated to take their medicines regularly at this stage than later on in the PMTCT cascade [18, 50]. Attention to the prominent reasons for this, including non-disclosure of HIV-positive status, side effects of ART, and perception that the baby is safe post-delivery might be useful [28]. Ensuring that women are ready for Option B+ and HIV-positive status disclosure are factors that can be stressed to improve lifelong ART adherence. HIV-positive gravid women should not be hurried to start on Option B+ ART on the same day of HIV diagnosis but be sufficiently counseled and supported to ensure that they are ready for the lifelong ART. Facilities should have mechanisms such as use of peers to detect women who are ART non-adherent early enough so that they can be given targeted supportive adherence counseling [24]. These peers should be well-trained to acquire knowledge and skills necessary for detecting non-adherence. Adequate adherence results into viral suppression and subsequently less risk of MTCT of HIV [51] as endorsed in the UNAIDS concept of undetectable = untransmittable [52].

Most of the issues around ART prescription, swallowing and early adherence among HIV-positive gravid and lactating women that were identified in this study are critical and can be addressed by strengthening the existing strategies. Such strengthening would focus on provision of adequate general and targeted counseling, and social support and early tracking of women. Although some study eligible women declined to participate in the study, their baseline characteristics did not vary from those who participated except for the categories of casual worker and housewife under the variable "Occupation". Although some earlier studies found a positive association between occupation/employment and adherence [53], similar to our study, other studies reported no association between socio-demographic and economic variables and adherence to ART [54, 55]. Therefore, our study findings can be generalizable to women in settings similar to where the study was conducted such as regional referral hospitals, general hospitals and HC IIIs.

Implications for practice, public health and policy

Our study results have implications for practice, public health and policy. These mainly revolve around expectant females and lactating mothers, their close networks and health providers.

Understanding the benefits of lifelong ART, early ART initiation, optimal ART adherence, and HIV status disclosure could heighten uptake of and adherence to ART [56, 57]. Addressing barriers to non-adherence such as long distances to health facilities, fear of side effects, non-disclosure of HIV status to anyone, and perception that the baby is safe from HIV infection post-delivery is crucial [58, 59] and calls for more time and adequate information during PMTCT health education and counselling. Additionally, health workers should be cognizant of challenges women face with uptake and adherence, such as unwillingness and unreadiness to start lifelong ART, as well as stigma which deters disclosure of HIV-positive results, and should work to adequately counsel and support them.

Ministry of Health should institute appropriate pre-and in-service training, guidelines, supervision, and mentorship for health workers to enhance quality PMTCT counseling. Furthermore, inadequate counselling due to lack of time and health workers could be addressed through strategies such as task shifting using peers to address human resource gaps. Finally, women who are not ready for lifelong ART should be given time and support to accept newly diagnosed HIV-positive status before ART initiation.

5.6 Strengths and limitations

To our knowledge, this is among the first studies that has documented detailed day-to-day critical steps in the preparation and ART initiation such as prescription, uptake, readiness, motivation and early adherence of Option B+ medicines among pregnant women. The study used data from a prospective cohort of HIV-positive expectant females complemented with data from qualitative interviews. Use of the integrated mixed methods study approach facilitated greater understanding of issues around prescription, swallowing, and uptake of, and adherence to lifelong ART among expectant and lactating women. Unfortunately, uptake and adherence were assessed by self-report which could

have introduced social desirability bias. However, the two outcome variables were measured using a series of questions. In addition, previous studies used self-report while measuring uptake and adherence [22, 60, 61]. Our study had a limitation of recall bias since we used a 30-days recall method to assess adherence. Nevertheless, prior studies have used the same technique to measure ART adherence [61-63]. Using individual interviews might have resulted into social desirability bias but this was minimized by use of well-trained and experienced data collectors, establishing of rapport, use of probes, conducting regular debriefing sessions, and research team meetings [64].

5.7 Conclusions

Most women received ART prescription on the same day they were diagnosed HIV-positive. Uptake of Option B+ in the first two months after HIV counseling, testing and ART initiation among females seeking ANC service is high in this setting. However, early adherence to Option B+ ART remains suboptimal especially in the lower facility. Disclosure of HIV status and readiness to start ART at time of prescription, a reflection of quality of counseling are important determinants of optimal adherence. Women still require time to internalize or accept the newly learnt HIV status and to be provided with more information prior to starting Option B+ ART.

Acknowledgements

The authors appreciate the study participants and the respective in-charges of Masaka RRH, Mityana GH, Luwero HC IV, Kyanamukaka HC IV, and Ssunga and Katikamu HC IIIs for their sustained support given to us throughout the study period. Additionally, special thanks go to the district health office of Masaka, Mityana, and Luwero that provided us with the necessary support to conduct the study. We appreciate the research assistants who carried out data collection and transcription. Special thanks also go to Mr. Edward Were and Mr. Ronald Ssenyonga who supported us in data management and analysis.

Author Abbreviations

A.M.: Aggrey David Mukose

E.B.: Esther Buregyeya

F.M.: Fredrick Makumbi

R.W.: Rhoda K. Wanyenze

Author Contributions

Conceptualization: Aggrey David Mukose, Fredrick Makumbi, Esther Buregyeya, Joshua Musinguzi, Rhoda K. Wanyenze.

Formal analysis: Aggrey David Mukose, Hilde Bastiaens, Fredrick Makumbi, Rhoda K. Wanyenze.

Funding acquisition: Joshua Musinguzi, Rhoda K. Wanyenze.

Investigation: Aggrey David Mukose, Fredrick Makumbi, Esther Buregyeya, Joshua Musinguzi, Rhoda K. Wanyenze.

Methodology: Aggrey David Mukose, Fredrick Makumbi, Esther Buregyeya, Joshua Musinguzi, Rhoda K. Wanyenze.

Project administration: Rose Naigino.

Supervision: Hilde Bastiaens, Fredrick Makumbi, Jean-Pierre Van Geertruyden, Rhoda K. Wanyenze.

Validation: Aggrey David Mukose, Rhoda K. Wanyenze.

Visualization: Aggrey David Mukose, Hilde Bastiaens, Fredrick Makumbi.

Writing – original draft: Aggrey David Mukose.

Writing – review & editing: Aggrey David Mukose, Hilde Bastiaens, Fredrick Makumbi, Esther Buregyeya, Rose Naigino, Joshua Musinguzi, Jean-Pierre Van Geertruyden, Rhoda K. Wanyenze.

Competing interests: The authors have declared that no competing interests exist.

Funding: This study was funded by the Global Fund through the Ministry of Health-Uganda [Grant Number: UGD-708-G07-H]. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

1. UNAIDS. Fact Sheet 2015: Global Statistics. Geneva: 2015.
2. Cleland JG, Ndugwa RP, Zulu EM. Family planning in sub-Saharan Africa: progress or stagnation? Bulletin of the World Health Organization. 2011;89:137-43.
3. UNAIDS. Towards an HIV-free generation: Ending the vertical transmission of HIV. Brief. France: 2011.
4. WHO. PMTCT Strategic Vision 2010–2015: Preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals. Geneva, Switzerland: WHO, 2010.
5. UNAIDS. Global Plan Towards the Elimination of New HIV Infections among Children by 2015 and Keeping their Mothers Alive 2011-2015. 20 Avenue Appia CH-1211 Geneva 27, Switzerland: 2011.
6. UNAIDS. The Gap Report, 2014. 20 Avenue Appia CH-1211 Geneva 27, Switzerland 2014.
7. UNAIDS. 2015 Progress report on the Global Plan. 20 Avenue Appia 1211 Geneva 27, Switzerland: UNAIDS, 2015.
8. WHO. Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants Programmatic update 2012. 20 Avenue Appia, 1211 Geneva 27, Switzerland: 2012.
9. Godfrey E, editor PMTCT Implementation in Uganda: Option B Plus Experience 2013; Entebbe, Uganda 2013.
10. Okonji JA, Zeh C, Weidle PJ, Williamson J, Akoth B, Masaba RO, et al. CD4, viral load response, and adherence among antiretroviral-naïve breast-feeding women receiving triple antiretroviral prophylaxis for prevention of mother-to-child transmission of HIV in Kisumu, Kenya. Journal of acquired immune deficiency syndromes (1999). 2012;61(2):249-57.
11. Huang Z, Jin M, Zhou H, Dong Z, Zhang S, Han J, et al. The Uptake of Prevention of Mother-to-Child HIV Transmission Programs in China: A Systematic Review and Meta-Analysis. PloS one. 2015;10(8): e0135068.
12. Tudor Car L, Brusamento S, Elmoniry H, van Velthoven MH, Pape UJ, Welch V, et al. The uptake of integrated perinatal prevention of mother-to-child HIV transmission programs in low- and middle-income countries: a systematic review. PloS one. 2013;8(3): e56550.

13. Kohler PK, Okanda J, Kinuthia J, Mills LA, Olilo G, Odhiambo F, et al. Community-based evaluation of PMTCT uptake in Nyanza Province, Kenya. *PloS one*. 2014;9(10): e110110.
14. van Lettow M, Bedell R, Landes M, Gawa L, Gatto S, Mayuni I, et al. Uptake and outcomes of a prevention-of mother-to-child transmission (PMTCT) program in Zomba district, Malawi. *BMC public health*. 2011;11: 426.
15. Bannink-Mbazzi F, Lowicki-Zucca M, Ojom L, Kabasomi SV, Esiru G, Homsy J. High PMTCT program uptake and coverage of mothers, their partners, and babies in northern Uganda: achievements and lessons learned over 10 years of implementation (2002-2011). *Journal of acquired immune deficiency syndromes (1999)*. 2013;62(5): e138-45.
16. Price AJ, Kayange M, Zaba B, Chimbwandira FM, Jahn A, Chirwa Z, et al. Uptake of prevention of mother-to-child-transmission using Option B+ in northern rural Malawi: a retrospective cohort study. *Sexually transmitted infections*. 2014;90(4):309-14.
17. Kreitchmann R, Harris DR, Kakehasi F, Haberer JE, Cahn P, Losso M, et al. Antiretroviral adherence during pregnancy and postpartum in Latin America. *AIDS patient care and STDs*. 2012;26(8):486-95.
18. Mellins CA, Chu C, Malee K, Allison S, Smith R, Harris L, et al. Adherence to antiretroviral treatment among pregnant and postpartum HIV-infected women. *AIDS care*. 2008;20(8):958-68.
19. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. *Aids*. 2012;26(16):2039-52.
20. Nassali M, Nakanjako D, Kyabayinze D, Beyeza J, Okoth A, Mutyaba T. Access to HIV/AIDS care for mothers and children in sub-Saharan Africa: adherence to the postnatal PMTCT program. *AIDS care*. 2009;21(9):1124-31.
21. Ickovics JR, Wilson TE, Royce RA, Minkoff HL, Fernandez MI, Fox-Tierney R, et al. Prenatal and postpartum zidovudine adherence among pregnant women with HIV: results of a MEMS substudy from the Perinatal Guidelines Evaluation Project. *Journal of acquired immune deficiency syndromes*. 2002;30(3):311-5.
22. Ebuy H, Yebyo H, Alemayehu M. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, northern Ethiopia. *International journal of*

- infectious diseases: IJID : official publication of the International Society for Infectious Diseases. 2015;33:123-9.
23. Kamuyango AA, Hirschhorn LR, Wang W, Jansen P, Hoffman RM. One-year outcomes of women started on antiretroviral therapy during pregnancy before and after the implementation of Option B+ in Malawi: A retrospective chart review. *World journal of AIDS*. 2014;4(3):332-7.
 24. Billioux A, Nakigozi G, Newell K, Chang LW, Quinn TC, Gray RH, et al. Durable Suppression of HIV-1 after Virologic Monitoring-Based Antiretroviral Adherence Counseling in Rakai, Uganda. *PloS one*. 2015;10(5): e0127235.
 25. WHO. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection Recommendations for a Public Health Approach Second Edition 2016. 20 Avenue Appia, 1211 Geneva 27, Switzerland: WHO, 2016.
 26. UNAIDS. The AIDS epidemic can be ended by 2030 Geneva, Switzerland: 2016.
 27. WHO. End HIV/AIDS by 2030: Framework for action in the WHO African Region, 2016-2020. 2017.
 28. Buregyeya E, Naigino R, Mukose A, Makumbi F, Esiru G, Arinaitwe J, et al. Facilitators and barriers to uptake and adherence to lifelong antiretroviral therapy among HIV infected pregnant women in Uganda: a qualitative study. *BMC pregnancy and childbirth*. 2017;17(1):94.
 29. Naigino R, Makumbi F, Mukose A, Buregyeya E, Arinaitwe J, Musinguzi J, et al. HIV status disclosure and associated outcomes among pregnant women enrolled in antiretroviral therapy in Uganda: a mixed methods study. *Reproductive Health*. 2017;14(1):107.
 30. Doyle L, Brady A-M, Byrne G. An overview of mixed methods research—revisited. *Journal of research in nursing*. 2016;21(8):623-35.
 31. Maxwell JA, Mittapalli K. Realism as a stance for mixed methods research. *Handbook of mixed methods in social & behavioral research*. 2010:145-68.
 32. Shannon-Baker P. Making paradigms meaningful in mixed methods research. *Journal of Mixed Methods Research*. 2016;10(4):319-34.
 33. Creswell JW, Plano Clark VL. *Designing and Conducting Mixed Methods Research*. Thousand Oaks, CA: SAGE 2011.
 34. Creswell JW, Plano Clark VL, Gutmann ML, Hanson WE. Advanced mixed methods research designs. *Handbook of mixed methods in social and behavioral research*. 2003;209:240.

35. Creswell JW. Research Design: Qualitative, Quantitative and Mixed Approaches. Fourth ed. Markanich M, editor. California, USA: SAGE; 2014.
36. Mukose AD, Bastiaens H, Buregyeya E, Naigino R, Makumbi F, Musinguzi J, et al. Health Provider Perspectives of Health Facility Preparedness and Organization in Implementation of Option B+ among Pregnant and Lactating Women in Central Uganda: A Qualitative Study. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2019;18:2325958219833930.
37. MOH. Consolidated Guidelines for Prevention and Treatment of HIV in Uganda. In: ACP, editor. Kampala, Uganda: MOH; 2016. p. 154.
38. Turan JM, Nyblade L. HIV-related Stigma as a Barrier to Achievement of Global PMTCT and Maternal Health Goals: A Review of the Evidence. *AIDS and behavior*. 2013;17(7):2528-39.
39. Ahmed S, Kim MH, Abrams EJ. Risks and benefits of lifelong antiretroviral treatment for pregnant and breastfeeding women: a review of the evidence for the Option B+ approach. *Current Opinion in HIV and AIDS*. 2013;8(5):474-89.
40. Aizire J, G Fowler M, M Coovadia H. Operational issues and barriers to implementation of prevention of mother-to-child transmission of HIV (PMTCT) interventions in Sub-Saharan Africa. *Current HIV Research*. 2013;11(2):144-59.
41. Mannheimer S, Friedland G, Matts J, Child C, Chesney M. The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2002;34(8):1115-21.
42. Cheek J. An untold story? Doing funded qualitative research: Sage Publications; 2000.
43. Guest G, Bunce A, Johnson L. How many interviews are enough? An experiment with data saturation and variability. *Field methods*. 2006;18(1):59-82.
44. Barros AJ, Hirakata VN. Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. *BMC medical research methodology*. 2003;3(1):21.
45. Bradley EH, Curry LA, Devers KJ. Qualitative Data Analysis for Health Services Research: Developing Taxonomy, Themes, and Theory. *Health Services Research*. 2007;42(4):1758-72.
46. Crabtree BFM, William L. Doing qualitative research. 2nd ed. Thousand Oaks, Calif. ; London: SAGE; 1999.

47. Uganda National Council for Science and Technology (UNCST). 2014. National Guidelines for Research involving Humans as Research Participants. , (2014).
48. MoH. Uganda Population-Based HIV Impact Assessment (UPHIA) 2016–2017. MOH Uganda; 2017.
49. Stranix-Chibanda L, Brummel S, Pilotto J, Mutambanengwe M, Chanaiwa V, Mhembere T, et al. Slow Acceptance of Universal Antiretroviral Therapy (ART) Among Mothers Enrolled in IMPAACT PROMISE Studies Across the Globe. *AIDS and behavior*. 2019;23(9):2522-31.
50. Okawa S, Chirwa M, Ishikawa N, Kapyata H, Msiska CY, Syakantu G, et al. Longitudinal adherence to antiretroviral drugs for preventing mother-to-child transmission of HIV in Zambia. *BMC pregnancy and childbirth*. 2015;15:258.
51. Hosseinipour M, Nelson JAE, Trapence C, Rutstein SE, Kasende F, Kayoyo V, et al. Viral Suppression and HIV Drug Resistance at 6 Months Among Women in Malawi's Option B+ Program: Results From the PURE Malawi Study. *Journal of acquired immune deficiency syndromes (1999)*. 2017;75 Suppl 2:S149-s55.
52. UNAIDS. Undetectable= Untransmittable. Public health and HIV Viral Load Suppression. 2018.
53. Nachega JB, Uthman OA, Peltzer K, Richardson LA, Mills EJ, Amekudzi K, et al. Association between antiretroviral therapy adherence and employment status: systematic review and meta-analysis. *Bulletin of the World Health Organization*. 2014;93:29-41.
54. Peltzer K, Pengpid S. Socioeconomic factors in adherence to HIV therapy in low-and middle-income countries. *Journal of health, population, and nutrition*. 2013;31(2):150.
55. Azmach NN, Hamza TA, Husen AA. Socioeconomic and demographic statuses as determinants of adherence to antiretroviral treatment in HIV infected patients: A systematic review of the literature. *Current HIV research*. 2019;17(3):161-72.
56. Lumbantoruan C, Kermode M, Giyai A, Ang A, Kelahe M. Understanding women's uptake and adherence in Option B+ for prevention of mother-to-child HIV transmission in Papua, Indonesia: A qualitative study. *PloS one*. 2018;13(6):e0198329.
57. Ross AJ, Aung M, Campbell L, Ogunbanjo GA. Factors that positively influence adherence to antiretroviral therapy by HIV and/or AIDS patients and their caregivers. *African Journal of Primary Health Care & Family Medicine*. 2011;3(1).

58. Wasti SP, Simkhada P, Randall J, Freeman JV, van Teijlingen E. Factors Influencing Adherence to Antiretroviral Treatment in Nepal: A Mixed-Methods Study. *PloS one*. 2012;7(5):e35547.
59. Curioso WH, Kepka D, Cabello R, Segura P, Kurth AE. Understanding the facilitators and barriers of antiretroviral adherence in Peru: a qualitative study. *BMC public health*. 2010;10(1):1-8.
60. Tsegaye D, Deribe L, Wodajo S. Levels of adherence and factors associated with adherence to option B+ prevention of mother-to-child transmission among pregnant and lactating mothers in selected government health facilities of South Wollo Zone, Amhara Region, northeast Ethiopia, 2016. *Epidemiology and Health*. 2016;38:e2016043.
61. Phillips T, Cois A, Remien RH, Mellins CA, McIntyre JA, Petro G, et al. Self-Reported Side Effects and Adherence to Antiretroviral Therapy in HIV-Infected Pregnant Women under Option B+: A Prospective Study. *PloS one*. 2016;11(10):e0163079.
62. Psaros C, Smit JA, Mosery N, Bennett K, Coleman JN, Bangsberg DR, et al. PMTCT Adherence in Pregnant South African Women: The Role of Depression, Social Support, Stigma, and Structural Barriers to Care. *Annals of Behavioral Medicine*. 2020;54(9):626-36.
63. Byakika-Tusiime J, Crane J, Oyugi JH, Ragland K, Kawuma A, Musoke P, et al. Longitudinal antiretroviral adherence in HIV+ Ugandan parents and their children initiating HAART in the MTCT-Plus family treatment model: role of depression in declining adherence over time. *AIDS and behavior*. 2009;13(1):82-91.
64. Bergen N, Labonté R. "Everything is perfect, and we have no problems": detecting and limiting social desirability bias in qualitative research. *Qualitative health research*. 2020;30(5):783-92.

CHAPTER 6:

Suboptimal Adherence to Lifelong ART, and its predictors among HIV- positive pregnant and breastfeeding women in three districts of Central Uganda: a repeated measures analysis

Aggrey David Mukose^{1, 2*}, Jean-Pierre Van Geertruyden², Fredrick Makumbi¹, Esther Buregyeya³, Rose Naigino⁴, Joshua Musinguzi⁵, and Rhoda K. Wanyenze³.

¹ Department of Epidemiology and Biostatistics, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda

² Global Health Institute, Department of Epidemiology and Social Medicine, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

³ Department of Disease Control and Environmental Health, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda

⁴ Makerere University School of Public Health, Kampala, Uganda

⁵ Ministry of Health, Kampala, Uganda

*Corresponding Author: Aggrey David Mukose; E-mail: amukose@musph.ac.ug

Tel: +256772427800; Present address: Department of Epidemiology and Biostatistics, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda.

Submitted.

6.1 Abstract

Background: Although lifelong ART among HIV-positive pregnant and breastfeeding women has been scaled-up for the elimination of mother-to-child transmission of HIV, few studies have examined suboptimal adherence to lifelong ART levels using repeated measures analysis.

Methods: A prospective cohort study was conducted among 385 HIV- positive pregnant and breastfeeding women who were followed up for 18 months after enrolment at three public health facilities in Central Uganda. Repeated measures using mixed effects logistic model was used to determine the predictors of suboptimal adherence to lifelong ART using odds ratio as a measure of association and a corresponding 95% confidence interval.

Results: The 30-day suboptimal adherence levels were highest at month 2 (23.2%) but varied between 12%-13.9% at month 4, 6, 10, 14, and 18 post study enrolment visits. In the adjusted analysis, disclosure of HIV-positive status to anyone, AOR = 0.50 (0.30 – 0.84), spousal support, AOR = 0.43 (0.28 – 0.67), and motivation from health providers to start lifelong ART, AOR = 0.19 (0.07 – 0.51) were associated with lower odds of suboptimal adherence. Unreadiness to start taking ART, AOR = 2.38 (1.26 – 4.50), HIV-related stigma, AOR =1.70 (1.05 – 2.75), and receipt of HIV care from Luwero HC IV, AOR=5.36 (2.62 - 10.98) were associated with higher odds of suboptimal adherence.

Conclusion: Disclosure of HIV-positive status, spousal support, and motivation from health providers to start ART attenuate suboptimal adherence while HIV related-stigma and unreadiness to start taking ART immediately increase the risk of suboptimal adherence.

6.2 Introduction

Globally, 38.4 million people were living with HIV while 28.7 million people were accessing antiretroviral therapy (ART) in 2021. In the same year, 81% of pregnant women living with HIV had access to ART to prevent mother-to-child transmission (MTCT) of HIV. Of these, 90% were residing in eastern and southern Africa [1].

In Uganda, the number of HIV-positive pregnant and breastfeeding women initiated on ART for the elimination of MTCT (e-MTCT) of HIV has been drastically increasing. The number increased from 52% in 2011 to 92% in 2020, and to 96% in 2021[2, 3]. Consequently, the number of new paediatric HIV infections has been declining [4].

Uganda has been implementing lifelong ART for prevention of mother-to-child transmission (PMTCT) of HIV since September 2012 [5] and great achievements have been registered. However, a number of bottlenecks such as HIV-related stigma, non-retention in care, and suboptimal adherence to lifelong ART persist [4, 6]. These challenges hinder the achievement of e-MTCT and yet PMTCT of HIV remains pivotal for the achievement of an AIDS-free generation by 2030.

Suboptimal adherence to lifelong ART refers to taking <95% of the dispensed ART, whereas optimal adherence means taking $\geq 95\%$ of the dispensed ART [7-9]. Achieving and sustaining optimal adherence are essential in ensuring the success of ART [10]. Whilst suboptimal adherence to lifelong ART among pregnant and breastfeeding women increases the risk of; HIV transmission to the infant and or spouse as a consequence of un-suppressed viral load, drug-resistance HIV strains due to episodic ART exposure, limited treatment efficacy, resulting in disease progression as well as reducing future treatment options for the mother [11-13].

Studies have reported variations in adherence levels during pregnancy and post-delivery. A systematic review and meta-analysis conducted to assess adherence to ART during pregnancy and postpartum in low- and middle-income countries found that the pooled proportion of women with adequate adherence levels was higher during antepartum (75.7%) than during postpartum (53.0%). However, this review included studies from the pre-lifelong ART era [14]. Similarly, a 2-arm cluster randomized controlled trial conducted

in Zimbabwe found that suboptimal adherence among women who were initiated on ART during pregnancy increased over the 14 months follow-up. The suboptimal adherence increased from 18.9% at one month post ART initiation to 42.3% at one year after ART commencement [15].

Adeniyi et al (2018) found ART suboptimal adherence of 31% among pregnant women in the Eastern Cape, South Africa [16]. While, a nationwide study conducted in Burkina Faso in 2019-2020 reported a suboptimal adherence to ART of 13.4% among pregnant and breastfeeding women [17]. In Ethiopia, a systematic review and meta-analysis showed an overall pooled estimate of suboptimal adherence of 15.8% among pregnant and lactating women. In the same study, the pooled suboptimal adherence level was 14.4% among pregnant women, and 18.1% among both pregnant and postpartum women [18].

Comparably, studies in Uganda have shown different levels of suboptimal adherence to lifelong ART among pregnant and breastfeeding women. In a prospective study conducted in western Uganda, suboptimal adherence levels varied in pregnancy and postpartum periods. Median adherence was reported to be stable during pregnancy, with 51.3% of the study participants having optimal adherence [19]. Moreover, full adherence was found to be 51%, 19%, and 20.5% at 6, 12, and 18 months postpartum respectively though the sample sizes were small [20]. Likewise, a cohort study conducted in urban South Africa and rural Uganda found median adherence to ART for women during pregnancy, postpartum and non-pregnancy-related periods at 94%, 90%, 90% respectively in the Uganda cohort [21].

Mothers who sustain optimal lifelong ART adherence during pregnancy, delivery and breastfeeding have a significantly reduced risk of HIV transmission to their children. Addressing the factors responsible for suboptimal adherence will contribute to the achievement of viral suppression. This will result in better health for the women, reduction of MTCT of HIV and HIV transmission to an HIV-negative spouse which contributes to ending HIV as a public health threat by 2030 [22], and the achievement of target 3.3 of sustainable development goal (SDG) 3[23].

Therefore, this study was conducted to follow up pregnant and breastfeeding women in three districts of Central Uganda so as to determine levels of suboptimal adherence, and its predictors using repeated measures analysis. Many of the previous studies assessing adherence to lifelong ART among pregnant and breastfeeding women have largely been cross-sectional, retrospective records reviews or focus on overall mean, and median adherence levels. Given the weaknesses of the previous studies, our current study used a unique aspect, where suboptimal adherence was prospectively determined in a cohort of HIV- positive pregnant and lactating women followed up for 18 months. The study design and use of repeated measures enabled the researchers to prospectively assess changes both between and within individual women's behaviors during and after pregnancy in three different settings in Central Uganda. Finally, use of repeated measures helps in assessment of the effects of the covariates on suboptimal adherence over the study period. Understanding the predictors of suboptimal adherence over time will inform the development of targeted interventions to minimize or eliminate suboptimal adherence to lifelong ART among pregnant and breastfeeding women so as to improve their health and achieve e-MTCT of HIV.

6.3 Methods

Study sites

This study was conducted in Central Uganda in the districts of Masaka, Mityana and Luwero. These districts were purposively selected because they were among the 'Central 1' districts with the highest HIV prevalence [24], and were prioritized for the phase 1 scale-up of life-long ART among pregnant and post-partum HIV-positive women in 2012. Three health facilities were purposively included in the study namely; Masaka Regional Referral Hospital (RRH), Mityana General Hospital (GH), and Luwero Health Centre (HC) IV. These were the high HIV-positive patient volume [25] health facilities in each of the selected districts.

Study population

HIV-positive pregnant women aged 15-49 years, who started on lifelong ART within four weeks of ART initiation or who were ART naïve were eligible for study enrolment.

Pregnancy was determined either through self-report or a pregnancy test by health workers attending to the antenatal care (ANC) women at the health facility. All eligible women were enrolled consecutively at each study site between October 2013 and August 2014, and followed up until March 2016. The enrolment at each study site was done consecutively until the desired sample size was achieved.

Data collection

Data were prospectively collected over a period of 18 months on enrolled women to primarily determine uptake of lifelong ART, adherence to lifelong ART, and retention in HIV care. Serial quantitative surveys were conducted at baseline/enrollment; every two months post study enrolment up to month 6, and then every four months up to month 18 were conducted (Month 0, 2, 4, 6, 10, 14, and 18) making a total of seven interviews. Study follow-up interviews were aligned with the scheduled clinic visits as much as possible to minimize inconvenience to the women.

A well-trained and experienced female research assistant was stationed at each study health facility to collect the data through face-to-face structured interviews using a tool with both pre-coded and open-ended questions at every study visit. ART adherence was assessed through self-report by asking for the number of ART doses missed in the 30 days preceding the study interview.

Study variables

For this study's purpose, suboptimal lifelong ART adherence was the outcome variable, defined as taking less than 95% of the once-a-day ART prescription (<29 doses) in the 30 days preceding each follow-up interview [7-9].

The independent variables included; age in completed years categorized into two groups of 15-24 and ≥ 25 years, marital status classified as married, never married, or widowed/separated to capture their marital status Highest level of education completed grouped as either no formal education, primary, secondary or tertiary level education.

Study participants were asked and assessed for their readiness to start taking (swallowing) their lifelong ART medicines immediately or delay at the time they started taking their ART. The responses were recorded as immediately or later.

Other variables included; disclosure of HIV-positive status to anyone, knowledge of partner's HIV status, belonging to a social group, disclosure of being on lifelong ART to anyone, and experiencing HIV related stigma because of one's HIV status which were recorded as yes or no. Spousal support was measured by asking the participants, who had spouses if the spouse gave the participant transport money to attend the ART clinic, or reminded her to take ART or escorted the participant to pick her ART. Responses were recorded as yes or no. To measure motivation to start ART, participants were asked what motivated them to start taking ART. The responses were; to protect my baby, to protect myself, to protect my spouse and the health provider advised me. These were categorized as yes and no. Follow-period was defined as the month at which follow-up visits after study enrolment were scheduled to take place, which was recorded as month 2, 4, 6, 10, 14, and 18.

Statistical analysis

Data are accrued from a prospective cohort study of 507 HIV+ pregnant women who were enrolled to determine uptake of lifelong ART. This analysis included all the 410 women, who were prescribed and had started swallowing ART by the first follow-up visit at month 2. However, only women who had at least three follow-up visits (385) were included in the repeated measures analysis. The women who had fewer than three follow-up visits were excluded from the repeated measures analysis because less than three observations for a given woman do not fit a linear trend [26, 27].

The median and interquartile range were computed for the age of the women. Frequencies and percentages were computed and presented for categorical variables.

The mixed effects logistic model was used to assess the predictors of suboptimal adherence to lifelong ART using the backward elimination method by removing the most insignificant variables. The mixed effects model was chosen because it enables the modeling of correlated repeated measures data and time-varying covariates. The

confounding and time interactions among covariates were examined. The different covariance structures were compared to determine the structure that best fits the model using the Bayesian Information Criterion (BIC) [28, 29]. The model that included a covariance structure with the lowest BIC was chosen. Stata version 17 was used in the analysis.

Ethical approval

Ethical clearance was obtained from the Institutional Review Board (IRB) at the Makerere University School of Public Health Higher Degree and Research Ethics Committee (HDREC) and at the Uganda National Council for Science and Technology (UNCST). Additionally, permission to conduct the study was sought from the district health officers (DHOs) and health facility in-charges, and informed individual written consent was obtained from all study participants. Women aged 15-17 years were considered as emancipated minors because they were pregnant as per the UNCST ethics committee guidelines [30].

6.4 Results

Table 6.1 shows the characteristics of the study participants from the three study sites namely; Masaka RRH, Mityana GH, and Luwero HC IV. The majority (79.0%, 324/410) of the women had disclosed their HIV-positive status to someone. Two-thirds (67.8%, 278/410) did not belong to any social group. Most (46.5%, 190/409) women were seeking care from Mityana GH. The median age (IQR) was 24 (21-28) years. Half (50.6%, 207/409) of the enrollees were young women (15-24 years), and 80% (329/409) were married. Catholic (48.9%, 200/409) was the most common religion, followed by Protestants (20.3%). Almost all (95.3%, 389/408) intended to deliver from the health facility where they were receiving ANC services.

Table 6. 1: Baseline sample characteristics

Variable	n (%)
HIV-positive status disclosure to anyone	
Yes	324 (79.0)
No	86 (21.0)
Belongs to a social group	
Yes	132 (32.2)
No	278 (67.8)
Age group (Years)	
15 -24	207(50.6)
≥25	202(49.4)
Health facility	
Masaka RRH	132 (33.3)
Mityana GH	190 (46.5)
Luwero HC IV	87 (21.3)
Marital Status	
Currently married	329 (80.4)
Never married	50 (12.2)
Widowed/Separated	30 (7.3)
Highest education level completed	
No formal education	15 (3.7)
Primary	196 (47.9)
Secondary	188 (46.0)
Tertiary	9 (2.2)
Primary occupation	
Peasant farmer	79 (19.4)
Employed	45 (11.1)
Business/commercial	138 (33.9)
House wife	92 (22.6)
Unemployed	53 (13.1)
Religion	
Catholic	200 (48.9)
Protestant	83 (20.3)
Born again	42 (10.3)
Moslem	73 (17.9)
Others	11 (2.7)
Sexual partner tested for HIV*	
Yes	61 (39.6)
No	85 (55.2)
Intends to deliver from current health facility	
Yes	389 (95.3)
No	19 (4.7)
ART status disclosure to anyone	

Yes	96 (35.8)
No	172 (64.2)
Experienced HIV related stigma	
Yes	31 (7.6)
No	376 (92.4)
Spousal/Husband support*	
Yes	299 (72.9)
No	86 (20.9)
Not applicable	25 (6.1)
Readiness to start taking ART	
Immediately	306 (83.4)
Later	61 (16.6)
Motivation to start ART	
Protect baby	
Yes	331 (90.2)
No	36 (9.81)
Protect self	
Yes	330 (92.7)
No	26 (7.3)
Protect spouse*	
Yes	27 (7.6)
No	337 (91.8)
Health provider	
Yes	39 (11.0)
No	315 (89.0)
Others motivation sources	
Yes	13 (3.5)
No	351 (95.6)
Currently has a sexual partner	
Yes	372 (91.0)
No	37 (9.1)

* Only those who reported having a sexual partner at the time of the interview

Table 6.2 shows the comparison of characteristics of study participants who were included in the repeated measures analysis (had ≥ 3 study visits) to those who were not (i.e., had only 1 or 2 study visits). Women who were included in the analysis and those who were excluded had similar baseline characteristics except for the HIV status disclosure to anyone categories ($p = 0.014$).

Table 6. 2: Comparison of baseline characteristics of study participants included in the repeated measures analysis and those who were excluded

Variable	Inclusion into repeated measures analysis		p-value
	only 1 or 2 visits n (%)	3 visits or more n (%)	
Health facility			
Masaka RRH	7 (5.3)	125 (94.7)	0.617
Mityana GH	14 (7.4)	175 (92.6)	
Luwero HC IV	4 (4.5)	84 (95.5)	
Adherence levels			
Optimal Adherence	19 (6.0)	296 (94.0)	0.919
Suboptimal adherence	6 (6.3)	89 (93.7)	
HIV-positive status to anyone			
No	10 (11.8)	75 (88.2)	0.014
Yes	15 (4.6)	310 (95.4)	
Health provider advice			
No	20 (6.2)	302 (93.8)	0.566
Yes	4 (9.5)	38 (90.5)	
Experienced HIV Stigma			
No	25 (6.6)	352 (93.4)	0.371
Yes	0 (0.0)	30 (100.0)	
Readiness to start taking ART			
Immediately	20 (6.5)	286 (93.5)	0.995
Later	4 (6.6)	57 (93.4)	
Age (Years)			
15- 24	16 (7.7)	191 (92.3)	0.167
≥25	9 (4.5)	193 (95.5)	

* Only those who reported having a sexual partner at the time of the interview

Figure 6.1 shows the 30-day suboptimal adherence levels over the follow-up period. Overall suboptimal adherence levels were 23.2%, 13.9%, 13.6%, 13.8%, 12.7%, and 12% at month 2, 4, 6, 10, 14, and 18 visit post study enrolment respectively. Suboptimal adherence was highest in Luwero HC IV and lowest in Mityana GH.

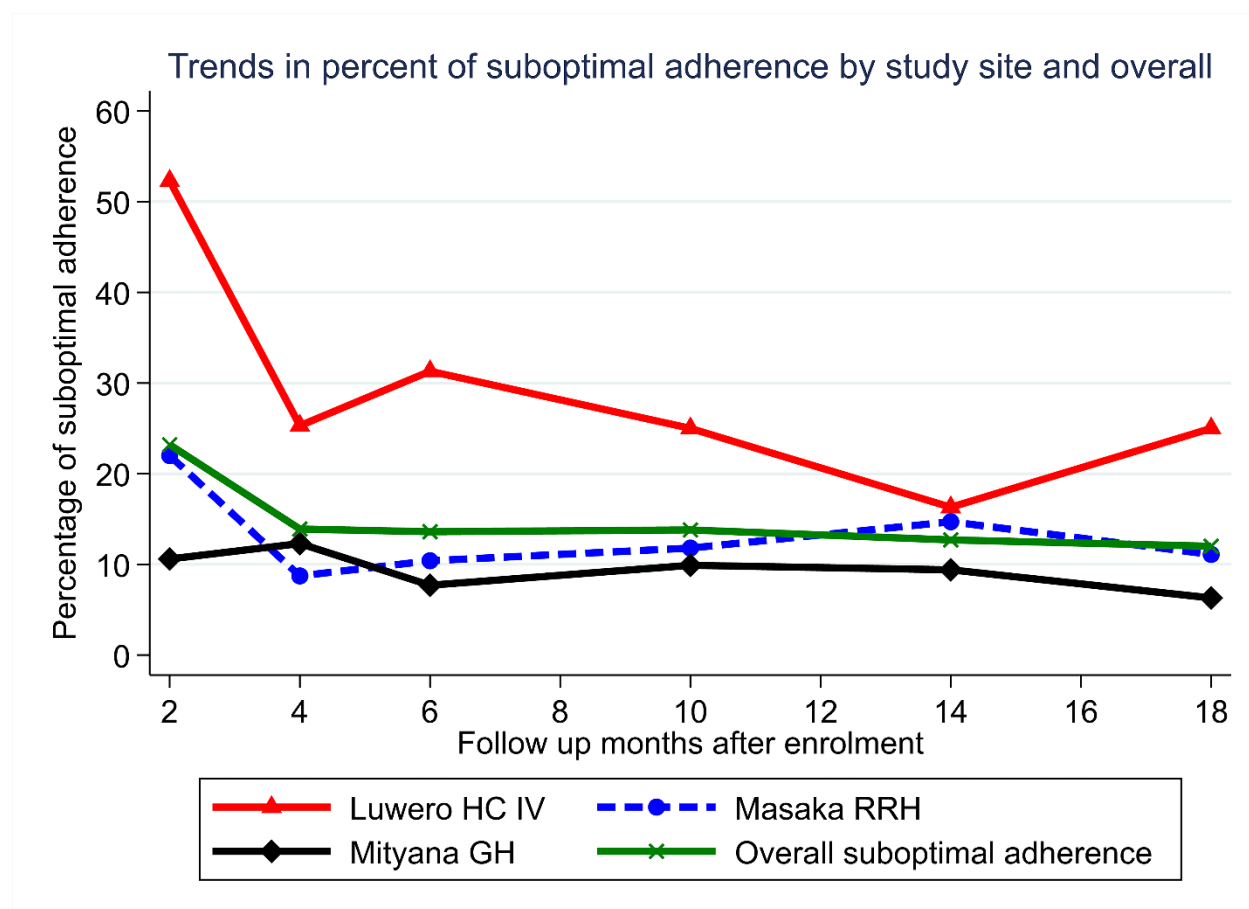


Figure 6.1: Suboptimal adherence levels during the follow-up period

Predictors of suboptimal adherence to lifelong ART

Table 6.3 shows predictors of the 30-day suboptimal adherence, unadjusted and adjusted odds ratios (AORs).

In the adjusted analysis, factors associated with lower odds of 30-day suboptimal adherence were; disclosure compared to non-disclosure of HIV-positive status to anyone, AOR = 0.50 (0.30 – 0.84), having versus lack of spousal/husband support, AOR = 0.43

(0.28 – 0.67), receipt compared to non-receipt of motivation from health providers to start lifelong ART, AOR = 0.19 (0.07 – 0.51), and follow up visit at month 4, 6, 10, 14 and 18 compared to month 2 post study enrolment, AOR = 0.37 (0.22-0.63), 0.43 (0.25-0.73), 0.48 (0.29-0.81), 0.33 (0.19- 0.57), and 0.31 (0.18-0.55) respectively. Factors associated with higher odds of suboptimal adherence were being unready to start taking lifelong ART AOR = 2.38 (1.26 – 4.50) compared to being ready to start taking lifelong ART immediately, reported experience of HIV-related stigma compared to those who did not, AOR =1.70 (1.05 – 2.75), and receipt of HIV care from Luwero HC IV, AOR=5.36 (2.62 - 10.98), relative Masaka RRH.

Table 6. 3: Predictors of suboptimal adherence to lifelong ART among pregnant and breastfeeding women in Central Uganda

Variable	Un adj. OR (95%)	p-value	AOR (95% CI)	p-value
Age-group (Years)				
15-24	1.0		1.0	
≥25	0.46 (0.27 – 0.81)	0.006	0.89 (0.54 – 1.48)	0.654
Marital status				
Married	1.0			
Never married	1.03 (0.43 – 2.47)	0.944		
Widowed/separated	2.05 (0.73 – 5.80)	0.174		
Highest level of education completed				
No formal education	1.0			
Primary	1.91 (0.41 – 8.81)	0.408		
Secondary	1.69 (0.36 – 7.85)	0.502		
Tertiary	0.94 (0.07 – 12.12)	0.961		
Readiness to start taking ART				
Immediately	1.0		1.0	
Later	4.56 (2.28 – 9.12)	<0.001	2.38 (1.26 – 4.50)	0.008
Primary occupation				
Peasant farmer	1.0			
Employed	0.91 (0.31 – 2.68)	0.870		
Business/commercial	0.85 (0.38 – 1.89)	0.683		
House wife	2.09 (0.91 – 4.83)	0.084		
Unemployed	2.99 (1.15 – 7.78)	0.024		
Health facility				
Masaka RRH	1.0		1.0	
Luwero HC IV	4.70 (2.38 – 9.28)	<0.001	5.36 (2.62 – 10.98)	<0.001
Mityana GH	0.56 (0.30 – 1.05)	0.073	0.75 (0.40 – 1.42)	0.376
Religion				
Catholic	1.0			
Protestant	0.87 (0.42 – 1.83)	0.715		

Born again	1.38 (0.55 – 3.48)	0.494		
Moslem	1.23 (0.59 – 2.60)	0.579		
Others	0.82 (0.15 – 4.59)	0.818		
ART disclosure to anyone				
No	1.0			
Yes	0.83 (0.37 – 1.86)	0.654		
Knowledge of partner's HIV status*				
No	1.0			
Yes	1.19 (0.40 – 3.57)	0.752		
Belongs to a social group				
No	1.0			
Yes	0.75 (0.52 – 1.09)	0.133		
HIV-positive status disclosure to anyone				
No	1.0	1.0	1.0	
Yes	0.36 (0.22 – 0.58)	<0.001	0.50 (0.30 – 0.84)	0.008
Experienced HIV stigma				
No	1.0		1.0	
Yes	1.06 (0.71 – 1.59)	0.775	1.54 (1.01 – 2.51)	0.032
Spousal/Husband support*				
No	1.0		1.0	
Yes	0.36 (0.24 – 0.53)	0.433	0.43 (0.28 – 0.67)	<0.001
Motivation to start ART				
Protect baby				
No	1.0			
Yes	0.17 (0.08 – 0.38)	<0.001		
Protect self				
No	1.0			
Yes	0.16 (0.06 – 0.39)	<0.001		
Protect spouse*				
No	1.0			
Yes	0.35 (0.10 – 1.20)	0.095		
Health provider				
No	1.0		1.0	
Yes	0.40 (0.15 – 1.05)	0.063	0.19 (0.07 – 0.51)	<0.001
Follow-up month				
Month 2	1.0		1.0	
Month 4	0.36 (0.22 – 0.59)	<0.001	0.37 (0.22 – 0.63)	<0.001
Month 6	0.37 (0.23 – 0.60)	<0.001	0.43 (0.25 – 0.73)	0.002
Month 10	0.40 (0.25 – 0.65)	<0.001	0.48 (0.29 – 0.81)	0.006
Month 14	0.33 (0.20 – 0.55)	<0.001	0.33 (0.19 – 0.57)	<0.001
Month 18	0.32 (0.19 – 0.53)	<0.001	0.31 (0.18 – 0.55)	<0.001

* Only those who reported having a sexual partner at the time of the interview

6.5 Discussion

Overall, the percent of women with suboptimal adherence decreased over the 18-months follow-up period. The percent of women with suboptimal adherence was highest at month 2 follow-up visit, declined sharply at month 4 follow-up visit, and thereof, a gradual decline to almost constant levels was observed. Overall suboptimal adherence to lifelong ART was higher among women receiving care from Luwero HC IV compared to those from Masaka RRH.

Although the suboptimal adherence levels were relatively low, efforts should be made to ensure that all pregnant and breastfeeding women attain optimal lifelong ART adherence perpetually so as to achieve viral suppression. Viral suppression results in good health for the women, reduced risk of HIV transmission to the child(ren) and the HIV-negative partner thus contributing attainment ending HIV as a public health threat by 2030[31]. The higher suboptimal levels at the beginning of the follow-up period might be attributed to the fact that the women were still getting used to the new HIV diagnosis and ART with its associated side effects [21]. However, over time on treatment, women get used to ART, HIV disclosure improves, and HIV stigma lessens [32] leading to lower levels of suboptimal adherence. Emphasis should be put on vigilance in counseling HIV-positive pregnant and breastfeeding women on issues of living with HIV, and lifelong ART adherence before and soon after initiating ART.

This study identified predictors of suboptimal adherence to inform e-MTCT programming. Women who had disclosed their HIV-positive status to anyone were less likely to have suboptimal adherence compared to those who had not disclosed to anyone. Our study findings are comparable to previous studies conducted elsewhere [33-35]. Disclosure of one's HIV-positive status has the potential to reduce fear of being seen while swallowing daily ART medications, may enable one seek psychosocial support, and consequently reduce suboptimal adherence. Efforts should be made to facilitate disclosure of HIV-positive status especially to individuals who can offer ART adherence support.

Our study showed that women who received spousal support in form of transport money to attend the ART clinic or reminder to take ART or being escorted to pick ART had lower

odds of suboptimal adherence. The findings conform to those in a study conducted in South Africa where lack of spousal financial partner support was associated with suboptimal adherence [36]. The findings are also supported by our qualitative results in which support from spouses was a facilitator of optimal adherence [37]. Spousal support is crucial in ART adherence, as it can greatly impact the health outcomes of people living with HIV. Spouse support can help in several ways. First, emotional support from a spouse can reduce stress, anxiety, and depression, which are common barriers to medication adherence. A supportive spouse can also provide practical support, such as reminding their partner to take their medication, helping them manage side effects, and assisting with medication refills. However, it is important to note that not all HIV-positive pregnant and breastfeeding women have supportive spouses, and that social support can come from other sources, such as other family members, friends or healthcare providers. In cases where spousal support is not feasible, healthcare providers can play an important role in providing support and education about ART adherence. Undeniably, our study findings show that women who were motivated by health providers to start lifelong ART, were 81% times less likely to have suboptimal adherence compared to those who didn't. This finding is supported by a study that was conducted in Rwanda [32]. Women on lifelong ART in Rwanda testified that messages from health workers encouraged them to remain adherent. This highlights the critical role health workers play in supporting women on lifelong ART. Health providers should use innovative PMTCT information and motivation right from the diagnosis of HIV, initiation of ART and throughout care and treatment to ensure that women sustain optimal lifelong ART adherence.

The odds of suboptimal adherence were lower at month 4, 6, 10, 14 and 18 compared to month 2 post study enrolment visit. Our results are supported by a qualitative study that was conducted in Rwanda [32]. In the Rwanda study, women reported that they got support from various people including peers and relatives to stay on ART for life during the challenging time of coping with ART. This motivated them to ensure optimal adherence overtime.

Our data also reveal that women who were unready to start taking lifelong ART immediately at the time they started taking their ART had higher odds of suboptimal adherence compared to those who were ready to start immediately. This is consistent

with a study that was conducted in four sub-Saharan African settings, where HIV-positive expectant women who didn't feel ready to initiate ART immediately after testing positive became non-adherent along the way [38]. By contrast women who receive adequate counselling and support, start on lifelong ART and remain adherent [39]. PMTCT programs should continually give adequate information and support to HIV-positive pregnant and breastfeeding women to ensure that they are ready to start and maintain taking lifelong ART.

Women who ever experienced stigma due to being HIV-positive had higher odds of suboptimal adherence compared to those who hadn't experienced HIV related stigma. This finding is consistent with studies done in South Africa and Nigeria [16, 35, 40]. HIV stigma may occur within health facilities, homes and communities. Stigma hinders seeking for HIV care and uptake of HIV services, disclosure of HIV status, and seeking for psychosocial support which are key in averting suboptimal ART adherence [41]. HIV-positive pregnant and breastfeeding women should be screened for HIV-related stigma at every clinic visit so that appropriate counseling and support for its control is given throughout the PMTCT cascade.

Seeking HIV care from a lower-level health facility (Luwero HC IV) was a predictor of suboptimal adherence compared to getting care from a regional referral hospital (Masaka RRH). This is similar to findings from studies conducted in Ethiopia and Malawi whereby the level of health facility was associated with adherence to lifelong ART [42, 43]. Findings from the study conducted in selected government health facilities of South Wollo Zone, Amhara Region, northeast Ethiopia indicated that mothers who received lifelong ART services from hospitals were less likely to adhere than those who attended health centers [43]. Similarly, a cohort study conducted in Malawi established that women receiving lifelong ART for PMTCT from district hospitals and urban health centers were more likely to have suboptimal adherence compared to those receiving care from faith-based health facilities or central hospitals. Conversely, our results show that women who sought care from the HC IV had higher odds of suboptimal adherence compared to those who received care from the hospitals. This finding might imply that there are differences in how lifelong ART services are offered to pregnant and postpartum women in regards to level of health facilities in varying contexts.

6.6 Study strengths and limitations

We used a prospective cohort where women were followed up during pregnancy and post-delivery. Our study had a large enough sample size. Finally, use of repeated measures analysis enabled us to; further increase the sample size- individual women were their own control, evaluate time varying covariates in determining the suboptimal adherence patterns, and assess changes both between and within individual women's behaviors during and after pregnancy.

Our study had a limitation of measuring the outcome through self-reports which could have underestimated adherence levels due to recall and social desirability bias. However, our study assessed suboptimal adherence and individuals who state they are non-adherent nearly always are [13]. Additionally, previous studies have used similar measurements [14]. Finally, the findings of our study have to be interpreted bearing in mind; changes such as new interventions designed to address suboptimal adherence that have happened over time.

6.7 Conclusions and recommendations

The 30-day suboptimal adherence levels were highest at month 2 (23.2%) but varied between 12%-13.9% at month 4, 6, 10, 14, and 18 follow up visits. Disclosure of HIV-positive status to anyone, spousal support, and receiving motivation from health providers to start lifelong ART reduced the risk of suboptimal adherence. However, suboptimal adherence was higher among women who were not ready to start taking lifelong ART immediately, those who reported having ever experiencing HIV -related stigma, and those who sought care from Luwero HC IV.

We recommend that innovative, context, and HIV- positive women specific PMTCT information, motivation and support interventions to eliminate suboptimal adherence be designed and given throughout the PMTCT cascade. The information should be delivered by health care providers, as well as other individuals like peers and key family members. Furthermore, Ministry of Health should encourage mutual learning across facilities so as to share experiences around suboptimal adherence.

Authors' abbreviations

A.D.M.: Aggrey David Mukose, J.P.: Jean-Pierre Van Geertruyden, F.M.: Fredrick Makumbi, E.B.: Esther Buregyeya, R.N.: Rose Naigino, J.M.: Joshua Musinguzi, R.K.W.: Rhoda K. Wanyenze

Authors' contributions

A.D.M., F.M., E.B., J.M., and R.K.W. contributed substantially to the article in relation to the study design; A.D.M., F.M., E.B., R.N., J.M., and R.K.W. contributed substantially to the article in relation to the study implementation; A.D.M. and F.M. carried out the analysis and interpretation of these data; E.B., R.N., J.M., J.P., and R.K.W. contributed substantially to the article in relation to the interpretation of the data. All authors should have been involved in the writing of the manuscript at draft and any revision stages, and have read and approved the final version. A.D.M., F.M., and R.K.W. are guarantors of the paper.

Acknowledgements

The authors wish to thank all study participants without whom this study wouldn't have been successful. Special thanks also go to the respective heads of facility for Masaka RRH, Mityana GH, and Luwero HC IV for their continued support rendered to us throughout the data collection process. We also acknowledge the tireless efforts of all study interviewers in collecting data at their respective study sites. Sincere thanks also go to Mr. Ronald Kusolo who supported us in data management and analysis.

Funding

This work was supported by the Global Fund through the Ministry of Health-Uganda [Grant Number: UGD-708-G07-H]. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests

None declared.

Ethical approval

The authors have observed high standards with respect to publication ethics as set out by the Commission on Publication Ethics (COPE) and International Committee of Medical Journal Editors (ICMJE).

Data Availability Statement

The data underlying this article cannot be shared publicly due to restrictions by the Makerere University School of Public Health Research, and Ethics Committee, some access restrictions apply to the data for reasons of safety and protection of study subjects and their institutions. Sensitive data was collected from patients and they didn't consent to open data access. However, criteria-eligible researchers with an interest in the data may request anonymized data access through the Chair, Research, and Ethics Committee on: The Chairperson Makerere University School of Public Health Research and Ethics Committee, P.O. Box 7072, Kampala. Email: sphrecadmin@musph.ac.ug, Telephone +256393291397.

References

1. UNAIDS. UNAIDS Fact Sheet 2022: Latest global and regional statistics on the status of the AIDS epidemic. 2022 [cited 2022 December 2022]; Available from: https://www.unaids.org/en/resources/documents/2022/UNAIDS_FactSheet.
2. MoH, Annual Health Sector Performance Report–FY 2014/2015, Planning, Editor. 2015, MoH: Kampala, Uganda. p. 154.
3. MoH, Annual Health Sector Performance Report Financial Year 2020/21, Planning, Editor. 2021: Kampala, Uganda.
4. UAC, Annual Joint AIDS Review Report FY 2021/22. 2022, UAC: Kampala Uganda.
5. MoH, Uganda HIV and AIDS Country Progress report., UACP, Editor. 2014, MoH: Kampala, Uganda. p. 73.
6. UAC, Uganda Annual Joint AIDS Review Report 2020/21. 2021, UAC: Kampala, Uganda.
7. Paterson, D.L., et al., Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of internal medicine*, 2000. **133**(1): p. 21-30.
8. Zhang, Y., et al., The impact of substance use on adherence to antiretroviral therapy among HIV-infected women in the United States. *AIDS and Behavior*, 2018. **22**: p. 896-908.
9. Siefried, K.J., et al., Socioeconomic factors explain suboptimal adherence to antiretroviral therapy among HIV-infected Australian adults with viral suppression. *PLoS One*, 2017. **12**(4): p. e0174613.
10. Starace, F., et al., Adherence to antiretroviral therapy: an empirical test of the information-motivation-behavioral skills model. *Health Psychology*, 2006. **25**(2): p. 153.
11. Cohen, M.S., et al., Prevention of HIV-1 infection with early antiretroviral therapy. *New England journal of medicine*, 2011. **365**(6): p. 493-505.
12. Ekstrand, M.L., et al., Suboptimal adherence associated with virological failure and resistance mutations to first-line highly active antiretroviral therapy (HAART) in Bangalore, India. *International health*, 2011. **3**(1): p. 27-34.
13. Paterson, D.L., B. Potoski, and B. Capitano, Measurement of adherence to antiretroviral medications. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 2002. **31**: p. S103-S106.
14. Nachega, J.B., et al., Adherence to antiretroviral therapy during and after pregnancy in low-, middle and high income countries: a systematic review and meta-analysis. *AIDS (London, England)*, 2012. **26**(16): p. 2039.

15. Erlwanger, A.S., et al., Patterns of HIV care clinic attendance and adherence to antiretroviral therapy among pregnant and breastfeeding women living with HIV in the context of Option B+ in Zimbabwe. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 2017. **75**: p. S198-S206.
16. Adeniyi, O.V., et al., Factors affecting adherence to antiretroviral therapy among pregnant women in the Eastern Cape, South Africa. *BMC infectious diseases*, 2018. **18**: p. 1-11.
17. Zoungrana-Yameogo, W.N., et al., Adherence to HIV Antiretroviral Therapy Among Pregnant and Breastfeeding Women, Non-Pregnant Women, and Men in Burkina Faso: Nationwide Analysis 2019–2020. *Patient preference and adherence*, 2022: p. 1037-1047.
18. Wubneh, C.A., et al., Adherence to option B+ and its association with disclosure status and counseling among HIV-positive pregnant and lactating women in Ethiopia: systematic review and meta-analysis. *Public Health*, 2022. **211**: p. 105-113.
19. Schnack, A., et al., Prevention of mother-to-child transmission of HIV in option B+ era: uptake and adherence during pregnancy in western Uganda. *AIDS patient care and STDs*, 2016. **30**(3): p. 110-118.
20. Decker, S., et al., Prevention of mother-to-child transmission of HIV: Postpartum adherence to Option B+ until 18 months in Western Uganda. *PloS one*, 2017. **12**(6): p. e0179448.
21. Matthews, L.T., et al., Adherence to HIV antiretroviral therapy among pregnant and postpartum women during the Option B+ era: 12-month cohort study in urban South Africa and rural Uganda. *Journal of the International AIDS Society*, 2020. **23**(8): p. e25586.
22. WHO, Global health sector strategy on HIV 2016-2021. Towards ending AIDS. 2016. 2016: Geneva, Switzerland.
23. WHO, Accelerating progress on HIV, tuberculosis, malaria, hepatitis and neglected tropical diseases: A new agenda for 2016-2030. 2016: Geneva, Switzerland.
24. MoH, Uganda AIDS Indicator Survey 2011, ACP, Editor. 2012, ICF International: Kampala, Uganda.
25. MoH, Consolidated Guidelines for Prevention and Treatment of HIV in Uganda 2016. 2016, MoH: Kampala, Uganda.
26. O'Connell, A.A. and D.B. McCoach, Applications of hierarchical linear models for evaluations of health interventions: demystifying the methods and interpretations of multilevel models. *Evaluation & the Health Professions*, 2004. **27**(2): p. 119-151.
27. Singer, J.D., J.B. Willett, and J.B. Willett, Applied longitudinal data analysis: Modeling change and event occurrence. 2003: Oxford university press.

28. Hamaker, E.L., et al., Model selection based on information criteria in multilevel modeling. *Handbook of advanced multilevel analysis*, 2011: p. 231-255.
29. Neath, A.A. and J.E. Cavanaugh, The Bayesian information criterion: background, derivation, and applications. *Wiley Interdisciplinary Reviews: Computational Statistics*, 2012. **4**(2): p. 199-203.
30. UNCST, National guidelines for research involving humans as research participants. 2014, UNCST: Kampala, Uganda.
31. Tsai, A.C., et al., How does antiretroviral treatment attenuate the stigma of HIV? Evidence from a cohort study in rural Uganda. *AIDS and Behavior*, 2013. **17**: p. 2725-2731.
32. Gill, M.M., et al., Understanding antiretroviral treatment adherence among HIV-positive women at four postpartum time intervals: qualitative results from the kabeho study in Rwanda. *Aids patient care and Stds*, 2017. **31**(4): p. 153-166.
33. Larsen, A., et al., Longitudinal adherence to maternal antiretroviral therapy and infant Nevirapine prophylaxis from 6 weeks to 18 months postpartum amongst a cohort of mothers and infants in South Africa. *BMC infectious diseases*, 2019. **19**: p. 1-13.
34. Unge, C., et al., Long-term adherence to antiretroviral treatment and program drop-out in a high-risk urban setting in sub-Saharan Africa: a prospective cohort study. *PloS one*, 2010. **5**(10): p. e13613.
35. Psaros, C., et al., PMTCT adherence in pregnant South African women: the role of depression, social support, stigma, and structural barriers to care. *Annals of Behavioral Medicine*, 2020. **54**(9): p. 626-636.
36. El-Khatib, Z., et al., Adherence and virologic suppression during the first 24 weeks on antiretroviral therapy among women in Johannesburg, South Africa-a prospective cohort study. *BMC public health*, 2011. **11**(1): p. 1-13.
37. Buregyeya, E., et al., Facilitators and barriers to uptake and adherence to lifelong antiretroviral therapy among HIV infected pregnant women in Uganda: a qualitative study. *BMC pregnancy and childbirth*, 2017. **17**(1): p. 1-9.
38. McLean, E., et al., 'I wanted to safeguard the baby': a qualitative study to understand the experiences of Option B+ for pregnant women and the potential implications for 'test-and-treat'in four sub-Saharan African settings. *Sexually transmitted infections*, 2017. **93**(Suppl 3).
39. Gugsu, S., et al., Exploring factors associated with ART adherence and retention in care under Option B+ strategy in Malawi: A qualitative study. *PLOS ONE*, 2017. **12**(6): p. e0179838.

40. Joseph, A., et al., Determinants of adherence to antiretroviral therapy among HIV-positive women accessing prevention of mother-to-child transmission services in Ebonyi State, Nigeria. *Annals of Medical and Health Sciences Research*, 2018. **8**(4).
41. Turan, J.M. and L. Nyblade, HIV-related stigma as a barrier to achievement of global PMTCT and maternal health goals: a review of the evidence. *AIDS and Behavior*, 2013. **17**: p. 2528-2539.
42. Haas, A.D., et al., Adherence to antiretroviral therapy during and after pregnancy: cohort study on women receiving care in Malawi's option B+ program. *Clinical infectious diseases*, 2016. **63**(9): p. 1227-1235.
43. Tsegaye, D., L. Deribe, and S. Wodajo, Levels of adherence and factors associated with adherence to option B+ prevention of mother-to-child transmission among pregnant and lactating mothers in selected government health facilities of South Wollo Zone, Amhara Region, northeast Ethiopia, 2016. *Epidemiology and health*, 2016. **38**.

CHAPTER 7:

Challenges and commonly used countermeasures in the implementation of lifelong antiretroviral therapy for PMTCT in Central Uganda: A health providers' perspective

Aggrey David Mukose^{1, 2}, Hilde Bastiaens^{2, 3}, Fredrick Makumbi¹, Esther Buregyeya⁴, Rose Naigino⁵, Joshua Musinguzi⁶, Jean-Pierre Van Geertruyden², and Rhoda K. Wanyenze⁴

¹ Department of Epidemiology and Biostatistics, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda

² Global Health Institute, Department of Epidemiology and Social Medicine, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

³ Department of Family Medicine and Population Health, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

⁴ Department of Disease Control and Environmental Health, School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda

⁵ Makerere University School of Public Health, Kampala, Uganda

⁶ Ministry of Health, Kampala, Uganda

PLoS ONE 18(1): e0280893. <https://doi.org/10.1371/journal.pone.0280893>

Received: May 23, 2022; Accepted: January 23, 2023

DOI: <https://doi.org/10.1371/journal.pone.0280893>

7.1 Abstract

Introduction: Uganda has implemented lifelong antiretroviral therapy for the prevention of mother-to-child HIV transmission since September 2012. Implementation of this strategy has been met with health provider and client challenges which have persisted up to date. This study explored providers' perspectives on the challenges and countermeasures of the implementation and scale-up of lifelong ART among pregnant and breastfeeding women.

Methods: A qualitative descriptive study was conducted whereby 54 purposively selected participants from six facilities in three districts of Central Uganda namely; Masaka, Mityana, and Luwero were recruited. A key informant interview guide was used to collect data from the study participants. The data were thematically analysed using Atlas-ti, Version 7.

Results: Study participants reported challenges under the themes of 1) inadequacy of HIV service delivery (lack of relevant training, health provider shortages, inadequate counselling, stock-outs of essential HIV commodities); 2) Non-utilization of HIV services (Non-disclosure of HIV- positive results, denial of HIV-positive results, fear to be followed up, unwillingness to be referred, large catchment area, lack of transport); and 3) Suboptimal treatment adherence (fear of ART side effects, preference for traditional medicines, low male partner involvement in care and treatment). Strategies such as on-job training, mentorship, task shifting, redistribution of HIV commodities across facilities, accompanying of women to mother-baby care points, ongoing counseling of women, peers, and family support groups were commonly used countermeasures.

Conclusions: This study highlights key challenges that health providers face in implementing lifelong antiretroviral therapy services among pregnant and postpartum women. Context-specific, innovative, and multilevel system interventions are required at national, district, health facility, community and individual levels to scale up and sustain the lifelong antiretroviral therapy strategy among pregnant and breastfeeding women.

7.2 Introduction

Adoption of lifelong antiretroviral therapy (ART) for all pregnant and breastfeeding women living with HIV regardless of CD4 count or clinical stage (Option B+) for prevention of mother-to-child transmission (PMTCT) of HIV started in Malawi in 2011[1]. Subsequently, this strategy was adopted by many countries in sub-Saharan Africa (SSA), including Uganda [2-4]. At that time, this choice was based on programmatic and operational reasons, particularly in generalized epidemics where there are high fertility rates, small birth intervals, poor access to CD4 testing, and a long duration of breastfeeding [5].

Evidence suggests that initiating ART in all pregnant and breastfeeding women would reduce HIV incidence and prevent HIV transmission in both current and future pregnancies [5]. Uganda adopted the lifelong ART strategy for pregnant and breastfeeding women in September 2012. By August 2013, the strategy had been scaled up in all the 112 districts across the country [6]. Moreover, Uganda started implementing the HIV “test and treat” policy for all children, pregnant and breastfeeding women, HIV-positive people with both TB or Hepatitis B co-infection and the HIV-positive individuals in sero-discordant relationships in 2014[7]. Besides, in the same year, Uganda adopted the World Health Organization’s recommendation for routine viral load testing as the standard of care compared to CD4 count for monitoring ART effectiveness [8]. However, in 2016, Uganda revised her “Consolidated guidelines for the prevention and treatment of HIV and AIDS” to include all adolescents and adults living with HIV on the “test and treat” policy. This policy involves providing lifelong ART to people living with HIV irrespective of CD4 count or World Health Organization (WHO) clinical stage [9]. These changes drastically increased the number of people living with HIV (PLHIV) who were initiated on ART which could end up constraining the health system [10]. Finally, in 2020, the Uganda Ministry of Health (MOH) rolled out revised HIV and AIDS prevention, and treatment guidelines which recommend the optimization of ART using Dolutegravir-based regimens as the preferred first line for all eligible PLHIV including pregnant and breastfeeding adolescent girls and women [11]. Typically, pregnant and lactating women are categorized under priority populations since they have a higher chance of acquiring or transmitting HIV. Besides, HIV-positive pregnant and postpartum women have unique

needs including access to and utilization of HIV services, retention in care and adherence [12, 13]. Consequently, the WHO anticipated that additional support would be required to ensure optimal adherence and retention in HIV care for HIV-positive women initiating lifelong ART since many would still be healthy [5]. As a result, mother-to-child transmission (MTCT) of HIV rate would rapidly abate. Although the MTCT rates in Uganda have declined over time, the desired level has not been achieved. For instance, a recent (2017-2019) impact evaluation study found that the overall MTCT rate in Uganda at 18 months post-delivery was 2.8% (95% CI: 2.0-3.9) [14] while an annual performance report showed that an estimated 5,300 MTCT infections occurred in the 2020/21 financial year [15]. Ergo, Uganda still lags behind in attaining the validation status for elimination of mother-to-child transmission (e-MTCT) of HIV.

To maximise the benefits of lifelong ART among pregnant and breastfeeding women, there is thus a need for a fully functional and organized health system to support the women and their infants. However, some studies have identified health system challenges in PMTCT implementation. Some of the challenges include; patient and health system difficulties such as poor communication and coordination among health system actors, poor clinical practices, and gaps in provider training [12]. A study conducted in Kenya identified insufficient training, staff and drug shortages, long queues, limited space and lack of patient-friendly services as some of the facility challenges in implementing lifelong ART among women on lifelong ART [16]. Although certain strategies have been implemented to address some of these challenges, a number of challenges such as antiretroviral drug (ARV) stock-outs, long distances to health facilities, low male partner involvement, and non-retention in care persist [17-19]. Relatedly, a review conducted to assess progress, gaps and research needs towards achieving UNAIDS targets for pregnant and postpartum women in SSA identified a number of research priorities which included; barriers to ART uptake, retention in care, and sustained ART adherence[20].

There is therefore a need for contextual studies to explore the challenges and countermeasures to inform policy and programmatic improvements. To that effect, this study aimed at exploring the health providers' perspectives of challenges along with the corresponding countermeasures to inform implementation of lifelong ART among HIV-

positive pregnant and breastfeeding women in central Uganda. Countermeasures are strategies that were used to overcome the challenges. Understanding the challenges and countermeasures in implementation of lifelong ART is critical to the success of the PMTCT of HIV program. The findings have potential to strengthen PMTCT programs to attain validation status for, achieve, and sustain e-MTCT of HIV and consequently contribute to the goal of ending AIDS as a public health threat by 2030[21, 22]. The results are also relevant for similar contexts and in countries that are still experiencing similar challenges in implementing the current policy of test and treat [3, 23-25].

7.3 Methods

Study design

A qualitative descriptive study was conducted among PMTCT services providers to elicit information on work challenges and countermeasures experienced during implementation of lifelong ART among HIV-positive pregnant and breastfeeding women in central Uganda.

Study sites

The study was conducted in six public health facilities from three largely rural districts. The study sites were: Katikamu Health Centre (HC) III and Luwero HC IV in Luwero district; Mityana General Hospital (GH) in Mityana district; Ssunga HC III, Kyanamukaka HC IV and Masaka Regional Referral Hospital (RRH) in Masaka district. These districts and facilities were selected because they were among the first to implement lifelong ART strategy in Uganda and had fully operational PMTCT programs. The facilities could thus give comprehensive information on challenges and countermeasures. HIV-positive pregnant, in labour, or post-delivery women accessed PMTCT services at the antenatal care (ANC), labour wards and postnatal care (PNC) clinics respectively.

Study population

Fifty-four participants took part in the study as key informants. They were grouped into formal and informal health providers. Formal providers were health workers who had received recognized training with a defined curriculum. They comprised midwives,

nurses, counselors, nursing assistants, store assistants (Assistant inventory management officer), dispensers, laboratory assistants, clinical officers, and medical doctors. Informal health providers were health workers who had not received formally recognized training and typically not mandated by any formal institution. Instead, they had some level of training through apprenticeships, seminars, and workshops [26]. Informal providers enrolled in the study were expert clients. Expert clients are people living with HIV who have disclosed their HIV status and are willing to support other HIV clients voluntarily. We included participants who had been involved in lifelong ART services provision to pregnant or breastfeeding women for at least one year. Eligible participants who were too sick or unavailable at the time of the interviews to participate in the study were excluded from the study.

Selection of study participants

Participants (health providers) were purposively selected based on their roles, workstation, and experience. The aim was to select participants from a broad and diverse sample of providers and clinics to get a comprehensive view on experiences and the organization of services concerning implementing lifelong ART. In total, 54 study participants were included.

This study was part of a larger study on implementation of lifelong ART among HIV-positive pregnant and breastfeeding women in Uganda. The objectives of the larger study were to determine the uptake of ART and other PMTCT related services by HIV+ pregnant women and their infants, and to assess retention in care and adherence to ART treatment. Concisely, the larger study enrolled 54 health providers, and 57 HIV-positive women for qualitative descriptive inquiry [27, 28]. In addition, we recruited 507 HIV-positive pregnant women who were prospectively followed during pregnancy, labour, after delivery and during breastfeeding for a total of 18 months to collect quantitative data [29, 30]. In the current manuscript, we analyse data from the 54 health providers to explore providers' perspectives on the challenges encountered and countermeasures while implementing the PMTCT program.

Data collection

Data were collected between April and May 2014 using a key informant interview guide. The guide was developed to explore challenges and countermeasures experienced during implementation of lifelong ART among HIV-positive pregnant and breastfeeding women. The semi-structured interview guide explored health providers' experiences about challenges in provision of lifelong ART for HIV-positive pregnant and breastfeeding women. Besides, countermeasures to deal with these challenges were explored. Table 7.1 shows the topics, questions and probes that were included in the study tool. The initial tool was pretested by some of the investigators and later discussed by the entire study team. We noted the consensuses and incongruities which we resolved through agreement. This ensured consistency in administration of the semi-structured key informant interview (KII) guide and interpretation of the questions. One-on-one interviews were conducted by four of the lead investigators (A.M., R.W., E.B., and R.N.). Each interview was audio-recorded with consent from the study participant and generally lasted 1.5 hours.

Table 7. 1: Topics, questions and probes that were included in the study tool

Topic	Questions	Probes
Challenges faced in supporting women on lifelong ART	What challenges do you face in supporting women on lifelong ART?	<ul style="list-style-type: none"> • Support for retention, adherence. • Drug stock-outs, staffing numbers, and trainings/skills Early infant diagnosis (EID) of HIV
challenges faced by pregnant women on Option B+	In your experience, what challenges do pregnant women on lifelong ART face?	<ul style="list-style-type: none"> • Loss to follow up, ART adherence, keeping clinic appointments, drug stock-outs. • Stigma, discrimination • Referrals across difference service points such as ANC and ART clinics.
Countermeasures to address the challenges	What measures has the health facility/clinic instituted to address the challenges and how effective are these strategies?	<ul style="list-style-type: none"> • Support for retention, adherence. • Drug stock-outs, staffing numbers and trainings/skills • EID • Loss to follow up, ART adherence, keeping clinic appointments. • Stigma, discrimination • Referrals across difference service points such as ANC and ART.

Data management and analysis

All audio-recorded data were transcribed verbatim; data in Luganda (local language) were concomitantly translated and transcribed into English. Final transcripts were stored securely on password-protected external drives. Data analysis was done using thematic analysis [31]. and comprised the following steps: familiarisation with the data by reading through all the data repeatedly to understand the data. A list of ideas from the data was generated, and this was used to develop codes for analysis which A.M., H.B., and R.W. later discussed, unified and organized around challenges and countermeasures in implementation of lifelong ART among pregnant and breastfeeding women. All transcripts were exported to Atlas software (Atlas.ti, Version 7 software, Berlin, Germany) to guide the coding process. Eventually, the codes were sorted into subthemes, categories, and themes. Analysis was undertaken by A.M., H.B., and R.W. regularly evaluated and discussed the entire process of analysis and output for quality control and to ensure that the interpretation was close to the content and supported reflexivity. Illustrative quotations have been presented to enhance the study findings.

Ethical considerations

Makerere University School of Public Health Higher Degrees, Research and Ethics Committee and the Uganda National Council for Science and Technology approved the study. Permission was also obtained from the study districts and facilities. Participants were assured of anonymity and confidentiality: interviews were conducted in a private environment and transcripts did not bear participant names, nor any other identifiable details. Written informed consent was obtained from each study participant. The informed consent included a section on publication of anonymized responses. Each participant received compensation of 10,000 Uganda Shillings (equivalent to 4USD at the time of the study) for their time.

7.4 Results

Characteristics of study participants

Table 7.2 shows the characteristics of health providers who participated in the study. Overall, 54 interviews were conducted with 22 midwives, 8 nursing assistants, 7 expert clients, 4 doctors, 4 store assistants, 3 clinical officers, 3 nurses, one counsellor, one dispenser and one laboratory assistant. Majority of the participants were female (76%, 41/54), while half had received training in provision of lifelong ART to pregnant and breastfeeding women. Participants had worked in HIV care for a median (IQR) of 5 (1-8) years.

Providers' perspectives of challenges and countermeasures

The challenges are arranged under three themes of; inadequacy of HIV service delivery, non-utilization of HIV services, and suboptimal treatment adherence. Under each theme; categories, sub-themes, and countermeasures are presented as shown in Figure 7.1.

Table 7. 2: Characteristics of study participants (n= 54)

Characteristic	Number (%)
District	
Masaka	34 (63.0)
Mityana	10 (18.5)
Luwero	10 (18.5)
Health Facility	
Masaka RRH	12 (22.2)
Mityana GH	10 (18.5)
Kyanamukaka HC IV	10 (18.5)
Luwero HC IV	10 (18.5)
Katikamu HC III	7 (13.0)
Ssunga HC III	5 (9.3)
Sex	
Female	41 (75.9)
Male	13 (24.1)
Cadre	
Midwife	22 (40.7)
Nursing assistant	8 (14.8)
Expert client	7 (13.0)
Doctor	4 (7.4)
Store assistant	4 (7.4)
Clinical officer	3 (5.5)
Nurse	3 (5.5)
Counsellor	1 (1.9)
Dispenser	1 (1.9)
Laboratory assistant	1 (1.9)

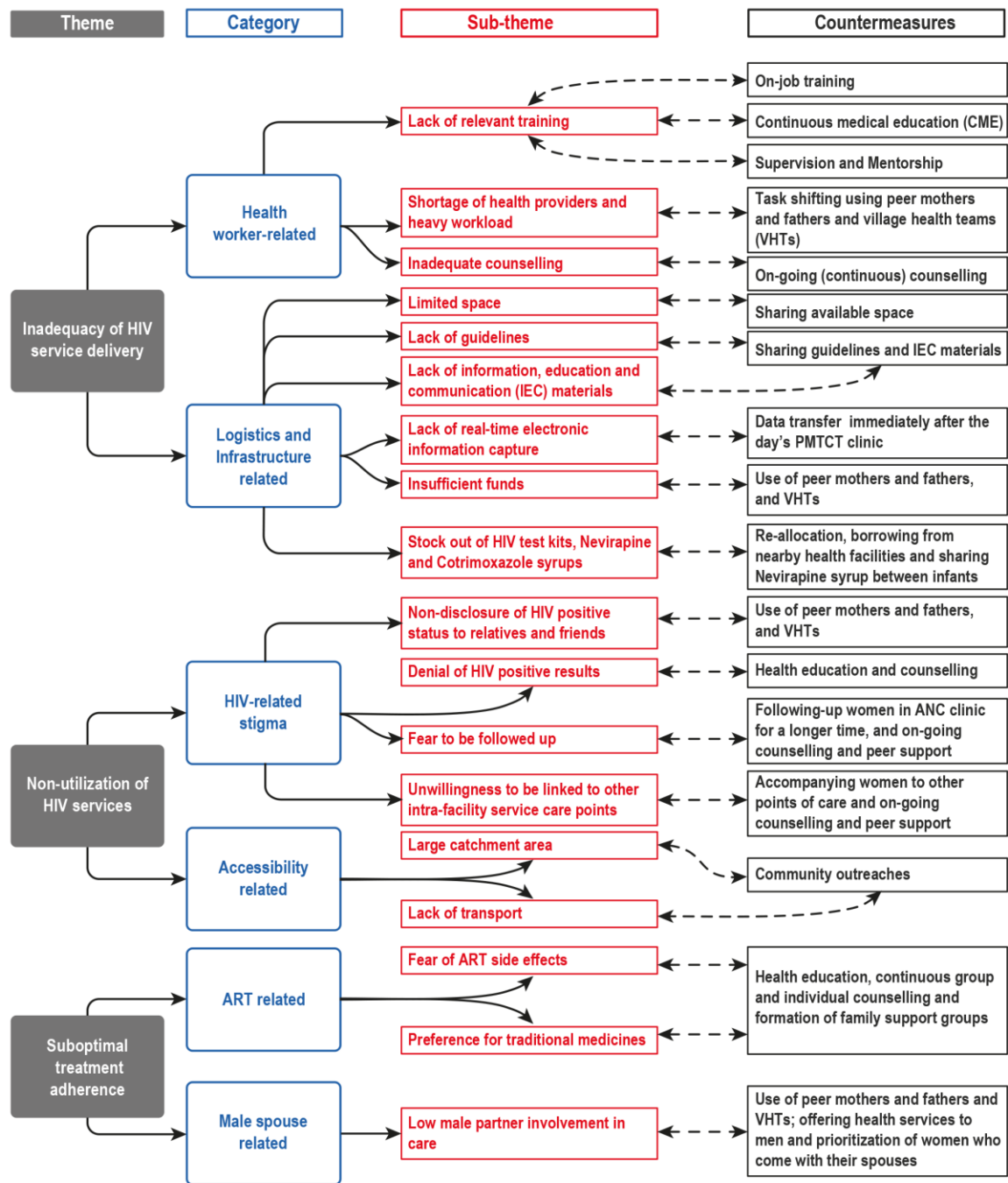


Figure 7.1: Illustrates the themes, categories, sub-themes, and countermeasures in implementation of lifelong ART services for PMTCT in three districts of Central Uganda

1. Inadequacy of HIV service delivery and countermeasures.

Two categories were identified under this theme: health worker-related; and logistics, and infrastructure-related.

a) Health worker-related. Four sub-themes were identified under this category.

Lack of relevant training

Half of the participants had not received training in the provision of ART for pregnant and breastfeeding women. Additionally, most interviewees reported a complete lack of training or lack of refresher training in lifelong ART provision among their colleagues. Among those directly involved in providing maternal, neonatal, and child health services; most of those who had not been trained were new at the facility. Participants also mentioned that, providers who were not directly involved in providing maternal, neonatal and child health services lacked relevant PMTCT training. These included laboratory, pharmacy and store staff.

“As a supplies officer [Store assistant], I was left out when trainings on lifelong ART for HIV-positive pregnant and breastfeeding women were going on. They brought these drugs and they just told me that these are lifelong ARVs.” (Health Provider, Hospital)

All participants underscored the importance of training more providers to build capacity for sustainable lifelong ART service provision. To address the training gaps, study participants mentioned several strategies that were being used to build provider capacity. These included: on-job training, continuous medical education (CME), and supervision and mentorship by the MOH, district health officials, and implementing partners including Mildmay Uganda and Protecting Families Against HIV/AIDS. Supervision and mentorship were being done once every three months.

“Supervision and mentorship are conducted quarterly [once in three months]. The ideal would have been every month but due to resource constraints, this is not possible.” (Health Provider, HCIV)

Shortage of health providers and heavy workload

Some participants highlighted that there were low numbers of some providers such as counsellors and clinical officers. In those cases, midwives were overloaded as they were expected to provide counselling, and maternal, neonatal, child and health services to many female clients and their children. The clinical workload was exasperated by the numerous PMTCT paperwork. The ensuing long queues affected staff attitudes who at times became flustered, and exhausted. Eventually, clients would experience delays at clinics.

“There are usually many clients [HIV-positive individuals] yet we have very few health workers. We may have just three health workers and as one is immunizing the babies, one may be filling various cards and registers while the other is examining the pregnant women and at the same time checking their cards. the queue may be so long and there is no way she can talk to one lady for so long.” (Health Provider, Hospital)

Participants noted that health facilities adopted task-shifting using expert clients and village health team members (VHTs), to overcome staff shortages and heavy workload. Task shifting was observed as being very helpful in reducing the heavy workload and patient waiting time.

“We have expert clients who are also peer mothers in the ANC clinic. They help to counsel these mothers and to follow them up. They support us a lot in caring for the mothers on lifelong ART.” (Health Provider, HC IV)

Inadequate counselling

All participants highlighted the importance of adequate and quality counselling to ensure lifelong ART uptake, adherence and retention in care by the women and their infants. However, many felt that the counselling offered was inadequate due to a lack of counselling training, a shortage of dedicated counsellors, and limited time to counsel women on the range of issues, amidst an overwhelming number of women who required the service.

“Counselling is not enough; the workload is too much and the counsellors are very few yet, we have bigger clinics, the PMTCT and the ART clinics. I think we have about two counsellors and the other health workers provide the counselling but it is not really conducted satisfactorily. If we

don't give the mothers continuous information, they will become reluctant.” (Health Provider, Hospital)

Inadequate counselling was addressed through offering continuous (on-going) counselling to women at every facility visit with emphasis on issues at hand.

“We offer on-going counselling to HIV-positive pregnant and breastfeeding mothers on lifelong ART every time they come back. We ask them the challenges they have met when they are at home taking the lifelong ART and then offer appropriate support.” (Health Provider, HC IV)

b) Logistics, and infrastructure-related. Under this category, six sub-themes were identified.

Limited space

Limited space was a prominent challenge cited by most participants. This was mostly attributed to the increased number of women seeking services, yet different services that had been integrated into the clinic were still offered in the same space. This resulted in congestion, which compromised privacy and confidentiality. Mothers were reportedly uncomfortable receiving services in such an environment.

“The place where they get the information is open and small, near a walk-way and there are so many activities taking place, it is extremely small. So, there are so many things that might divert their attention [when counselling is going on], we don't have any privacy.” (Health Provider, Hospital)

Limited space, especially for counselling was difficult to address because it was affecting all other departments and not only limited to maternal, neonatal, and child health clinics. Providers said that they continued to work in the available space but wished that government and implementing partners would set up new buildings or temporary structures like tents.

Lack of guidelines

Most participants noted that copies of PMTCT guidelines were limited. In some facilities, participants reported never seeing any lifelong ART guidelines for pregnant and

breastfeeding women. Where guidelines existed, health providers kept them in their consultation rooms and shared them when need arose.

Lack of information, education and communication (IEC) materials

PMTCT IEC materials were also lacking except for a few facilities that had such information on the walls.

“Yeah, there are some posters, but they are extremely few. I have seen one, but recently, they repainted the walls and I don’t know if they have put them up again.” (Health Provider, Hospital)

Additionally, participants noted that facilities lacked fliers and information packs that could be provided to mothers. A few participants felt these materials could be taken home by the women to assist their understanding and to enable them share with family members especially their spouses.

“It would be good to give HIV-positive mothers materials such as leaflets with lifelong ART information because it reminds the woman to take the ARVs. Additionally, if put on the table - and my husband doesn’t know that am HIV-positive; when my he comes and reads it, he will get the information and will realize that there is need to test for HIV.” (Health Provider, HC IV)

Lack of real-time electronic data capture system

In all the health facilities, participants highlighted that lack of real-time electronic data capture system was a challenge. They reported that they recorded patients’ data in PMTCT registers and on cards which were later given to staff in the records’ section for entry. Participants emphasized that time from data capture to electronic entry depended on the volume of patients and number of record assistants available. Once the data had been electronically entered it was used to track mothers and later their babies as well.

“We record the mother’s information on paper. Thereafter, we send it to the in-charge who verifies the information captured and then takes it to the records assistants for entry into the computer.” (Health Provider, HC III)

Insufficient funds

Many participants indicated that limited funding hindered making of phone calls, home visits and community out reaches to follow up women and their infants who missed clinic appointments.

“Follow-up and tracking of women and their exposed infants require funds for transport. We at times use bicycles but they are few and some places are far away. I wish the Ministry of Health comes to provide more funds, bicycles, and motorcycles.” (Health Provider Hospital)

Participants said that in addition to use of VHTs and expert clients, other strategies like health facility providers using facility and district vehicles, follow-up and track women despite the limited funding.

“We give the HIV-positive women addresses of the VHTs to go and follow-up on them. The VHTs go to check whether the mother and baby are still there and why they are not coming for their clinic visits or taking the ART.” (Health Provider, Hospital)

Stock-outs of HIV test kits, Cotrimoxazole and Nevirapine syrups

Most participants observed that health facilities occasionally faced shortage of HIV testing kits, Nevirapine and Cotrimoxazole syrups. However, it was acknowledged that at one point the shortage of testing kits was a country-wide challenge. Participants admitted that sometimes stock-outs were due to poor forecasting which was rectified by devising a mechanism for enhanced forecasting.

“We have been experiencing stock-outs for; testing kits and the syrup - baby syrup [meaning Nevirapine].” (Health Provider, HC IV)

Internal re-allocation of supplies and borrowing from nearby facilities were used to address this, and at other times, dividing of drugs was done.

“We would request Nevirapine syrup from the lower-level health units which are not very busy..... It reached a moment where we had to share the Nevirapine syrup among two babies.” (Health Provider, Hospital)

In cases where providers were completely constrained, they would inform the implementing partners who would then bring the logistics.

2. Non-utilization of HIV services and countermeasures

Two categories are presented: HIV-related stigma and accessibility related.

a) *HIV-related stigma*. Four sub-themes are presented under this category.

Non-disclosure of HIV-positive status

All study participants expressed that non-disclosure of HIV-positive status was a significant and common challenge. They highlighted that many HIV-positive women feared disclosing their HIV status and the women perceived it that they would be stigmatized. It was noted that some women didn't disclose their HIV-positive status to their partners since they weren't sure of their spouses' reaction to the HIV+ result. Of most concern to the women, was fear of negative impact on relationships.

"The man [spouse] will chase me away or run away from me, yet this is still a new marriage!"
(Health Provider, Hospital)

"She will then tell you, 'ah'! Musawo [health worker] leave me alone, what if I tell him [spouse] and he tells me that am the one who brought the virus!" Another one will say, "what if he [spouse] chases me away with my child..... just leave me alone". Actually, most of them do not tell them [spouses] about their HIV-positive status and being on ART." (Health Provider, Hospital)

The women ended up hiding their ARVs, missing appointments and not adhering to ART.

"The first challenge is non-disclosure of HIV-positive status! Mothers were initiated on lifelong ART during ANC and post-delivery, but even after all the counselling is done, some mothers refuse to disclose the positive HIV status to their partners. This mother's ART adherence may be affected because she may not be able to take the drugs when the husband is around. Secondly, she may fear to keep the drugs with her in the house." (Health Provider, HC IV)

Denial of HIV-positive results

During interviews, many participants reported that some women did not believe they were HIV-positive. Such women reportedly repeated the test at other facilities which delayed ART initiation.

“One woman said that she has been delivering all her children normally [meaning children who were HIV-negative] and now we are telling her that she is HIV-positive? How comes? In other words, she doubted her HIV status.” (Health Provider HC III)

Fear to be followed up

Participants noted that some women did not welcome being visited or followed up in the communities where they lived due to HIV-related stigma with some providing incorrect addresses and/or telephone numbers. Sometimes women switched off their phones. This affected follow-up and linkage to HIV community-based services.

“Yes, we try to call them, but it is hard to find them. When they get to know your telephone contact, they stop picking your calls! Sometimes, when you call them [women], they will tell you that they are busy. Others may tell you that they shifted to another place for the same services.” (Health Provider HC IV)

Participants said that the use of ongoing counselling, expert clients and VHT support were the strategies in place to overcome non-disclosure, and denial of HIV-positive results, and fear to be followed-up.

Unwillingness to be linked to other intra-facility service care points

There are established mechanisms to link women and their infants to different intra-facility service care points, however, several challenges were cited by study participants. For example, some women were unwilling to be linked for intra-facility HIV services mainly because of HIV – related stigma. Many participants reported that some women feared being seen in general HIV clinics by relatives, friends and or neighbours.

“After giving birth, the mothers are supposed to attend the EID and general HIV clinics from the other side and there are many other patients seated together there. So, some fear and are

unwilling to be linked to those other clinics. They prefer to stay at the PNC clinic where they are few and receive the clinic services quickly.” (Health Provider, Hospital)

To overcome this challenge providers cited various strategies. The time of follow-up within the PNC was extended at several facilities to address this lack of willingness to transfer to general HIV chronic care clinics. In four of the six facilities, women were staying in the PNC beyond the recommended six weeks after giving birth.

“Actually, we continue keeping them within the PNC clinic until the women are ready for referral/linkage to the ART clinic successfully before they deliver or after they have delivered.” (Health Provider, HC IV)

As another strategy, women were accompanied by either a midwife, a counsellor, an expert client, or a VHT member from one service point to another, to ensure successful linkage. For example, women would be accompanied from the ANC clinic to the infant immunization clinics or to the EID testing care point and general HIV clinic.

“Mothers who come here for their first time don’t know us or the different health service care points. I move with the mother showing her around and what is done until we reach the EID care point. There is a person responsible for EID, and then I introduce that medical worker to the mother.” (Health Provider, HC IV)

b) Accessibility related. Under this category, two sub-themes were identified. These were:

Large catchment areas

Some participants reported that they serve women who came from distant places to the study facilities. Facilities especially in rural areas that were close to the women didn’t offer lifelong ART services.

Lack of transport

Most HIV-positive pregnant women could not afford transport costs which impacted their ability to attend appointments.

Some women come from very far! They stay like 20 miles away from here. Such women have a challenge of transport coming here every month.” Health Provider HC IV.

To address accessibility-related challenges study participants noted that they used outreaches during which women on lifelong ART would be clinically evaluated and appropriately treated. Additionally, community members were engaged in health education and, HIV counselling and testing (HCT) which was envisaged to reduce community-related-HIV stigma. Besides, expert clients and VHTs would support the women to cope with the lifelong ART.

“We have three outreaches in a month. We have a number of landing sites where we conduct outreaches. We have our “Kizindalo” [big loud speaker] that we use to call and mobilize them. When they come, we counsel and test them. Those who test HIV-positive, are counselled and enrolled into care, while those who test negative are only counselled. We use the occasion to reduce stigma tendencies through health education” (Health Provider, HC IV)

However, it was noted that outreaches were expensive and time-consuming which calls for more resources and consequently result in sustainability challenges.

Furthermore, some participants reported that some female clients were given additional ARV supplies to reduce visits to clinics for collection of medication. This was anticipated to reduce on the transport costs.

“Some women who come from far are given ARVs for two months instead of one to reduce on the frequency of their clinic appointments. In addition, we have been provided with some fuel to take the ARVs and do HIV testing to the community through outreaches.” (Health Provider, Hospital)

3. Suboptimal treatment adherence and countermeasures

The categories under this theme were ART-related, and male spouse related.

a) *ART-related.* Two sub-themes are presented.

Fear of ART side effects

Most participants said that many women feared ART side effects, and some of which were reported to have been grave.

“She [HIV-positive mother] refused ARVs claiming that she will get a skin rash or even die. At least, she would take Septrin [Cotrimoxazole] but not ART]. She [HIV-positive mother] tells you that some of her relatives suffered from HIV and when they started taking ARVs, they got severe side effects and some actually passed away.” (Health Provider, HC III)

Preference for traditional medicines

Several study participants mentioned that some women would stop using ART and opt to use local herbs with a misconception that they would treat HIV as illustrated by the quote below;

“Some women stop taking their HIV drugs and resort ‘budomola’ meaning the local herbs used to treat HIV. Such mothers continue taking those herbs. But for us [health providers] here, we don’t support them to use those herbs because when they will give birth to HIV-positive babies in the long run.” (Health Provider, HC III)

Participants emphasized that fear of ART side effects and preference for traditional medicines were addressed using similar strategies. These included health education, continuous group and individual counselling, and formation of family support groups (FSGs).

Participants noted that FSGs had helped significantly in addressing these challenges through peer support.

“Family support groups are helpful; when one is HIV-positive, alone and gets a problem, it disturbs a lot but when one is in a group and another person mentions the very problem you are encountering, then you will realize that you are not alone. As a result, your mind is settled.” (Health Provider, HC III)

b) Male spouse related. Low male partner involvement in care was identified as the subtheme under this category.

Low male partner involvement in care

Low male partner involvement in care was a common finding. Participants noted that some women would even bring different men other than their partners whenever they are

told to bring their spouses. This was attributed to fear for consequences of HIV-positive status disclosure.

“We tell the women to come with their husbands for HIV counselling and testing, and treatment but majority don’t want. The mothers tell you that the men are busy while others are scared to come to health facilities.” (Health Provider, HC III)

Some men were reported to be unsupportive during ANC, delivery and PNC. Partner support related challenges intensified after delivery especially when the woman did not disclose her HIV status.

“We have very few husbands that accompany pregnant women and my fear is that when one doesn’t have a treatment partner, there is nobody to share with the challenges they are facing. If the man is not involved, what will happen if that woman depends on the man for financial support? At first, it was the pregnancy driving the man to give money to the pregnant mother to come for ANC, now that the baby has been delivered, what will be the reason for the husband to give transport to this mother to come for ART?” (Health Provider, Hospital)

There were various interventions across facilities to overcome low male involvement. In most facilities, women who came with their husbands were prioritized for health services. However, in other instances, men would actively be involved in the care that the wives received.

“Apart from health education that we provide, the men are there with us, when we are taking body weight and blood pressure; we also take theirs (the men). Inside the examination room, we also ask the husband if he is having any sickness and we give them the treatment. Moreover, after I examine the mother, I ask the spouse, [have you ever felt your baby’s heart beating from the uterus?] Then the person says no. Then I ask, “Do you wish to feel it beating?” When he agrees, I just put a foetal scope there, call him and give him instructions. When the husband hears the baby’s heart beating, you see that he is really excited.” (Health Provider, HC IV)

Participants reported providing health services to men such as health education, screening for, and treating common illnesses motivated the men to accompany their wives to the health facilities. In other facilities, study participants said that they didn’t prioritize those who came as couples but thanked and recognized men who had accompanied their wives. Other strategies to improve male involvement encompassed

community outreach, continuous counselling, health education, use of FSGs and peer fathers/male champions.

“We realized that some of the strategies that we are using motivate men to come with their spouses for lifelong ART services. The strategies include giving health education on topics like HIV, care for pregnant and breastfeeding women, medical male circumcision, sexually transmitted infections (STIs) and non-communicable diseases. Other approaches that we use are offering men health services such as screening for STIs, non-communicable diseases like hypertension and diabetes mellitus.” (Health Provider, Hospital)

One participant said that they were exploring the possibility of encouraging men to be involved in care for their spouses. He suggested that they were going to target men when they come to visit their wives in the health facility which is common in the first few hours after delivery. This would be an opportunity to encourage male involvement since most men come to check on their wives and the new-born infants.

“Normally when the woman delivers, that is when her husband comes to see or pick her and the new-born. So, we are making an attempt to see whether we can use that as a time to counsel men as well. It is an opportunity that we have, to talk to the men.” (Health Provider, HC IV)

7.5 Discussion

This study explored challenges and countermeasures in the implementation of lifelong ART for pregnant and breastfeeding women from the health providers' perspective in three districts in Central Uganda. Major challenges were: a lack of in-service and/or refresher training on lifelong ART, shortage of health providers, inadequate counselling, lack of real-time electronic data capture system, and stock-outs of HIV test kits, Nevirapine syrup and Cotrimoxazole syrups which might result in inadequate lifelong ART service delivery. Other major challenges such as non-disclosure of HIV-positive status, fear to be followed up, large catchment area, and lack of transport suggest non-utilization of lifelong ART services. While challenges like fear of ART side effects, and low partner involvement in care could lead to suboptimal treatment adherence lifelong ART among pregnant and postpartum women.

Several strategies were being used and proposed to address the identified challenges. These included on-job training, continuous medical education, task shifting, on-going counselling, FSGs, re-allocation of HIV commodities, use of peers, and conducting community outreaches.

The Uganda MOH working with U.S. President's Emergency Plan For AIDS Relief (PEPFAR) and implementing partners have addressed some of the challenges such as training inadequacies, stock-outs, retention in care challenges, and staff shortages to ensure that Uganda remains on track to achieve both the UNAIDS and national 95-95-95 targets. Strategies that were employed to address the gaps include increasing funding for ARV procurement and stock monitoring, supply chain reform improvement, human resource performance management, improving referral and linkage structures, use of short message services, phone calls, and home visits to track the lost women and HIV exposed infants, bring back mother and baby campaign, and supporting outreaches [19, 32, 33]. Recent reports indicate that several of these challenges still exist including inadequate number of health workers, increased workload, lack of training, insufficient supplies and commodities, suboptimal ART adherence, non-disclosure of positive HIV status, low retention in care rates and low male partner involvement in care [17, 34-36]. Likewise, we earlier reported challenges around adherence and non-disclosure of HIV-positive status from the clients' perspective [27, 30]. Therefore, this study adds to existing literature on challenges in implementation of lifelong ART among pregnant and breastfeeding women from the health providers' perspective. The study also describes approaches that were used to address the challenges. Addressing these persistent challenges will fast track the achievement and sustainability of e-MTCT outcomes towards ending AIDS as a public health threat by 2030 [21, 22].

Lack of relevant training and inadequate counselling

Quality of e-MTCT services continues to experience some flaws which should be addressed [35]. Challenges that result in inadequate HIV service delivery might be contributors to low quality e-MTCT services. Many health providers had not received training on PMTCT lifelong ART service provision. This was mostly among providers who were new in the facilities and those who were not directly involved in offering lifelong ART

services. On the other hand, some of the previously trained providers lacked refresher training. Congruent with our findings, a study conducted in India, found that some health providers lacked training on PMTCT services [18]. Other studies including a systematic review and another study done among health care providers at four health facilities in western Kenya revealed that the PMTCT training received by health providers was insufficient [12, 16, 37]. Furthermore, despite the adoption and implementation of the innovative differentiated service delivery (DSD) models for HIV services in Uganda in 2016, a study found that health workers in 600 out of 1,800 health facilities providing ART had not yet been trained in DSD delivery [36]. This suggests persistent gaps in HIV service delivery training in Uganda. Our study finding calls for e-MTCT training of more health providers and refresher trainings for those who were already trained. Innovative trainings such as web based, virtual and modular would be more appropriate and cost-effective since they reduce movements of health providers from their work stations. Additionally, the web based and virtual designs could be appropriate in the current context of COVID-19 pandemic.

Moreover, the trainings could be designed to address gaps in counselling that our study identified as one of the major challenges. Although adequate counselling was earlier reported to be the reason for the women to start swallowing ART on the same day it was prescribed[29], this might have targeted the newly diagnosed HIV pregnant women. The counselling inadequacies might be partially attributed to lack of or insufficient training on e-MTCT services, limited time for counselling, overwhelming numbers of individuals who require HIV services, and a lack of trained counsellors. Adequate counselling is essential especially in preparing pregnant and breastfeeding women for lifelong ART [38]. It prepares the women for the lifelong journey of ART. In contrast, inadequate counselling results in low utilization of PMTCT services [39] which would deter the achievement of e-MTCT of HIV. Most challenges identified such as the denial of HIV+ results, fear of ART side effects, fear to be followed up and non-disclosure HIV status can be solved using good counselling skills.

Shortage of health providers

Shortage of health providers was another challenge identified by this study. Staffing inadequacy in Uganda is not only a PMTCT challenge but rather cuts across various programs [40]. Notably, our study identified counsellors and clinical officers as some of the health providers who were inadequately staffed. Unfortunately, this shortage in the PMTCT program is worsened by the extensive patient and documentation load associated with HIV service provision [41]. Similar to our study, a validation study on the path to e-MTCT of HIV and Syphilis in Uganda (2010-2018) showed that at facility and district level, 50% (64) and 54% (32) respectively, had inadequate staff in both category and numbers offering PMTCT services [17]. Correspondingly, a study in Nigeria revealed a huge lack of doctors, nurses and midwives to available to deliver PMTCT services [23]. Task shifting using non-formal health providers such as expert clients (peer/mentor mothers and fathers), community linkage facilitators and VHTs has been adopted to address this challenge. However, the number of this cadre of health workers remains low [42]. Non-formal providers might have more time with women on lifelong ART because some of them live within the same communities. Expert clients have lived HIV experience, placing them in a better position to handle HIV-related stigma challenges. Nevertheless, the use of a mix of formal health workers, expert clients and other informal volunteer workers calls for more innovation to ensure delivery of quality services and sustainability [43-45]. The MOH and implementing partners should ensure adequate training, supervision and mentorship of expert clients, linkage facilitators and VHTs to enable them work effectively.

Lack of real-time electronic information capture, guidelines, and IEC materials

Absence of real-time electronic data capture system and limited supply of PMTCT guidelines and communication materials was noted as a shortfall. This finding is similar to results from a study in Malawi where health workers reported lack of information technology infrastructure which resulted in use of paper-based methods of data capture and storage [46]. Paper-based data has limitations such as storage, unreadable, double work, time consuming, and errors during entry into the electronic medical record system, and difficulties in analyses [46, 47]. In India, it was found that real-time electronic data

capture systems improve health provider work style, data capture, linkage across different clinics and overall satisfaction with PMTCT work [48, 49]. MOH in collaboration with the donors should strengthen scale up of electronic medical records to enable real-time data capture, easy and timely analysis to inform decision making. Additionally, more copies of PMTCT guidelines should be distributed to health facilities to enhance standardized practice. Participants felt that PMTCT communication materials would be useful in disseminating information to individuals, families and communities especially men who are reluctant to visit health facilities. Client IEC materials have the potential to reduce HIV related stigma and hence increase utilization of PMTCT of HIV services [50]. Appropriate, context specific and easy to understand client PMTCT IEC materials should be availed to health facilities and communities.

Stock-outs of HIV test kits, Nevirapine and Cotrimoxazole syrups

Our findings show occasional stock-outs of HIV test kits, Nevirapine and Cotrimoxazole syrups. This is consistent with findings from a study in India, where study participants reported shortages of HIV testing kits, and Nevirapine for infants [18]. However, a study from health facility surveys in six SSA countries had varied results. Stock-outs of HIV test kits and ARVs were common in Tanzanian health facilities [51]. Stock-outs might suggest poor forecasting, management, and monitoring of these essential HIV commodities. A lack of HIV testing kits, Nevirapine and Cotrimoxazole syrups is unacceptable. HIV testing is the entry point for primary and secondary prevention as well as care and treatment, while the ARVs supply chain is a major component of a systematic program for the prevention and treatment of HIV/AIDS [52-54]. Health facilities with stock-outs would make arrangements to get these from facilities that had enough stock. This is in line with the MOH redistribution strategy [7]. Although the Uganda MOH with support from partners is closely undertaking ARV stock monitoring and management using the Web-Based ARV Ordering and Reporting System [19], these findings underscore the need for all e-MTCT of HIV stakeholders to work together to avert the recurrent stock-outs of HIV commodities. This could be done by strengthening the supply chain management capacity at national, regional, district and health facility levels which would ensure accurate and timely ordering and provision of appropriate real-time stock status data at health facilities.

Unwillingness to be referred

Health providers noted that some women refused to be referred to other HIV intra-facility service care points. The women preferred to remain in the antenatal clinic even after giving birth which was attributed to HIV- related stigma. This finding is similar to results from a study that was done in Nigeria. Participants reported that HIV-positive women feared to get services from designated places in the health facilities [55]. Refusal to receive services from other HIV care points is likely to result in loss-to-follow up along the PMTCT cascade. Facilities used various approaches to ensure that women are not lost during the linkage process. Strategies used included accompanying women from one service point to another, following up referrals that were given to women and only referring women when they were ready. This was to ensure that women reach the point of referral. However, accompanying women could be a challenge and not feasible where health providers face staff shortages and heavy workload.

Large catchment area and lack of transport

Despite the target by the Uganda MOH that 85% of population to reside within a distance of 5km from a health facility, distance to health facilities remains a challenge [56, 57]. Our study highlights the challenge of large catchment areas and lack of transport. These findings concur with those from Ethiopia and South Africa where restricted physical access, and transportation to PMTCT sites were barriers to utilization of PMTCT services [58, 59]. Expert clients, linkage facilitators, VHTs and community outreaches were being employed to address this challenge. Nonetheless, these strategies are costly and unsustainable. Given that several women and other clients on test and treat attend HC IIIs and IIs for both ANC and immunization yet these facilities often lack comprehensive HIV services, the MOH ought to strengthen HIV services at HC IIIs, accredit large volume HC IIs to provide comprehensive HIV services.

Low male partner involvement in care

Men are the main decision-makers in a home especially in Africa [60, 61]. They thus influence women's access to maternal, neonatal and child health services, and thus impacting their health outcomes [61]. Male involvement in implementation of the lifelong ART strategy affects uptake, adherence and retention in care [62-64]. Low male partner involvement in care for lifelong ART among pregnant and breastfeeding women stood out in our study findings as a challenge. Consistent with our study, findings from studies conducted elsewhere show low male partner involvement in care [65-67]. For example, in Mwanza region –Tanzania the study showed that only 24.7% of mothers indicated that their male partners were involved in PMTCT, whereas only 20.9% of men from a study in Ethiopia had a high involvement index in PMTCT services [66, 67].

Facilities in our study were engaging some strategies to improve male involvement in lifelong ART services but providers reported that the impact was limited possibly because they were still in infancy stages. Strategies include community sensitization of men about benefits of ANC and lifelong ART, having male friendly services for men who accompany their spouses and offering quality services. Strategies such as use of mentor fathers/champions, health education, community sensitizations and screening of non-communicable diseases for men might have a great potential to improve male involvement in lifelong ART services. Regrettably, male partner involvement has remained a gap in the PMTCT of HIV program [17]. The countermeasures that our study identified to address low male involvement could be implemented in other African country settings so as to accommodate male partners in attending, ANC, delivery, and PNC services with their female partners. Albeit, more innovations such as age and population specific dialogues are needed to overcome low male partner involvement in e-MTCT of HIV.

7.6 Strengths and limitations

A broad range of providers implementing the PMTCT program were interviewed which enabled us to explore challenges and countermeasures within the facilities. The data was collected in 2014 and some of the findings may not be applicable in the current context.

In addition, the PMTCT program has gone through a number of transitions in the last decade. For example, the last transition is the change to Dolutegravir ART-based regimen [11]. Viral load monitoring has become the standard of care compared to CD4 count. These changes may have implications on our results. However, several of the findings remain relevant and can be transferred to other facilities and settings with Uganda and beyond. Use of key informant interviews might have resulted into social desirability bias but this was minimized by use of experienced data collectors, establishing of rapport, use of probes, and conducting regular research team meetings.

7.7 Conclusions and Recommendations

The study identified persistent challenges that were negatively impacting HIV service delivery and use, and subsequently treatment adherence. A number of countermeasures were being used to address these challenges. We recommend that; providers including community support groups offering lifelong ART services to pregnant and postpartum women should receive regular training, supervision, and mentorship. Training on lifelong ART services should start during the pre-service period for all clinical students. Adequate personalized pre-ART and continuous counselling should be offered to HIV-positive pregnant and breastfeeding women. Facilities should be supported to ensure that they; are well stocked with lifelong ART and health supplies, and acquire real-time electronic data capture system. Ministry of health should scale-up the strategy of task shifting using peers, VHTs, and male champions, and consider accreditation of the large volume HC IIs and those in distant rural areas to provide e-MTCT services. Research to assess the effectiveness of the key countermeasures is recommended so as to inform adoption and scale up.

Acknowledgement

The authors wish to thank all study participants without whom this study wouldn't have been successful. Special thanks also go to the respective heads of facility for Masaka RRH, Mityana General Hospital, Luwero HC IV, Kyanamukaka HC IV, Ssunga and Katikamu HC IIIs for their continued support rendered to us throughout the data collection process. We also acknowledge the tireless efforts of all study interviewers in collecting data at their respective study sites.

Author Abbreviations

A.M.: Aggrey David Mukose

E.B.: Esther Buregyeya

H.B.: Hilde Bastiaens

R.N: Rose Naigino

R.W.: Rhoda K. Wanyenze

Author Contributions

Conceptualization: Aggrey David Mukose, Fredrick Makumbi, Esther Buregyeya, Joshua Musinguzi, Rhoda K. Wanyenze.

Formal analysis: Aggrey David Mukose, Hilde Bastiaens, Rhoda K. Wanyenze.

Funding acquisition: Joshua Musinguzi, Rhoda K. Wanyenze.

Investigation: Aggrey David Mukose, Fredrick Makumbi, Esther Buregyeya, Rhoda K. Wanyenze.

Methodology: Aggrey David Mukose, Esther Buregyeya, Rhoda K. Wanyenze.

Project administration: Rose Naigino.

Supervision: Hilde Bastiaens, Jean-Pierre Van Geertruyden, Rhoda K. Wanyenze.

Visualization: Aggrey David Mukose, Hilde Bastiaens.

Writing – original draft: Aggrey David Mukose.

Writing – review & editing: Aggrey David Mukose, Hilde Bastiaens, Fredrick Makumbi, Esther Buregyeya, Rose Naigino, Joshua Musinguzi, Jean-Pierre Van Geertruyden, Rhoda K. Wanyenze.

Competing interests: The authors have declared that no competing interests exist.

Funding: This study was funded by the Global Fund through the Ministry of Health-Uganda [Grant Number: UGD-708-G07-H]. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

1. Schouten EJ, Jahn A, Midiani D, Makombe SD, Mnthambala A, Chirwa Z, et al. Prevention of mother-to-child transmission of HIV and the health-related Millennium Development Goals: time for a public health approach. *The Lancet*. 2011;378(9787):282-4.
2. CDC. Impact of an innovative approach to prevent mother-to-child transmission of HIV--Malawi, July 2011-September 2012. Atlanta, Georgia, United States: Centers for Disease Control Prevention, 2013 1545-861X Contract No.: 8.
3. Kalua T, Barr BAT, Van Oosterhout JJ, Mbori-Ngacha D, Schouten EJ, Gupta S, et al. Lessons learned from option B+ in the evolution toward “test and start” from Malawi, Cameroon, and the United Republic of Tanzania. *Journal of acquired immune deficiency syndromes (1999)*. 2017;75(Suppl 1):S43.
4. NAC. National 2012 global AIDS response progress report: Malawi country report. Lilongwe, Malawi: The Malawi, National AIDS Commission, 2012.
5. WHO. Consolidated Guidelines on the use of Antiretroviral drugs for Treating and Preventing HIV infection: Recommendations for a Public Health Approach. Geneva, Switzerland: World Health Organization, 2016 978 92 4 154968 4.
6. Godfrey E. PMTCT Implementation in Uganda: Option B Plus Experience 2013 [cited 2013]. Available from: http://www.vaccineenterprise.org/sites/default/files/02-Esiru_0.pdf).
7. MOH. Consolidated guidelines for prevention and treatment of HIV in Uganda. In: ACP, editor.: MOH; 2014.
8. UAC. The Uganda HIV and AIDS Country Progress Report July 2015-June 2016. Kampala, Uganda: 2016 26 August 2016.
9. MOH. Consolidated guidelines for prevention and treatment of HIV in Uganda. In: ACP, editor. Kampala, Uganda: MOH; 2016. p. 154.
10. Mikkelsen E, Hontelez JAC, Jansen MPM, Bärnighausen T, Hauck K, Johansson KA, et al. Evidence for scaling up HIV treatment in sub-Saharan Africa: A call for incorporating health system constraints. *PLOS Medicine*. 2017;14(2):e1002240. doi: 10.1371/journal.pmed.1002240.
11. MOH. Consolidated Guidelines for the Prevention and Treatment of HIV and AIDS in Uganda 2020. Kampala, Uganda: MOH; 2020. p. 245.

12. Colvin CJ, Konopka S, Chalker JC, Jonas E, Albertini J, Amzel A, et al. A systematic review of health system barriers and enablers for antiretroviral therapy (ART) for HIV-infected pregnant and postpartum women. *PloS one*. 2014;9(10):e108150. doi: 10.1371/journal.pone.0108150. PubMed PMID: 25303241; PubMed Central PMCID: PMC4193745.
13. UNAIDS. Women and HIV: a spotlight on adolescent girls and young women. 2019.
14. MOH. Impact of the National Program for Prevention of Mother– to-Child Transmission of HIV in Uganda, Evaluation Report 2017 - 2019. Kampala, Uganda: Ministry of Health, AIDS; 2022 January 2022.
15. MOH. Annual Health Sector Performance Report Financial Year 2020/21. Kampala, Uganda: MOH; 2021. p. 156.
16. Helova A, Akama E, Bukusi EA, Musoke P, Nalwa WZ, Odeny TA, et al. Health facility challenges to the provision of Option B+ in western Kenya: a qualitative study. *Health policy and planning*. 2017;32(2):283-91.
17. MOH. Progress Report for Validation on the Path to Elimination of Mother-to- Child Transmission of HIV and Syphilis in Uganda (2010-2018). In: ACP, editor. Kampala, Uganda: MOH; 2019. p. 80.
18. Suryavanshi N, Mave V, Kadam A, Kanade S, Sivalenka S, Kumar VS, et al. Challenges and opportunities for outreach workers in the Prevention of Mother-to-Child Transmission of HIV (PMTCT) program in India. *PloS one*. 2018;13(9): e0203425. doi: 10.1371/journal.pone.0203425.
19. PEPFAR. PEPFAR Uganda Country Operational Plan (COP) 2019 Strategic Direction Summary April 12, 2019. Washington, DC, USA. 2019: PEPFAR, 2019.
20. Abuogi LL, Humphrey JM, Mpody C, Yotebieng M, Murnane PM, Clouse K, et al. Achieving UNAIDS 90-90-90 targets for pregnant and postpartum women in sub-Saharan Africa: progress, gaps and research needs. *Journal of virus eradication*. 2018; 4:33-9.
21. UAC. National HIV and AIDS Strategic Plan 2015/2016- 2019/2020: An AIDS Free Uganda, My Responsibility! Uganda AIDS Commission, Republic of Uganda. Kampala, Uganda: Uganda AIDS Commission, 2015 2015.
22. UNAIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic. Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS, 2014.
23. Olakunde BO, Adeyinka DA, Olawepo JO, Pharr JR, Ozigbu CE, Wakdok S, et al. Towards the elimination of mother-to-child transmission of HIV in Nigeria: a health

- system perspective of the achievements and challenges. *International health*. 2019;11(4):240-9.
24. Etoori D, Kerschberger B, Staderini N, Ndlangamandla M, Nhlabatsi B, Jobanputra K, et al. Challenges and successes in the implementation of option B+ to prevent mother-to-child transmission of HIV in southern Swaziland. *BMC Public Health*. 2018;18(1):1-9.
 25. Gugsu S, Potter K, Tweya H, Phiri S, Sande O, Sikwese P, et al. Exploring factors associated with ART adherence and retention in care under Option B+ strategy in Malawi: A qualitative study. *PloS one*. 2017;12(6): e0179838.
 26. Sudhinaraset M, Ingram M, Lofthouse HK, Montagu D. What is the role of informal healthcare providers in developing countries? A systematic review. *PloS one*. 2013;8(2): e54978.
 27. Buregyeya E, Naigino R, Mukose A, Makumbi F, Esiru G, Arinaitwe J, et al. Facilitators and barriers to uptake and adherence to lifelong antiretroviral therapy among HIV infected pregnant women in Uganda: a qualitative study. *BMC pregnancy and childbirth*. 2017;17(1):1-9.
 28. Mukose AD, Bastiaens H, Buregyeya E, Naigino R, Makumbi F, Musinguzi J, et al. Health Provider Perspectives of Health Facility Preparedness and Organization in Implementation of Option B+ among Pregnant and Lactating Women in Central Uganda: A Qualitative Study. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2019; 18:2325958219833930.
 29. Mukose AD, Bastiaens H, Makumbi F, Buregyeya E, Naigino R, Musinguzi J, et al. What influences uptake and early adherence to Option B+ (lifelong antiretroviral therapy among HIV-positive pregnant and breastfeeding women) in Central Uganda? A mixed methods study. *PloS one*. 2021;16(5):e0251181.
 30. Naigino R, Makumbi F, Mukose A, Buregyeya E, Arinaitwe J, Musinguzi J, et al. HIV status disclosure and associated outcomes among pregnant women enrolled in antiretroviral therapy in Uganda: a mixed methods study. *Reproductive health*. 2017;14(1):1-11.
 31. Braun V. Using thematic analysis in psychology. *Qualitative Research in Psychology*. 2006; 3:77/101.
 32. MOH. Implementation Guide for Differentiated Service Delivery Models of HIV Services in Uganda. Kampala, Uganda: MOH, ACP; 2017 June 2017.

33. PEPFAR. PEPFAR Uganda Country Operational Plan (COP) 2018 Strategic Direction Summary Washington, DC, USA. 2018: 2018 April 17, 2018.
34. MOH. National Plan For Elimination of Mother-to-Child Transmission of HIV, Syphilis and Hepatitis B (2020/21 – 2023/24). 2020.
35. MOH. Annual Health Sector Performance Report Financial Year 2019/20 Kampala, Uganda: MOH; 2020.
36. Zakumumpa H, Rujumba J, Kwiringira J, Katureebe C, Spicer N. Understanding implementation barriers in the national scale-up of differentiated ART delivery in Uganda. *BMC health services research*. 2020;20(1):1-16.
37. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. *Journal of the International AIDS Society*. 2013; 16:18588. doi: 10.7448/IAS.16.1.18588. PubMed PMID: 23870277; PubMed Central PMCID: PMC3717402.
38. Chung MH, Richardson BA, Tapia K, Benki-Nugent S, Kiarie JN, Simoni JM, et al. A randomized controlled trial comparing the effects of counseling and alarm device on HAART adherence and virologic outcomes. *PLoS Med*. 2011;8(3):e1000422.
39. Hampanda K. Vertical Transmission of HIV in Sub-Saharan Africa: Applying Theoretical Frameworks to Understand Social Barriers to PMTCT. *ISRN Infectious Diseases*. 2013; 2013:420361. doi: 10.5402/2013/420361.
40. Koutsoumpa M, Odedo R, Banda A, Meurs M, Hinlopen C, Kramer K, et al. Health workforce financing in Uganda: challenges and opportunities. *European Journal of Public Health*. 2020;30(Supplement_5). doi: 10.1093/eurpub/ckaa165.525.
41. Sande O, Burtcher D, Kathumba D, Tweya H, Phiri S, Gugsu S. Patient and nurse perspectives of a nurse-led community-based model of HIV care delivery in Malawi: a qualitative study. *BMC public health*. 2020; 20:1-8.
42. CSOs. The People's Voice Uganda: Community Priorities - PEPFAR Country Operational Plan 2020. CSOs, 2020 2020.
43. Callaghan M, Ford N, Schneider H. A systematic review of task-shifting for HIV treatment and care in Africa. *Human resources for health*. 2010;8(1):8.
44. Celletti F, Wright A, Palen J, Frehywot S, Markus A, Greenberg A, et al. Can the deployment of community health workers for the delivery of HIV services represent an effective and sustainable response to health workforce shortages? Results of a multicountry study. *Aids*. 2010;24: S45-S57.

45. WHO. Serving the needs of key populations: Case examples of innovation and good practice on HIV prevention, diagnosis, treatment and care. 2017 9241512539.
46. Kumwenda W, Kunyenje G, Gama J, Chinkonde J, Martinson F, Hoffman I, et al. Information management in Malawi's prevention of Mother-to-Child Transmission (PMTCT) Program: Health workers' perspectives. *Malawi Medical Journal*. 2017;29(4):306-10.
47. Gourlay A, Wringe A, Todd J, Michael D, Reniers G, Urassa M, et al. Challenges with routine data sources for PMTCT programme monitoring in East Africa: insights from Tanzania. *Global Health Action*. 2015;8(1):29987. doi: 10.3402/gha.v8.29987.
48. Suryavanshi N, Kadam A, Kanade S, Gupte N, Gupta A, Bollinger R, et al. Acceptability and feasibility of a behavioral and mobile health intervention (COMBIND) shown to increase uptake of prevention of mother-to-child transmission (PMTCT) care in India. *BMC public health*. 2020; 20:1-11.
49. Thomas DSK, Bull S, Nyanza EC, Hampanda K, Liedtke M, Ngallaba SE. An mHealth pilot designed to increase the reach of prevention of mother-to-child transmission of HIV (PMTCT) across the treatment cascade in a resource-constrained setting in Tanzania. *PloS one*. 2019;14(2):e0212305. doi: 10.1371/journal.pone.0212305.
50. McDougal L, Moteetee MM, Mohai F, Mphale M, Mahanty B, Motaung B, et al. Lesotho's Minimum PMTCT Package: lessons learned for combating vertical HIV transmission using co-packaged medicines. *Journal of the International AIDS Society*. 2012;15(2):17326. doi: <https://doi.org/10.7448/IAS.15.2.17326>.
51. Church K, Machiyama K, Todd J, Njamwea B, Mwangome M, Hosegood V, et al. Identifying gaps in HIV service delivery across the diagnosis-to-treatment cascade: findings from health facility surveys in six sub-Saharan countries. *Journal of the International AIDS Society*. 2017;20(1):21188.
52. Altevogt BM, Wizemann TM, Norris SMP, Pankevich DE. Improving access to essential medicines for mental, neurological, and substance use disorders in sub-Saharan Africa: workshop summary: National Academies Press; 2014.
53. Spisak C, Morgan L, Eichler R, Rosen J, Serumaga B, Wang A. Results-based financing in Mozambique's central medical store: a review after 1 year. *Global Health: Science and Practice*. 2016;4(1):165-77.
54. Branson BM. The future of HIV testing. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2010;55: S102-S5.

55. Dirisu O, Eluwa G, Adams E, Torpey K, Shittu O, Adebajo S. "I think this is the only challenge... the stigma" Stakeholder perceptions about barriers to Antenatal care (ANC) and Prevention of mother-to-child transmission (PMTCT) uptake in Kano state, Nigeria. *PloS one*. 2020;15(4): e0232028. doi: 10.1371/journal.pone.0232028.
56. MOH. Health Sector Development Plan 2015/16 - 2019/20. Kampala, Uganda: MOH; 2015. p. 110.
57. EPRC. Universal Health Coverage in Uganda: The critical health infrastructure, healthcare coverage and equity. Kampala, Uganda: EPRC, 2017 June 2017.
58. Akal CG, Afework DT. Status of prevention of mother-to-child transmission (PMTCT) services utilization and factors affecting PMTCT service uptake by pregnant women attending antenatal care clinic in selected health facilities of Afar Regional State, Ethiopia. *Journal of environmental and public health*. 2018;2018.
59. Habedi D. Healthcare workers' perspectives on availability and accessibility of the prevention of mother-to-child-transmission programme in North West province, South Africa. *African Journal of AIDS Research*. 2020;19(1):24-33.
60. Mosha I, Ruben R, Kakoko D. Family planning decisions, perceptions and gender dynamics among couples in Mwanza, Tanzania: a qualitative study. *BMC public health*. 2013;13(1):1-13.
61. Yargawa J, Leonardi-Bee J. Male involvement and maternal health outcomes: systematic review and meta-analysis. *Journal of Epidemiology and Community Health*. 2015;69(6):604-12. doi: 10.1136/jech-2014-204784.
62. Alemayehu M, Etana B, Fisseha G, Hailelassie K, Yebyo H. The role of male partner involvement on mother's adherence to PMTCT care and support, Tigray, Northern Ethiopia. *Fam Med Med Sci Res*. 2014;3(04).
63. Belato DT, Mekiso AB, Begashaw B. Male partners involvement in prevention of mother-to-child transmission of HIV services in Southern Central Ethiopia: in case of Lemo District, Hadiya Zone. *AIDS research and treatment*. 2017;2017.
64. Nyondo AL, Chimwaza AF, Muula AS. Exploring the relevance of male involvement in the prevention of mother-to-child transmission of HIV services in Blantyre, Malawi. *BMC International Health and Human Rights*. 2014;14(1):1-12.
65. Yah CS, Tambo E. Why is mother-to-child transmission (MTCT) of HIV a continual threat to new-borns in sub-Saharan Africa (SSA). *Journal of infection and public health*. 2019;12(2):213-23.

66. Elias M, Mmbaga EJ, Mohamed AA, Kishimba RS. Male partner involvement in the prevention of mother-to-child transmission of HIV infection in Mwanza Region, Tanzania. *The Pan African Medical Journal*. 2017;27.
67. Amano A, Musa A. Male involvement in PMTCT and associated factors among men whom their wives had ANC visit 12 months prior to the study in Gondar town, North west Ethiopia, December, 2014. *Pan African Medical Journal*. 2016;24(1).

CHAPTER 8:

GENERAL DISCUSSION

This thesis explored the health provider perspectives on health facility preparedness, organization, challenges, and countermeasures, determined uptake of, and adherence to lifelong ART and its predictors among pregnant and lactating women living with HIV during the implementation of lifelong ART for PMTCT in Central Uganda.

The UNAIDS Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive [1] provided the foundation for country-led movements towards the elimination of new HIV infections among children and keeping their mothers alive by 2015. Whereas this plan made some achievements, it expired before the targets were fully met. To reinforce the gains of the Global plan, UNAIDS started the Start Free, Stay Free, and AIDS-free initiative in 2016 [2]. This initiative also ran up to 2020 and the progress report of the initiative revealed that there were substantial achievements but many gaps remained [3]. Moreover, UNICEF and its partners released a road map in 2020 which has key guidance on support to pregnant and breastfeeding women living with HIV to ensure retention in HIV care, adherence to lifelong ART, and provision of early services to HIV exposed infants so as to achieve e-MTCT [4]. Most recently, the WHO developed the triple elimination initiative of MTCT of HIV, Syphilis and Hepatitis B virus and consequently in 2021 developed the Global guidance on criteria and processes for validation of elimination of the three diseases [5]. Globally, only 16 countries have been validated for elimination of HIV and/or syphilis as by the end of 2022 [6, 7]. In 2021, Botswana, a sub-Saharan Africa like Uganda was the first high-burden HIV country to be certified for achieving an important milestone (silver tier) on the path to e-MTCT of HIV by the WHO [8, 9]. Due to the prevailing challenges in meeting set targets, WHO released the global strategies to move forward the achievements so far attained and address existing bottlenecks. The strategies stretch from 2022 to 2030 [10]. Finally, in line with the UNAIDS 95-95-95 targets, the UNAIDS unveiled a report in 2023 “The path that ends AIDS” the pathways for ending aids by 2030 [11]. This report states that there is a path to end AIDS by calling for preparedness to address other pandemic

challenges, and advance progress across the Sustainable Development Goals. At a country level, the Uganda Modes of HIV Transmission study for 2022 [12], the Annual Joint AIDS Review report for 2022 [13], and the 2023 mid-term review of the national HIV/AIDS strategic plan that runs from 2020- 2025 [14] have revealed great strides in its HIV response but also chronic gaps and areas of stagnation that require attention if the country is to attain the UNAIDS and WHO targets of aids elimination by 2030. Failure to meet some of the set targets has been attributed to disruptions that were caused by the COVID-19 pandemic [15, 16]. Therefore, our sub studies contribute important data to inform both these international and national efforts.

The sub-studies present important PMTCT programmatic implementation perspectives that are relevant to e-MTCT practice, policy, and future HIV research. The early tremendous gains in achieving e-MTCT are reported to have slowed [4, 15]. Therefore, these perspectives inform the UNICEF, WHO, and UNAIDS strategic plan of going the “last mile” to e-MTCT of HIV as well as the Uganda HIV strategic plan towards the elimination of HIV as a public health threat [4, 5, 10, 11, 17].

Our study revealed that training, supervision, and mentorship of health providers were key drivers in the implementation of lifelong ART for PMTCT of HIV in Uganda. This finding is also supported by studies conducted in similar contexts [18-21]. Training health workers on the use of lifelong ART strategy for e-MTCT of HIV is critical to the success of triple e-MTCT programs [22, 23] and should be considered at the onset, scale-up and sustainability of these programs. A recent study that was conducted in New Delhi, India showed that training of health workers on the latest information about the prevention and management of viral hepatitis increased their knowledge which subsequently changed their attitudes and practices towards the prevention and management of viral hepatitis [24]. However, training alone may not have a great impact on health worker performance and should be supplemented with other measures such as supervision and mentorship [20, 25, 26]. In our study, health providers preferred mentorship to supervision because they perceived it to be non-accusatory, and alluded to it as a non-fault-finding approach. Trained, supervised, and mentored health providers can deliver accurate information and counseling, identify expectant and lactating women living with HIV, provide high-quality

and well-coordinated e-MTCT of HIV services throughout the care and treatment cascade. Training, supervision, and mentorship strengthen the health work force can improve health intervention coverage [27] and is recommended by the WHO [28]. In this way, the global health sector strategies on, HIV, viral hepatitis and sexually transmitted infections would be effectively implemented to contribute to the triple e-MTCT of HIV, syphilis, and HBV [10] which will subsequently contribute to the attainment of the UNAIDS AIDS free generation goal. This study therefore recommends, regular, sustained, and context-specific training, supervision, and mentorship for e-MTCT of HIV health providers in low resource settings with similar research context.

Relatedly, counseling pregnant and lactating women living with HIV emerged as a major factor in countering stigma and stimulated initiation into lifelong ART for the PMTCT cascade, and was noticeably enhance-able through training. Indeed, we observed that uptake of Option B+ ART (prescription and swallowing of ART) was nearly universal by two months of follow-up. Most women started taking their ART on the same day of prescription, although, prescription and uptake of ART varied by health facility attributable to differences in practices such as assessing women for readiness to start ART, giving women time to get ready, providing adequate counseling, and ensuring that women understood the benefits of Option B+ ART. This finding is supported by results from a systematic review that looked at health system barriers and enablers for ART for pregnant and breastfeeding women living with HIV [29]. Women on lifelong ART for PMTCT face a myriad of challenges that can be solved through timely, regular, adequate, and context appropriate counseling. Counseling services can provide emotional and psychological support, help women take up ART, overcome the fear of ART side effects, adhere to lifelong ART, overcome HIV -related stigma, and support informed decision-making about reproductive health [30]. Consequently, providing appropriate information, motivation, and support, counseling services can help women achieve optimal health outcomes for themselves and their infants.

Furthermore, we established that support mechanisms for pregnant and breastfeeding women living with HIV were key ingredients of the PMTCT services, employable during preparations and implementation of the lifelong ART approach for PMTCT of HIV. Support

mechanisms are cardinal for pregnant and breastfeeding women living with HIV on lifelong ART to manage their condition, overcome HIV-stigma related challenges, stay healthy, and prevent MTCT of the virus [31]. Support mechanisms can help women manage their medication, side effects, mental health, nutrition, and access to care, and improve their overall quality of life [32]. Our study, like in other studies found that the support mechanisms were provided through health providers, peers, spouses, and relatives and were reportedly important in improving uptake and adherence to lifelong ART and retention in care among pregnant and lactating mothers [32, 33]. This calls for multi-stakeholder involvement and coordination in line with engaging affected communities which is one of the UNAIDS building block for a successful HIV response [34].

We observed that in the earlier stages of the cohort study, adherence was suboptimal and later improved over time during the follow-up period. Our study findings are similar to those of a study that was conducted in Malawi [35] and Cameroon [36]. Adherence to lifelong ART among pregnant and breastfeeding women living with HIV may rise over time due to various reasons such as; improved understanding, and acceptance of the importance of ART. As expectant and lactating women living with HIV receive more information about the benefits of ART, they potentially become more motivated to adhere to their ART. Evidence suggest that overtime, patients on ART start to experience fewer side effects, receive more social support from healthcare providers, family members, and friends, inevitably contributing to improvements in adherence to lifelong ART [36]. Moreover, as HIV-related stigma decreases, people living with HIV may feel more comfortable disclosing their HIV status and seeking support, which lead to increased adherence to ART [37]. More studies have also shown that over time, as people living with HIV become familiar with the healthcare system, they increasingly become comfortable in accessing care and ultimately improve their adherence to ART [38]. These findings emphasize the need for more attention and support for clients in the early phases of HIV care and treatment to shorten the learning curve and ensure earlier optimal adherence for better treatment outcomes.

In this study, we found several factors that predict suboptimal adherence. The factors included patient readiness to start lifelong ART, HIV status disclosure, HIV related stigma, spousal support, and health provider motivation. Suboptimal adherence to lifelong ART among pregnant and breastfeeding women can have severe consequences for the mother, her infant, spouse, and the healthcare system. These consequences include; unsuppressed HIV viral load, increased risk of MTCT of HIV, increased risk of HIV drug resistance, poor maternal health outcomes, and increased healthcare costs [39-42].

On the other hand, optimal adherence to lifelong ART among pregnant and breastfeeding women living with HIV potentially contributes to achieving the UNAIDS 95-95-95 targets by increasing the number of people diagnosed with HIV who receive sustained ART, achieving viral suppression, and preventing MTCT of HIV. Consequently, e-MTCT will be realized. Our study indicates that it is therefore vital to provide continuous women friendly education, counseling, support, and resources to ensure and sustain optimal adherence to ART. Achievement of optimal adherence among pregnant and breastfeeding mothers living with HIV may culminate into reduction of new paediatric vertical HIV infections which remain high in Uganda. Actually, in 2021, it was noted that many (44%) of these new HIV vertical infections resulted from women started on lifelong ART but later defaulted during pregnancy and breastfeeding [13].

In addition, our study found that women who received spousal (male) partner support had lower odds of suboptimal adherence; concordant with findings from studies conducted in other settings [43, 44] but discordant with a study conducted in western Uganda where male involvement was not associated with adherence [45]. The discrepancy could have resulted from the difference in measuring male involvement and sample sizes that the two studies used. Unfortunately, like other studies [46, 47], our findings (sub study IV) revealed that male involvement in PMTCT of HIV services remains a challenge during the implementation of lifelong ART for PMTCT. Male involvement in the care of expectant and lactating women living with HIV is key for the psychological support, adherence to treatment, family planning, improved health outcomes and subsequently e-MTCT [48]. However, spousal support can only be obtained if the woman has disclosed her HIV positive status to the spouse. Sadly, HIV related stigma, discrimination and violence still impede the disclosure efforts [49]. This calls for measures to engage men through multi-

faceted approaches that may include; raising awareness, sensitizing healthcare providers, involving male peers, integrating PMTCT services into male-friendly clinics, and providing incentives to improve male participation in PMTCT of HIV services. For example, some studies have reported that efforts to achieve these strategies may include: involvement of health care providers and equipping them with skills of encouraging men to participate in maternal health programs [50] and subsequently provide them with the necessary information and support to be effective partners in the care of their HIV-positive partners. Efforts to engage men in PMTCT of HIV should consider the specific contexts in order to achieve the desired positive health outcomes like couple HIV testing, providing emotional and practical support to women, increasing the use of effective contraception methods, and improving child care and support [51, 52].

Additional challenges in this study were identified as logistical and infrastructural-related. These included a lack of; PMTCT guidelines, IEC materials, real-time electronic data capture systems, sufficient funding, and HIV test kits. Accessibility-related challenges such as large catchment areas and lack of transport were also highlighted. These findings are supported by results from other studies [49, 53]. These challenges should be addressed urgently through the Uganda national HIV and AIDS strategic plan [17], the HIV response through the UNAIDS building blocks [34], the WHO global health sector strategies on HIV, viral hepatitis and sexually transmitted infections [10] so as to achieve e-MTCT of these infections. Logistic and infrastructural-related challenges may result in negative implications for the delivery of e-MTCT services. The absence of e-MTCT guidelines can lead to inconsistencies in the delivery of services, including HIV testing, prophylaxis, treatment, and follow-up care for the mother-baby pairs. It has been established that standardized guidelines are crucial to ensure that all health workers follow a standardized approach that is based on the best available evidence and practice [54]. IEC materials are important tools for health workers to educate mothers, fathers, and communities on the importance of PMTCT services and the steps they need to take to protect their children from HIV, syphilis and HBV [55]. These materials should be culturally appropriate, easy to understand, and available in the local languages. Real-time electronic data capture systems are essential for monitoring the progress of PMTCT services and identifying areas for improvement. Real time electronic data capture

systems enable health workers to capture and analyze data on health services delivery including the uptake of HIV testing, the provision of prophylaxis, treatment, adherence, and the retention of mothers and children in care in real-time. Accordingly, this can improve patient management, and provider timely decision-making [56]. The stockout of HIV test kits can significantly impede the delivery of PMTCT services. HIV testing is a vital first step in the PMTCT cascade (for both the mother, and the baby at the age of ≥ 18 months), and the lack of test kits can delay or prevent access to care. It is essential that health facilities have good forecasting so as to have an adequate supply of HIV test kits at all times to ensure timely testing and initiation of PMTCT services to avoid missed opportunities. Accessibility-related challenges can significantly impact the effective utilization of PMTCT services. For example, being far from health facilities that offer e-MTCT services and lack of transport, can result in failure to test for HIV, initiate lifelong ART, remain in care, and adhere to the ART medications [20]. By addressing accessibility-related challenges, the provision of e-MTCT services can be enhanced, leading to improved health outcomes for both mothers and their children especially in line with the targets of start free, stay free, and AIDS free campaign [2, 3].

Lack of funding continues to be a challenge in Uganda and globally, adequate funds are required for delivery of effective and sustainable prevention and treatment e-MTCT interventions [10, 13, 34]. There is dependency on donor funding with little financial support from national budgets [23]. Availability of funding to timely procure logistics and infrastructure in health facilities that provide e-MTCT services is crucial. Addressing the logistical and infrastructural challenges would fit in the UNAIDS pathways to success in the HIV response resulting into; collection and use reliable, granular and timely data, removal of the societal and structural inequalities to HIV related services, resources and tools, equitable access to medicines and other health technologies, provision of accessible HIV prevention and treatment services to protect people's health and well-being, and adoption of innovative approaches based on guidelines and latest science [10, 34].

Task shifting was one of the countermeasures identified that effectively address the challenge of health worker shortages and heavy workload. This is also supported by available literature [57, 58] and it is seen as one of the approaches that can augment the

achievement of e-MTCT of HIV, and or syphilis, and HBV and has been recommended in many settings [10, 23, 59-63]. This strategy shifts tasks from highly trained health professionals to other cadres of health workers with less training, such as community health workers. Task shifting in our study was done using expert clients (peer/mentor mothers and fathers), community linkage facilitators, and VHTs.

Strengths and limitations

Our study had a number of strengths which included; the use of mixed methods which enabled data and methodological triangulation, understanding the perspectives of key players in the implementation of lifelong ART for PMTCT of HIV; the health providers, the pregnant women, and postpartum mothers living with HIV. In addition, undertaking a prospective cohort improved methodological robustness and eliminated biases that would otherwise be accrued if we employed retrospective methods. The main limitation in our study is the substantial time passage between data collection and the completion of this thesis work, which are attributable to a number of factors including delays in the publication process as well as personal, family, medical, financial, and work-related challenges. Despite these challenges, efforts were made and papers were published in peer reviewed journals between 2019 and 2023 out of these data as the first author, and presentations at scientific meetings; at the local and international levels were also made. Moreover, the data in the monograph provides important incites that are still relevant to inform current national and global efforts towards the triple e-MTCT of HIV, syphilis and HBV.

8.1 Conclusions and recommendations

1. Regular, sustained and context specific training, supervision, and mentorship of health providers are crucial in the implementation of lifelong ART for e-MTCT of HIV. Innovative and health-provider-friendly strategies such as virtual and digital platforms should be used to improve triple e-MTCT training, supervision, and mentorship of health workers (Paper I).
2. Counseling and support mechanisms for pregnant and postpartum women remain a cornerstone in the e-MTCT cascade. These should be individual, community, and context-specific to ensure maximum benefits from the PMTCT interventions

and achieve the desired health outcome and program goals (Papers I and IV). More specifically, audio and e-counselling modalities may be explored to address gaps in staffing norms.

3. Suboptimal adherence continues to be a challenge yet it has grave negative consequences on achieving viral suppression which is key to the e-MTCT of HIV, good health outcome of the mother, and reduced risk of HIV transmission to an HIV-negative spouse (Papers II, III, and IV).
4. Spousal support augments optimal adherence to lifelong ART for pregnant and breastfeeding women, yet low male involvement in PMTCT persists as a big challenge. Innovative and culturally appropriate strategies such as couple prioritization, male incentivized services like screening for diseases should be employed to encourage men to participate in PMTCT programs and provide them with the necessary information and support to enhance their care efforts to their HIV-positive partners (Papers III and IV).
5. Logistical and infrastructural-related challenges were a major hindrance to the implementation of PMTCT services. Governments, donors, implementing partners, and health providers should ensure the availability of logistics, commodities and supplies for delivery of timely and quality triple e-MTCT services. Additionally, MOH should consider the accreditation of the large volume HC IIs and those in distant rural areas, and continue providing community outreach programs to provide e-MTCT services so as to address the accessibility-related challenges (Paper IV)
6. Task shifting was a strategy that was being used to address the challenge of human resource shortages and heavy work load. Regular supervision and mentorship by MOH, implementing partners, district health officials, and health facility in-charges to individuals carrying out the role of task shifting should be guaranteed. This will improve the delivery of e-MTCT services in settings with few highly skilled health workers to meet the increasing demand for HIV services in this era of universal test and treat (Paper IV).

8.2 Recommendation for further research

In general, low male partner involvement in health care has been a persistent challenge. However, if male partners are involved in PMTCT programs, the benefits are well documented [59]. Male involvement in PMTCT services is critical as it promotes shared decision-making, can encourage women to go for ANC early, supports women's uptake of HIV testing, lifelong ART, adherence to lifelong ART, and other health services such as family planning, and enhances family support. All these men's roles are key in each of the four PMTCT prongs that are used in moving towards achieving e-MTCT of HIV. We, therefore, recommend research that will lead to the development of interventions and strategies that encourage male spouse involvement in e-MTCT services as well as agency for the women to overcome some of the financial and other socioeconomic challenges, and to negotiate for enhanced partner support.

Furthermore, qualitative research around integrating e-MTCT services into male-friendly clinics is important. Men may be hesitant to attend ANC clinics due to the perception that these services are primarily designed for women. However, male-friendly clinics that offer e-MTCT services could encourage male participation by providing a welcoming and supportive environment.

References

1. UNAIDS, U., *Countdown to ZERO: global plan towards the elimination of new HIV infections among children by 2015 and keeping their mother alive*. 2011: UNAIDS.
2. UNAIDS, P. *Start Free, Stay Free, AIDS Free*. 2020 [cited 2023 13/11/2023]; Available from: <https://free.unaids.org/>.
3. UNAIDS, *Progress towards the Start Free, Stay Free, AIDS Free targets; 2020 Report*. 2020, Joint United Nations Programme on HIV/AIDS.
4. UNICEF, U.a.W., *Key considerations for programming and prioritization. Going the 'Last Mile' to EMTCT: A road map for ending the HIV epidemic in children*. 2020, UNICEF: New York, USA.
5. WHO, *Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV, syphilis and hepatitis B virus*. 2021.
6. WHO. *Countries which have received WHO validation*. 2022 [cited 2023 25/11/2023]; Available from: <https://www.who.int/initiatives/triple-elimination-initiative-of-mother-to-child-transmission-of-hiv-syphilis-and-hepatitis-b/validation>.
7. Elgalib, A., et al., *Elimination of mother-to-child transmission of HIV, syphilis and viral hepatitis B: A call for renewed global focus*. International Journal of Infectious Diseases, 2023. **127**: p. 33-35.
8. WHO. *Botswana is first country with severe HIV epidemic to reach key milestone in the elimination of mother-to-child HIV transmission*. 2021 [cited 2023 25 November 2023]; Available from: <https://www.afro.who.int/countries/botswana/news/botswana-first-country-severe-hiv-epidemic-reach-key-milestone-elimination-mother-child-hiv>.
9. UNAIDS. *Botswana is first country with severe HIV epidemic to reach key milestone in the elimination of mother-to-child HIV transmission*. 2021 2023 [cited 2023 25 November 2023]; Available from: https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2021/december/emtct_botswana.
10. WHO, *Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030*. 2022.
11. UNAIDS, *The path that ends AIDS: UNAIDS Global AIDS Update 2023*, in Licence: CC BY-NC-SA 3.0 IGO. 2023, Joint United Nations Programme on HIV/AIDS; 2023. : Geneva.
12. UAC, *Uganda HIV Modes of Transmission HIV Prevention Synthesis - 2022*. 2023, UAC: Kampala, Uganda.

13. UAC, *Annual Joint AIDS Review Report FY 2021/22 FINAL*. 2022, UAC: Kampala, Uganda.
14. UAC, *Mid-Term Review of the National HIV AND AIDS Strategic Plan 2020/21-2024/25*. 2023, UAC: Kampala, Uganda.
15. UNAIDS, *IN DANGER: UNAIDS Global AIDS Update 2022*. 2022, Joint United Nations Programme on HIV/AIDS; 2022: Geneva.
16. WHO, *Pulse survey on continuity of essential health services during the COVID-19 pandemic: interim report, 27 August 2020*. 2020, WHO.
17. UAC, *The National HIV AND AIDS Strategic Plan 2020/21–2024/25: Ending the HIV and AIDS epidemic: Communities at the forefront*. 2020, UAC: Kampala, Uganda.
18. Deussom, R., et al., *Systematic review of performance-enhancing health worker supervision approaches in low-and middle-income countries*. Human Resources for Health, 2022. **20**(1): p. 2.
19. Kamiru, H., et al., *Effectiveness of a training program to increase the capacity of health care providers to provide HIV/AIDS care and treatment in Swaziland*. AIDS care, 2009. **21**(11): p. 1463-1470.
20. Manzi, A., et al., *Mentorship and coaching to support strengthening healthcare systems: lessons learned across the five Population Health Implementation and Training partnership projects in sub-Saharan Africa*. BMC health services research, 2017. **17**(3): p. 5-16.
21. Jongen, C., J. McCalman, and R. Bainbridge, *Health workforce cultural competency interventions: a systematic scoping review*. BMC health services research, 2018. **18**: p. 1-15.
22. Horwood, C., et al., *A continuous quality improvement intervention to improve the effectiveness of community health workers providing care to mothers and children: a cluster randomised controlled trial in South Africa*. Human resources for health, 2017. **15**: p. 1-11.
23. Cohn, J., et al., *Eliminating mother-to-child transmission of human immunodeficiency virus, syphilis and hepatitis B in sub-Saharan Africa*. Bulletin of the World Health Organization, 2021. **99**(4): p. 287.
24. Rastogi, A., et al., *Capacity building of healthcare workers: Key step towards elimination of viral hepatitis in developing countries*. PLOS ONE, 2021. **16**(6): p. e0253539.
25. Rowe, A.K., et al., *How can we achieve and maintain high-quality performance of health workers in low-resource settings?* The Lancet, 2005. **366**(9490): p. 1026-1035.

26. Feyissa, G.T., D. Balabanova, and M. Woldie, *How effective are mentoring programs for improving health worker competence and institutional performance in Africa? A systematic review of quantitative evidence*. Journal of multidisciplinary healthcare, 2019: p. 989-1005.
27. Li, X., et al., *Improving hepatitis B birth dose coverage through village health volunteer training and pregnant women education*. Vaccine, 2017. **35**(34): p. 4396-4401.
28. WHO, *Health policy and system support to optimize community health worker programmes for HIV, TB and malaria services: an evidence guide*. 2020.
29. Colvin, C.J., et al., *A systematic review of health system barriers and enablers for antiretroviral therapy (ART) for HIV-infected pregnant and postpartum women*. PloS one, 2014. **9**(10): p. e108150.
30. Takah, N.F., I.T. Kennedy, and C. Johnman, *The impact of approaches in improving male partner involvement in the prevention of mother-to-child transmission of HIV on the uptake of maternal antiretroviral therapy among HIV-seropositive pregnant women in sub-Saharan Africa: a systematic review and meta-analysis*. BMJ open, 2017. **7**(11): p. e018207.
31. Phillips, T.K. and L. Myer, *Shifting to the long view: engagement of pregnant and postpartum women living with HIV in lifelong antiretroviral therapy services*. Expert Review of Anti-infective Therapy, 2019. **17**(5): p. 349-361.
32. Phiri, S., et al., *Impact of facility-and community-based peer support models on maternal uptake and retention in Malawi's option B+ HIV prevention of mother-to-child transmission program: a 3-arm cluster randomized controlled trial (PURE Malawi)*. JAIDS Journal of Acquired Immune Deficiency Syndromes, 2017. **75**: p. S140-S148.
33. Topp, S.M., et al., *"Most of what they do, we cannot do!" How lay health workers respond to barriers to uptake and retention in HIV care among pregnant and breastfeeding mothers in Malawi*. BMJ Global Health, 2020. **5**(6): p. e002220.
34. UNAIDS, *Pathways to success in the HIV response: 2023 UNAIDS Global AIDS Update*. 2023, UNAIDS: Geneva, Switzerland.
35. Haas, A.D., et al., *Adherence to Antiretroviral Therapy During and After Pregnancy: Cohort Study on Women Receiving Care in Malawi's Option B+ Program*. Clinical Infectious Diseases, 2016. **63**(9): p. 1227-1235.
36. Atanga, P.N., et al., *Retention in care and reasons for discontinuation of lifelong antiretroviral therapy in a cohort of Cameroonian pregnant and breastfeeding HIV-positive women initiating 'Option B+' in the South West Region*. Tropical Medicine & International Health, 2017. **22**(2): p. 161-170.

37. Chadambuka, A., et al., *Acceptability of lifelong treatment among HIV-positive pregnant and breastfeeding women (Option B+) in selected health facilities in Zimbabwe: a qualitative study*. BMC public health, 2018. **18**(1): p. 1-8.
38. van Loggerenberg, F., et al., *A qualitative study of patient motivation to adhere to combination antiretroviral therapy in South Africa*. AIDS patient care and STDs, 2015. **29**(5): p. 299-306.
39. Cherutich, P., et al., *Detectable HIV viral load in Kenya: data from a population-based survey*. PloS one, 2016. **11**(5): p. e0154318.
40. Nevrekar, N., et al., *Self-reported Antiretroviral Adherence: Association With Maternal Viral Load Suppression in Postpartum Women Living With HIV-1 From Promoting Maternal and Infant Survival Everywhere, a Randomized Controlled Trial in Sub-Saharan Africa and India*. J Acquir Immune Defic Syndr, 2023. **92**(1): p. 76-83.
41. Hosseinipour, M., et al., *Viral Suppression and HIV Drug Resistance at 6 Months Among Women in Malawi's Option B+ Program: Results From the PURE Malawi Study*. J Acquir Immune Defic Syndr, 2017. **75 Suppl 2**(Suppl 2): p. S149-s155.
42. Landes, M., et al., *Low detectable postpartum viral load is associated with HIV transmission in Malawi's prevention of mother-to-child transmission programme*. Journal of the International AIDS Society, 2019. **22**(6): p. e25290.
43. van Lettow, M., et al., *Impact of inter-partner HIV disclosure patterns in Malawi's PMTCT program: A mixed-method study*. PloS one, 2019. **14**(7): p. e0219967.
44. Zacharius, K.M., et al., *Low adherence to Option B+ antiretroviral therapy among pregnant women and lactating mothers in eastern Tanzania*. PloS one, 2019. **14**(2): p. e0212587.
45. Decker, S., et al., *Prevention of mother-to-child transmission of HIV: Postpartum adherence to Option B+ until 18 months in Western Uganda*. PloS one, 2017. **12**(6): p. e0179448.
46. Ghoma Linguissi, L.S., et al., *Prevention of mother-to-child transmission (PMTCT) of HIV: a review of the achievements and challenges in Burkina-Faso*. HIV/AIDS-Research and Palliative Care, 2019: p. 165-177.
47. Melis, T. and Y. Fikadu, *Magnitude and determinants of male partner involvement in PMTCT service utilization of pregnant women attending public health facilities of Ethiopia, 2021: a systematic review and meta-analysis*. AIDS Research and Therapy, 2022. **19**(1): p. 8.

48. Odeny, B., et al., *Male partner antenatal clinic attendance is associated with increased uptake of maternal health services and infant BCG immunization: a national survey in Kenya*. BMC pregnancy and childbirth, 2019. **19**: p. 1-9.
49. Hodgson, I., et al., *A systematic review of individual and contextual factors affecting ART initiation, adherence, and retention for HIV-infected pregnant and postpartum women*. PLoS one, 2014. **9**(11): p. e111421.
50. August, F., et al., *Community health workers can improve male involvement in maternal health: evidence from rural Tanzania*. Global health action, 2016. **9**(1): p. 30064.
51. Daniele, M.A.S., *Male partner participation in maternity care and social support for childbearing women: a discussion paper*. Philosophical Transactions of the Royal Society B, 2021. **376**(1827): p. 20200021.
52. Clark, J., et al., *Improving male involvement in antenatal care in low and middle-income countries to prevent mother to child transmission of HIV: a realist review*. PLoS One, 2020. **15**(10): p. e0240087.
53. Dzamboe, C.E., et al., *Structural elements availability for the provision of Prevention of Mother-to-Child Transmission of HIV services among health facilities in the Volta Region of Ghana*. The Pan African Medical Journal, 2022. **41**.
54. Kredo, T., et al., *Guide to clinical practice guidelines: the current state of play*. International Journal for Quality in Health Care, 2016. **28**(1): p. 122-128.
55. Van Rompay, K.K., et al., *Empowering the people: development of an HIV peer education model for low literacy rural communities in India*. Human Resources for Health, 2008. **6**(1): p. 1-11.
56. Tweya, H., et al., *Developing a point-of-care electronic medical record system for TB/HIV co-infected patients: experiences from Lighthouse Trust, Lilongwe, Malawi*. BMC research notes, 2016. **9**(1): p. 1-10.
57. Naburi, H., et al., *The potential of task-shifting in scaling up services for prevention of mother-to-child transmission of HIV: a time and motion study in Dar es Salaam, Tanzania*. Human resources for health, 2017. **15**(1): p. 1-11.
58. Okoroafor, S.C. and C.D. Christmals. *Task Shifting and Task Sharing Implementation in Africa: A Scoping Review on Rationale and Scope*. in *Healthcare*. 2023. MDPI.
59. Taye, B.W., *A path to ending hepatitis C in Ethiopia: a phased public health approach to achieve micro-elimination*. The American Journal of Tropical Medicine and Hygiene, 2019. **101**(5): p. 963.

60. WHO, Integrated Regional Action Plan for viral hepatitis, HIV and sexually transmitted infections in South-East Asia, 2022–2026. 2022.
61. Chan, P.-L., et al., Regional progress towards hepatitis C elimination in the Western Pacific Region, 2015-2020. *Global Health & Medicine*, 2021. 3(5): p. 253-261.
62. Howell, J., et al., A global investment framework for the elimination of hepatitis B. *Journal of hepatology*, 2021. 74(3): p. 535-549.
63. Brennan, D.J., et al., “It’s a win for the clinic, it’s a win for the frontline, but, most importantly, it’s a win for the client”: Task Shifting HIV Prevention Services from Clinicians to Community Health Workers in Ontario, Canada. *Sexuality Research and Social Policy*, 2023. 20(2): p. 780-792
64. Judith, Y. and L.-B. Jo, *Male involvement and maternal health outcomes: systematic review and meta-analysis*. *Journal of Epidemiology and Community Health*, 2015. 69(6): p. 604.

Curriculum Vitae

1.0 ACADEMIC QUALIFICATIONS

- i. 2006-2008: MSc. Health Services Research, Case Western Reserve University, USA.
- ii. 1991 – 1996: Bachelor of Medicine and Bachelor of Surgery (MBChB), Makerere University, Uganda.

2.0 EMPLOYMENT

- i. August 1st, 2012 to date: Lecturer, Department of Epidemiology and Biostatistics, School of Public Health, College of Health Sciences, Makerere University
- ii. February 10th – 11th and March 5th – 7th 2014: Guest lecturer at the University of Stellenbosch, South Africa on the MPhil Health Systems and Services Research degree program
- iii. September 1st to 8th 2013: Acting Head of department of Epidemiology and Biostatistics, School of Public Health, College of Health Sciences, Makerere University
- iv. February 2010 to July 2012: Assistant lecturer at the School of Public Health, College of Health Sciences, Makerere University
- v. February 2010 to December 2018: Academic Coordinator Master of Health Services Research Program at the School of Public Health, College of Health Sciences, Makerere University
- vi. November 2011 to 2016: External examiner Mbarara University of Science and Technology

3.0 PROFESSIONAL MEMBERSHIP

- i. 2020 – Date: Member of Health Systems Global (HSG)
- ii. 2008 to date: Member of the Global Health Council
- iii. 2002 to date: Member of Uganda Society for Health Scientists
- iv. 1996 to date: Member of Uganda Medical Association

4.0 PUBLICATIONS

4.1 THESIS PUBLICATIONS

1. **Mukose AD**, Bastiaens H, Buregyeya E, Naigino R, Makumbi F, Musinguzi J, Van geertruyden JP, Wanyenze RK. Health provider perspectives of health facility

preparedness and organization in implementation of option B+ among pregnant and lactating women in central Uganda: a qualitative study. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*. 2019 Mar 5;18:2325958219833930.

2. **Mukose AD**, Bastiaens H, Makumbi F, Buregyeya E, Naigino R, Musinguzi J, Van geertruyden JP, Wanyenze RK. What influences uptake and early adherence to Option B+ (lifelong antiretroviral therapy among HIV-positive pregnant and breastfeeding women) in Central Uganda? A mixed methods study. *Plos one*. 2021 May 5;16(5):e0251181.
3. **Mukose AD**, Van geertruyden JP, Makumbi F, Buregyeya E, Naigino R, Musinguzi J, Wanyenze RK. Suboptimal Adherence to Lifelong ART, and its predictors among HIV- positive pregnant and breastfeeding women in three districts of Central Uganda: A repeated measures analysis. Submitted.
4. **Mukose AD**, Bastiaens H, Makumbi F, Buregyeya E, Naigino R, Musinguzi J, Van geertruyden JP, Wanyenze RK. Challenges and commonly used countermeasures in the implementation of lifelong antiretroviral therapy for PMTCT in Central Uganda: Health providers' perspective. *PloS one*. 2023 Jan 20;18(1): e0280893.

4.2 OTHER PUBLICATIONS

5. Njeru, P., Nassali, M., Muhumuza, C., Kaddamukasa, M., **Mukose, A.**, Wabwire, F., Haglund, M., Fuller, A. and Koltai, D., 2023. Health systems capacity for epilepsy care in Uganda: A survey of health facilities in Western Uganda. *Journal of the Neurological Sciences*, 455.
6. Natuhanya, C., Makumbi, F., **Mukose, A.D.** and Ssenkusu, J.M., 2023. Complete sources of cluster variation on the risk of under-five malaria in Uganda: a multilevel-weighted mixed effects logistic regression model approach. *Malaria Journal*, 22(1), p.317.
7. Ndyababo R, Nalugya A, Ssekamatte T, Nakafeero M, Kisakye A, **Mukose A.D.** Early infant diagnosis testing for HIV in a hard-to-reach fishing community in Uganda. *Plos one*. 2023 Jun 7;18(6): e0268416.
8. Namanda C, Atuyambe L, Ssali S, **Mukose A**, Tumwesigye NM, Makumbi FE, Tweheyo R, Gidudu A, Sekimpi C, Hashim CV, Nicholson M. A qualitative study of influences on the uptake of contraceptive services among people of reproductive age in Uganda. *BMC Women's Health*. 2023 Mar 25;23(1):130.
9. Makumbi FE, Nabukeera S, Tumwesigye NM, Namanda C, Atuyambe L, **Mukose A**, Ssali S, Ssenyonga R, Tweheyo R, Gidudu A, Sekimpi C. Socio-economic and education related inequities in use of modern contraceptive in seven sub-regions in Uganda. *BMC Health Services Research*. 2023 Feb 28;23(1):201.

10. Agiresaasi A, Nassanga G, Maina GW, Kiguli J, Nabiwemba E, Kiwanuka N, **Mukose A**, Tumwesigye NM. Effect of a communication intervention on alcohol use during pregnancy in post conflict Northern Uganda: a quasi-experimental study. *Substance Abuse Treatment, Prevention, and Policy*. 2022 Dec 12;17(1):80.
11. Ejalu, D.L., Irioko, A., Kirabo, R., **Mukose, A.D.**, Ekirapa, E., Kagaayi, J. and Namutundu, J., 2022. Cost-effectiveness of GeneXpert Omni compared with GeneXpert MTB/Rif for point-of-care diagnosis of tuberculosis in a low-resource, high-burden setting in Eastern Uganda: a cost-effectiveness analysis based on decision analytical modelling. *BMJ open*, 12(8), p.e059823.
12. Tumwesigye NM, Makumbi F, **Mukose A**, Atuyambe L, Namanda C, Ssali S, Tweheyo R, Gidudu A, Sekimpi C, Hashim CV, Nicholson M. Ability and willingness to pay for family planning services in low resource settings: evidence from an operational research. *African Health Sciences*. 2022 Apr 29;22(1):28-40.
13. Bbuye M, Muttamba W, Nassaka L, Nakyomu D, Taasi G, Kiguli S, Mayega RW, **Mukose AD**. Factors Associated with Linkage to HIV Care Among Oral Self-Tested HIV-positive Adults in Uganda. *HIV AIDS (Auckl)*. 2022 Feb 19;14:61-72. doi: 10.2147/HIV.S346951. PMID: 35221726; PMCID: PMC8867221.
14. Alitubeera, Phoebe Hilda, Juliet Ntuulo Mutanda, **Mukose Aggrey**, Olive Chiefe Kobusingye, Claire Biribawa, Andrew Tusubira, Patricia Eyu, and Noah Kiwanuka. "Prevalence, correlates of occupational percutaneous injuries and use of post exposure prophylaxis against HIV, Hepatitis B among health workers in Kampala, Uganda-May 2016." *Journal of Interventional Epidemiology and Public Health* 4, no. 13 (2021).
15. Naigino R, Makumbi F, **Mukose A**, Buregyeya E, Arinaitwe J, Musinguzi J, Kiene SM, Wanyenze RK. Resumption of Sexual Intercourse Among Postnatal Women Enrolled on Lifelong Antiretroviral Therapy in Uganda. *AIDS and Behavior*. 2021 Feb 19:1-1.
16. **Mukose AD**, Kebede S, Muhumuza C, Makumbi F, Komakech H, Bayiga E, Busobozi D, Musinguzi J, Kuznik A, Stegman P, Forsythe S. Costs and cost drivers of providing option B+ services to mother-baby pairs for PMTCT of HIV in Health Centre IV Facilities in Jinja District, Uganda. *BioMed Research International*. 2020 May 18;2020.
17. Nyangabyaki-Twesigye C, Mworozzi E, Namisi C, Nakibuuka V, Kayiwa J, Ssebunya R, **Mukose DA**. Prevalence, factors associated and treatment outcome of hyperbilirubinaemia in neonates admitted to St Francis hospital, Nsambya, Uganda: a descriptive study. *African health sciences*. 2020 Apr 20;20(1):397-405.
18. Lubogo M, Anguzu R, Wanzira H, Shour AR, **Mukose AD**, Nyabigambo A, Tumwesigye NM. Utilization of safe male circumcision among adult men in a

- fishing community in rural Uganda. *African Health Sciences*. 2019 Nov 6;19(3):2645-53.
19. Kweyamba M, Buregyeya E, Kusiima J, Kweyamba V, **Mukose AD**. Loss to follow-up among HIV-positive pregnant and lactating mothers on lifelong antiretroviral therapy for PMTCT in rural Uganda. *Advances in Public Health*. 2018 Oct;2018.
 20. Naigino R, Makumbi F, **Mukose A**, Buregyeya E, Arinaitwe J, Musinguzi J, Wanyenze RK. HIV status disclosure and associated outcomes among pregnant women enrolled in antiretroviral therapy in Uganda: a mixed methods study. *Reproductive health*. 2017 Dec; 14:1-1.
 21. Li M, Nyabigambo A, Navvuga P, Nuwamanya E, Nuwasiima A, Kaganda P, Asiimwe FT, Vodicka E, Mugisha NM, **Mukose A**, Kwesiga DK. Acceptability of cervical cancer screening using visual inspection among women attending a childhood immunization clinic in Uganda. *Papillomavirus Research*. 2017 Dec 1; 4:17-21.
 22. Buregyeya E, Naigino R, **Mukose A**, Makumbi F, Esiru G, Arinaitwe J, Musinguzi J, Wanyenze RK. Facilitators and barriers to uptake and adherence to lifelong antiretroviral therapy among HIV infected pregnant women in Uganda: a qualitative study. *BMC pregnancy and childbirth*. 2017 Dec;17(1):1-9.
 23. Mayanja Y, **Mukose AD**, Nakubulwa S, Omosa-Manyonyi G, Kamali A, Guwatudde D. Acceptance of treatment of sexually transmitted infections for stable sexual partners by female sex workers in Kampala, Uganda. *PLoS One*. 2016 May 12;11(5): e0155383.
 24. Akullian AN, **Mukose A**, Levine GA, Babigumira JB. People living with HIV travel farther to access healthcare: a population-based geographic analysis from rural Uganda. *Journal of the International AIDS Society*. 2016 Jan;19(1):20171.
 25. Musinguzi G, Bastiaens H, Wanyenze RK, **Mukose A**, Van geertruyden JP, Nuwaha F. Capacity of health facilities to manage hypertension in Mukono and Buikwe districts in Uganda: challenges and recommendations. *PloS one*. 2015 Nov 11;10(11): e0142312.
 26. Nevin PE, Pfeiffer J, Kibira SP, Lubinga SJ, **Mukose A**, Babigumira JB. Perceptions of HIV and safe male circumcision in high HIV prevalence fishing communities on Lake Victoria, Uganda. *PloS one*. 2015 Dec 21;10(12): e0145543.
 27. Muhumuza C, Gomersall JS, Fredrick ME, Atuyambe L, Okiira C, **Mukose A**, Ssempebwa J. Health care worker hand hygiene in the pediatric special care unit at Mulago National Referral Hospital in Uganda: a best practice implementation project. *JBHI Evidence Implementation*. 2015 Mar 1;13(1):19-27.
 28. Naigino R, Babikako H, Katamba A, **Mukose A**. Utilization of malaria diagnostic tests and receipt of anti-malarial drugs by febrile patients attending outpatient departments of health center IVs in Mukono district, Uganda. *International Journal of Infectious Diseases*. 2014 Apr 1; 21:366.

29. Simba D, **Mukose A**, Bazeyo W. Institutional capacity for health systems research in East and Central African Schools of Public Health: strengthening human and financial resources. Health research policy and systems. 2014 Dec;12(1):1-0.
30. Nangami MN, Rugema L, Tebeje B, **Mukose A**. Institutional capacity for health systems research in East and Central Africa schools of public health: enhancing capacity to design and implement teaching programs. Health Research Policy and Systems. 2014 Dec;12(1):1-5.
31. Musinguzi G, Bwayo D, Kiwanuka N, Coutinho S, **Mukose A**, Kabanda J, Sekabembe L, Nuwaha F. Sexual behavior among persons living with HIV in Uganda: implications for policy and practice. PloS one. 2014 Jan 23;9(1): e85646.
32. Tumuhamy N, Rutebemberwa E, Kwesiga D, Bagonza J, **Mukose A**. Client satisfaction with integrated community case management program in Wakiso District, Uganda, October 2012: A cross sectional survey. Health. 2013 Nov 11;2013.

5.0 SCIENTIFIC PRESENTATIONS

5.1 ORAL

1. Ainembabazi Bridget, Elizabeth Katana, **Aggrey David Mukose**. Prevalence of Advanced HIV Disease at Enrollment in Care and Associated Factors Among Adult Individuals During the Treat All Era at Selected Public Health Centres in Kampala, Uganda. The annual INTEREST 2023 Conference: 9-12 May 2023 in Maputo, Mozambique. <http://interestworkshop.org/sessions/mini-oral-abstract-presentations-4/>
2. **Aggrey Mukose**, Senait Kebede, Esther Bayiga, Fredrick Makumbi, et al (2016). Costs and cost drivers of Retaining a Mother-baby pair on Option B+, Jinja District-Uganda: The 9th International AIDS Economics Network (IAEN) Pre- AIDS 2016 conference Durban, South Africa 15-16 July 2016
3. **Aggrey Mukose**, Fred Makumbi, Fred Wabwire-Mangen, et al (2014). Improving Health Services Through Master of Health Services Research Program at Makerere University School of Public Health: A Multidisciplinary Training Program. Presented at the Joint Annual Scientific Health Conference of 10th Makerere University College of Health Sciences Annual Scientific Conference, 13th WHO Dr. Mathew Lukwiya Memorial Lecture, and 22nd UNACOH Annual Scientific Conference. September 24th -26th, 2014 at Imperial Royale Hotel, Kampala-Uganda.

5.2 POSTER

- I. **Aggrey David Mukose**, Fredrick Makumbi, Rhoda K. Wanyenze et al (2016). Uptake of and early adherence to lifelong ART (Option B+) and associated factors among pregnant women in Uganda. 21st International AIDS Conference, July 18-22, 2016, Durban, South Africa.