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Challenges and Promising Strategies for Maximizing Pregnant Women's Adherence and Retention in NIV Care in the Context of Option B+ in Kenya

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CHALLENGES AND PROMISING STRATEGIES FOR MAXIMIZING PREGNANT WOMEN'S ADHERENCE AND RETENTION IN HIV CARE IN THE CONTEXT OF OPTION B+ IN KENYA.

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CHALLENGES AND PROMISING STRATEGIES FOR MAXIMIZING PREGNANT WOMEN'S ADHERENCE AND RETENTION IN HIV CARE IN THE CONTEXT OF OPTION B+ IN KENYA.

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ABSTRACT

Under the current Kenyan guidelines, pregnant/postpartum women who test HIV-positive are immediately put on the lifelong antiretroviral (ART) therapy (Option B+) and are initiated into the prevention of mother-to-child (PMTCT) protocol. Gaps at each step of the PMTCT continuum undermine the positive impact of lifelong ART. Challenges at the individual, interpersonal, community, and health facility-levels contribute to these gaps. A community-based mentor mother (cMM) program tested under the Mother-Infant Visit Adherence and Treatment Engagement(MOTIVATE!) Trial (NICHD R01 R01HD080477; ClinicalTrials.gov#14-0331) is a potential approach to address these challenges.

The three manuscripts comprising this dissertation used qualitative and quantitative methods with the aims of understanding challenges to the implementation of the lifelong ART for pregnant/postpartum WLWH in southwestern rural Kenya at the healthcare facility level; evaluating the implementation and potential challenges related to the important PMTCT service of viral load (VL) testing during pregnancy/postpartum; and examining the potential effectiveness of a cMM program in addressing challenges related to adherence and retention in care.

This dissertation revealed important challenges related to the provision of a lifelong ART for pregnant/postpartum women, including Option B+ specific challenges, facility resource constraints, and lack of client-friendly services. Significant gaps also exist in VL testing. A large proportion of women are not getting VL measurements at crucial times during pregnancy/breastfeeding and do not receive VL testing according to current Kenyan guidelines. Women newly diagnosed with HIV during pregnancy, those who have not disclosed their status to their male partner, and women with a history of viremia, less engagement in HIV care, and those on a second-line ART regimen appear to be particularly vulnerable. Utilizing an adapted conceptual framework for the role of community health workers in facilitating patients' adoption of health behaviors, this study suggests that the cMM strategy has the potential to play an important role in enhancing PMTCT behaviors, and may also address barriers related to the provision of the Option B+ services and VL testing. Addressing these challenges may increase linkage, retention, and adherence to lifelong ART treatment for pregnant HIV-positive women in Kenya, contribute towards the elimination of mother-to-child transmission, and improve maternal/child outcomes.

Keywords: mother-to-child transmission of HIV, pregnancy, Kenya, viral load, community workers, mentor mothers

DEDICATION

I dedicate this work to my closest family. To my dad, Jan Medved, with whom I was granted only a short period of 15 years. *Ocko*, I'm so thankful for all the memories we shared together. I'd wish you could have had at least one campfire singing with your three daughters and six energetic grandkids. To my mom, Halina Baranowska Medved, for your support, encouragement, and for carrying the family forward after dad's passing. To my kids, Jakub and Kristyna, who inspire me to be the best version of myself. To my husband, Dr. Zdenek Hel, who introduced me to the world of global health and who is my constant academic inspiration; and to my sisters, Halina and Eva, for always having my back. Lastly, I dedicate this work to women and children everywhere.

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LIST OF ABBREVIATIONS

ANC	Antenatal Care
ART	Antiretroviral treatment
AZT	Azidothymidine
CHW	Community health worker
cMM	Community-based mentor mother
eMTCT	elimination of mother-to-child transmission
FACES	Family AIDS Care and Education Services
HIV	Human Immunodeficiency Virus
KEMRI	Kenya Medical Research Institute
KMMP	The Kenya Mentor Mother Program
MCH	Maternal and child health
MM	Mentor mother
MOH	Ministry of Health
MTCT	Mother-to-child transmission
NNRTI	Nucleoside reverse transcriptase inhibitor
PI	Protease inhibitor
PLWH	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PNC	Postnatal care
PP	Postpartum
PrEP	Pre-exposure prophylaxis
PWLWH	Pregnant women living with HIV

SSA	Sub-Saharan Africa
TDF	Tenofovir
UNAIDS	Joint United Nations Programme on HIV/AIDS
VL	Viral Load
WHO	World Health Organization
WLWH	Women living with HIV

INTRODUCTION

The HIV Epidemic, Prevention of Mother-to-Child Transmission (PMTCT) Guidelines and Option B+

HIV remains one of the most critical global health issues. In 2018, an estimated 37.9 million people were living with HIV (PLWH) worldwide.[1] The global community is still far from reaching the 2014 Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 goals (90% tested, 90% initiated on ART, and 90% achieving viral suppression). The achievement of the 90-90-90 targets by 2020 is, however, a crucial part of the effort to end the HIV epidemic by 2030.[2] As of 2018, approximately 79% of people living with HIV (PLWH) globally were aware of their HIV status, 62% were on antiretroviral therapy (ART), and 53% achieved viral suppression.[3] About 25.7 million PLWH live in Africa, most of them in the Sub-Saharan Africa (SSA) region, representing approximately 68% of PLWH globally. About 16.3 million Africans are on ART.[1] The demands on the national HIV programs and healthcare systems worldwide have intensified with 2016 WHO consolidated guidelines, recommending the Test & Treat all approach, scale-up of viral load testing, and the use of pre-exposure prophylaxis (PrEP) for populations at risk.[4]

Women are disproportionately affected by HIV. About 18.8 million women live with HIV (WLWH) worldwide[3], of whom about 90% live in SSA[5], and approximately 1.3 million WLWH are pregnant (PWLWH).[6] Children are a critical population in the fight against the HIV epidemic. An estimated 160,000 children under

15 years are still newly infected with HIV annually, 86% of these in the WHO African Region.[3] The majority of new infections are attributed to mother-to-child transmission (MTCT) occurring during pregnancy, labor, delivery, and breastfeeding.[6] Rates of MTCT range from 15-45% in the absence of any intervention.[5] However, MTCT rates have decreased from 22% in 2009 to 11% in 2017[7, 8] as the proportion of WLWH accessing ART has increased from 36% to 80% during the same time frame.[9] Despite this progress, additional efforts, including universal HIV testing and counseling for pregnant and breastfeeding women, increased coverage with effective PMTCT/ART regimens, targeted viral load monitoring protocols, and support for adherence are needed to achieve the Global Plan for the Elimination of New HIV Infections in Children (Global Plan)[10] goals to reduce new MTCT infections to less than 5% and keep mothers alive.[7, 9, 11]

In 2013, the World Health Organization (WHO) revised guidelines for the prevention of MTCT (PMTCT) and introduced new PMTCT regimen options to scale-up PMTCT services.[12] Table 1 below provides a comparison of eligibility criteria and treatment in the previously recommended regimens Option A and Option B, as compared to a currently recommended regimen for settings with generalized HIV epidemics, including Kenya[13], referred to as Option B+.[12] Option B+ is a PMTCT approach under which all pregnant and breastfeeding women are placed on life-long antiretroviral therapy (ART) immediately after HIV diagnosis, *regardless of CD4 count* and clinical stage. Infants receive daily nevirapine or azidothymidine (AZT) from birth through 4-6 weeks regardless of their feeding method. Logistically, Option B+ eliminates the need

for CD4 T-cell count testing to determine eligibility for ART, which previously served as a major barrier in resource-limited settings.[12]

Table 1
Comparison of PMTCT Regimens[12]

PMTCT Regimen:	**Treatment woman receives:**		**Treatment Infant receives:**
	CD4 count ≤ 350 cells/mm^3	CD4 count ≤ 350 cells/mm^3	
Option A	Triple ARV starting as soon as diagnosed and continued for life	AZT starting as early as 14 weeks of gestation; single-dose NVP and 1st dose of AZT/3TC at onset of labor; daily AZT/3TC through 7 days postpartum	Daily NVP from birth until 1 week cessation of breastfeeding; if not breastfed/mother is on treatment, through 4-6 weeks
Option B	Triple ARV starting as soon as diagnosed and continued for life	Triple ARVs starting as early as 14 weeks of gestation and continued through childbirth if not breastfeeding or until 1 week after cessation of breastfeeding	Daily NVP or AZT from birth through age 4-6 weeks regardless of infant feeding method
Option B+	Regardless of CD4 count, triple ARV starting as soon as diagnosed and continued for life		Daily NVP or AZT from birth through age 4-6 weeks regardless of infant feeding method

Note: Triple ARV: one of the recommended 3-drug fully suppressive treatment options. AZT =azidothymidine + zidovudine[ZDV]; NVP=nevirapine; 3TC=lamivudine

Lifelong ART for PWLWH was first rolled-out in 22 Global Plan Priority Countries[13], but has now been fully implemented in nearly all countries[14] (see Figure 1). Option B+ represents a promising approach expected to contribute towards goals set by the Global Plan substantially. In 2014, shortly after the implementation of a lifelong ART for PWLWH, many countries reported up to 60% decrease in MTCT rates compared to 2009.[15] Also, ART in pregnant women with high CD4 T cell counts is more effective in reducing MTCT during pregnancy than prophylaxis alone[16].

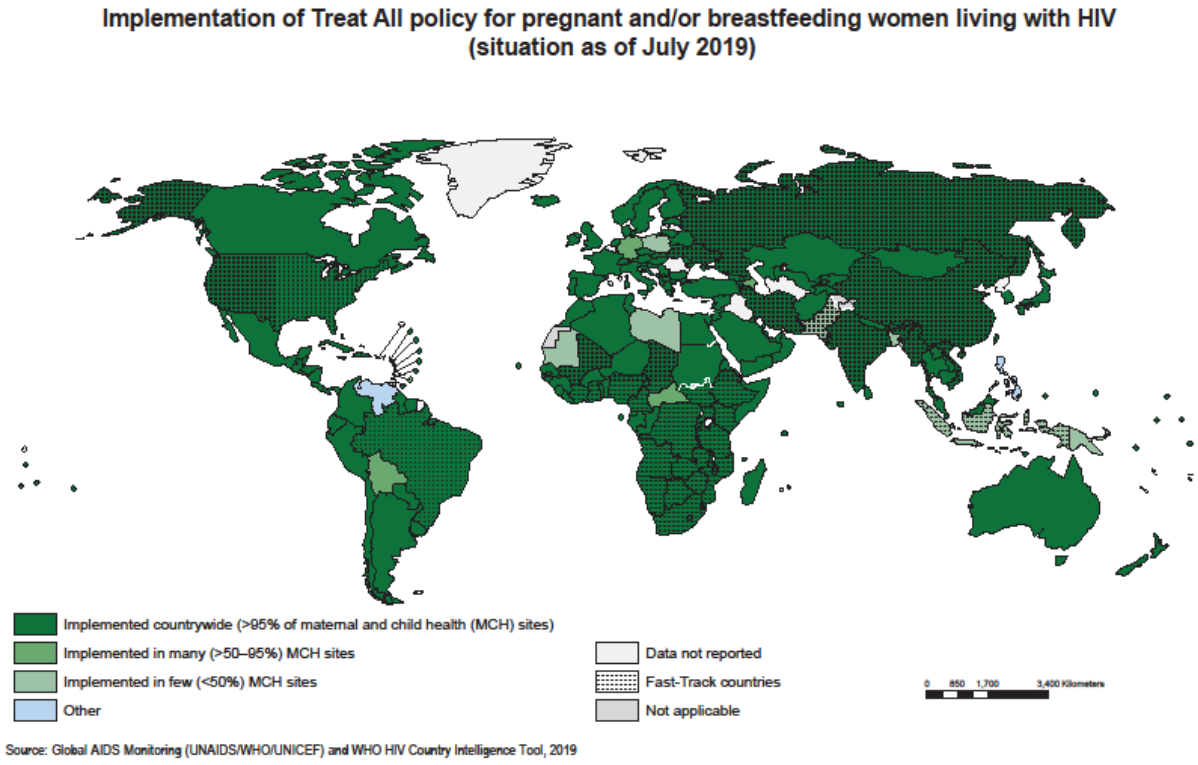

Figure 1. Current status of Treat All policy for pregnant and/or breastfeeding WLWH[14]

Option B+ might also facilitate a reduction in new HIV infections in serodiscordant couples and contribute to a general improvement in maternal well-being [17, 18]. Immediate treatment response compared to deferred treatment initiation at CD4 T cell count of fewer than 350 cells/mm^3 decreases the likelihood of AIDS, serious non-AIDS illness, and mortality [19, 20], increases a chance of viral suppression by the time of delivery, and decreases the likelihood of MTCT.[21] Research also suggests that Option B+ may be the most cost-effective regimen in the SSA setting [22-24].

However, persistent gaps in the PMTCT treatment continuum could undermine the expected positive impact of Option B+. Gaps at each step of the PMTCT continuum,

including women and infants who fail to engage in services at the stages of HIV testing, linkage to ART treatment, initiation, adherence, and retention) create the PMTCT cascade.[21] Acceptability of Option B+ among pregnant and breastfeeding women appears to be high; however, retention and adherence might undermine the positive impact of lifelong therapy.[25]. Other key challenges remain, including late antenatal care (ANC) initiation, not knowing HIV status prior to the pregnancy, non-disclosure of HIV status and fear of disclosure and intimate partner violence, delayed ART initiation, stigma, low postnatal care utilization, ever-changing guidelines, and side effects of ART.[26-28] With the growing evidence of ART effectiveness[15], the focus has shifted to efforts to promote pregnant women's linkage to care, ART adherence, and retention in care.

Viral Load (VL) testing is a key measure of the effectiveness of ART and patient adherence.[4] Literature shows that with good adherence, patients who are ART naïve normally achieve viral suppression within within 4-8 weeks of initiation of ART initiation.[29, 30] Despite the rapid increase in VL testing in many sub-Saharan African (SSA) countries, inadequante coverage and slow turn around for results of VL testing poses problems with timely clinical response.[32] In 2013, the World Health Organization (WHO) recommended that countries introduce targeted VL monitoring for pregnant and postpartum women.[33] With the increasing demands on the healthcare and laboratory systems[32, 34], it is pertinent to ensure that VL testing for pregnant, postpartum, and breastfeeding women is not neglected. These women have limited time for response to an elevated VL during pregnancy/postpartum in time to decrease the risk of vertical transmission to the infant.[35, 36] Sustained viral suppression during the

pregnancy and postpartum/breastfeeding periods is crucial; however, lack of performance of VL testing and long turnaround times for test results limit options for timely clinical decisions and interventions.[32]

HIV Epidemic and PMTCT Guidelines in Kenya

In 2018, 1.6 million Kenyans were living with HIV[37], the national HIV adult prevalence was 4.9% (4.5% men, 5.2% women)[38], and 46,000 people were newly infected.[37] The country is also struggling with reaching the 90-90-90 targets.[1] About 89% of Kenyans knew their HIV status, 69% of adults, and 61% of children were on treatment in 2018.[37]

The former Nyanza Province in southwestern Kenya, the setting of the studies in this dissertation, accounts for nearly one-third of all HIV infections in the country [39, 40]. The counties in the former Nyanza Province, Kisumu County (16.3%), Homa Bay County (20.7%), and Migori County (13.3%) are among the top five highest HIV-burden counties in Kenya.[41] This region represents 54% of the country's new infant HIV infections and 45% of its need for PMTCT services.[42] The ART coverage in adults in these counties ranges from 79% in Homa Bay to 90% in Kisumu.[38] In these counties, high total fertility rates (3.6-5.3) and underutilization of healthcare services (Kenya DHS 2014)[43] among women age 15-49 years interact with high HIV prevalence resulting in increased infections, MTCT, and delayed initiation into treatment for both women and infants.[44]

Kenya has been identified as one of the priority countries in the Global Plan for the elimination of new HIV infections in children [5, 45]. The Kenyan government formalized the roll-out of Option B+ in 2013.[46, 47] According to the guidelines, all HIV-positive pregnant and breastfeeding women should be initiated on ART immediately after being diagnosed with HIV. All missed opportunities for HIV diagnosis in these critical groups should be avoided. Therefore, unless a woman is known HIV-positive (KP), counseling and HIV testing should be conducted at the first antenatal (ANC) visit, in the third trimester, during labor and delivery, at the six-week postnatal (PNC) visit, at 6 months postpartum, and thereafter based on her risk category. HIV testing should also be offered to women who previously declined HIV testing, all male partners, and children of HIV-positive pregnant/ breastfeeding mothers to prevent further transmissions.[47]

In Kenya, about half of women (58%) have four or more antenatal visits, 65% deliver with a skilled birth attendant, and 60% do not receive postnatal care (Kenya DHS 2014).[43] Despite these challenges, the mother-to-child transmission (MTCT) rate at 18 months after birth decreased from 14% to 11.5% from 2014 - 2017. Overall, Kenya reports a 38% decrease in new HIV pediatric infections (children 0-14 years) between 2011-2017 and a 61% reduction in new HIV infections among pregnant women.[38]

The national viral load testing guidelines in Kenya were initiated in 2012 with a rapid scale-up of services over the subsequent years.[34] Viral load testing is available at no cost for qualifying patients on ART at all public health facilities. The standard viral load monitoring for PLWH requires viral load tests at 6 and 12 months after ART initiation, then annually thereafter, and more frequently if results show viremic failure (≥1,000 copies/ml). The guidelines require VL testing every 6 months for those 0-24 years, for all

during the first year of ART initiation, and for special populations, e.g., pregnant and breastfeeding women.[48] According to national guidelines in Kenya, pregnant women living with HIV should receive viral load monitoring at confirmation of pregnancy (if already on ART) or 6 months after ART initiation, and then every 6 months thereafter until the complete cessation of breastfeeding. Repeat testing is required for those with elevated VL.[48]

Demands on the healthcare and laboratory systems are rapidly increasing in Kenya. While in 2010, 440,000 patients were on ART and VL testing was done only for suspected cases of treatment failure; the number of tests increased rapidly to 237,000 in 2014 and to 1.2 million tests in 2018.[32] About 83-88% of the tests processed in 2018 were virally suppressed, while 73% achieved undetectable VL in Kenya in 2018.[49]

Scale-up of ART, Option B+, and intensified viral load monitoring are likely to increase the burden on already overwhelmed health care facilities and the current workforce.[50] UNAIDS recommends decentralization of services to the lowest levels, mobilization of affected communities in service provision, and in particular female empowerment.[51, 52] Existing research suggests that community involvement, especially the involvement of people living with HIV, is critical for PMTCT and, in particular, can improve retention in the PMTCT cascade.[53-58]

A mentor mother (MM) program strategy has been used in several countries to engage communities and promote successful PMTCT.[59] MMs are WLWH who have been through PMTCT in the past six months to two years, show good adherence to

treatment, and have disclosed their status. They are tasked with conducting one-on-one peer education to pregnant/postpartum WLWH on ART and other health-related topics, providing psychosocial support[11, 60-63] and giving encouragement for enrollment, adherence, and engagement in HIV care [62, 64]. MMs also participate in community health and PMTCT education and perform "defaulter tracing" of WLWH who drop out of care [10, 65, 66] Since its inception, health facility-based MMs have assisted more than 1.3 million WLWH, and the literature indicates that this approach may have contributed to reduced MTCT rates, improved ART adherence, increased uptake of early infant HIV diagnosis, and reduced workload for skilled health care workers.[67] Additionally, MM programs have been shown to be an innovative and cost-effective means to increase community employment and the availability of health services in underserved communities.[68] Research also shows that services provided by properly trained lay community health workers focusing on WLWH can promote adherence to healthy behavior through shared culture, language, and community.[69] A recent review by Schmitz, et.al.[70], demonstrates the positive impact of lay community health workers on WLWH-infant pairs in terms of increased MTCT awareness, retention, adherence to care, and infant testing.

The Kenya Mentor Mother Program (KMMP) was established in 2012.[66] In 2014, 325 facility-based mentor mothers were working at 236 healthcare facilities in Kenya.[65] Currently, the mentor mothers in Kenya provide services mainly within health care facilities for women who present for services. Community Health Workers (CHWs), where available, are based in the community, but are not HIV-focused and support a more comprehensive health agenda. They are generally volunteers or receive

a small stipend from supporting partner organizations, whereas MMs are women living with HIV who are salaried employees dedicated to PMTCT support.[66]

Community-Based Mentor Mother Intervention

Building on the success of facility-based MMs, the Mother-Infant Visit Adherence and Treatment Engagement (Motivate!) Study team (NICHD R01 R01HD080477; ClinicalTrials.gov #14-0331) was designed to test the implementation of a mentor mother program at the community level. Community-based mentor mothers (cMMs) are HIV-positive women with recent pregnancy experience living in the community who support uptake and retention in PMTCT services through home visits and other community outreach activities in the study communities in southwestern Kenya. Per protocol, cMMs should conduct a total of 13 home visits with each enrolled pregnant/postpartum woman living with HIV, including four visits during pregnancy and nine visits after the birth, to maximize adherence to ART during critical periods and reinforce maternal and child health (MCH) care and visits per Kenyan guidelines. Postnatal home visits are scheduled frequently after birth and within the first two months postpartum, i.e., during the critical period for PMTCT. The planned home visit schedule is provided in Table 1 below.

During antenatal visits, the focus of cMMs visit is primarily on the importance of adherence to ART drugs and completion of the recommended at least four ANC visits, necessary dietary supplements during pregnancy (folic acid/ferrous sulphate tablets), sleeping under insecticide-treated bednets, preparation of individual birth plans, and the

importance of delivery in a health facility. During the antenatal period, cMMs also check for any danger signs in pregnancy. Additionally, cMMs emphasize the importance of safe disclosure to the male partner, infant prophylaxis as prescribed at the health facility, immediate exclusive breastfeeding after birth, and they educate on immediate newborn care. During the postnatal visits, the cMMs support mothers living with HIVin initiating and sustaining breastfeeding, and when the time comes, weaning. The cMMs verify if the baby received vaccinations as scheduled, and discuss the importance of initiation of infant prophylaxis. Additionally, cMMs focus on health education related to family planning and birth spacing, and importantly ART adherence and retention in care. In case of any urgent health concern raised by the mother in regards to herself or her infant, the CMM makes an referral to the health facility.

Table 2

Recommended Home Visit Schedule in the MOTIVATE! Study cMM Intervention

cMM Visits During Pregnancy
First visit following a) the woman's first antenatal visit for pregnant known HIV-positive women or b) after the first HIV+ test in ANC for those newly diagnosed with HIV during pregnancy
Thereafter, monthly visits up until the birth[a]
cMM Visits in the Postpartum Period
Immediately after delivery (one day postpartum)
3-4 days postpartum
1 week postpartum
6 weeks postpartum (infant HIV test (PCR) performed around this time)
10 weeks postpartum (result of infant HIV test available)
14 weeks postpartum
6 months postpartum
9 months postpartum
12 months postpartum

[a]Four cMM visits are anticipated during the pregnancy period due to the common late initiation of antenatal care in this setting

Early experience with the implementation of the cMM strategy shows high acceptability rates. Outcomes and impact are currently being analyzed as part of the MOTIVATE! Study funded by the National Institute of Child Health and Human Development [grant number R01HD080477; ClinicalTrials.gov #14-0331]. The purpose of this parent study was to address potential barriers that may affect uptake and retention in HIV care for Option B+ in Nyanza, Kenya. Two evidence-based strategies (community-based mentor mothers and mobile phone text messages) are being tested to examine which strategy --alone or in combination—is more likely to maximize ART adherence and retention in care among pregnant women living with HIV and HIV-exposed infants in rural Kenya, using a 2x2 factorial cluster-randomized design.

Overview of the Dissertation

The aim of my dissertation project is to explore challenges and promising strategies for maximizing pregnant and postpartum women's adherence and retention in HIV care in the context of Option B+ roll-out in Kenya. In this context, the dissertation has a focus on viral load testing and community-based mentor mother strategies as promising approaches for addressing the challenges that have been identified.

I utilized the three-paper dissertation model. Taken together, these three papers aimed to illustrate some of the most important challenges to implementation of the lifelong antiretroviral therapy (Option B+) for pregnant and postpartum HIV-positive women in this setting (paper #1); evaluate the implementation and potential challenges related to viral load testing during pregnancy and postpartum, as one of the most

important biomedical indicators of ART adherence (paper #2); and examine the potential effectiveness of the community-based mentor mother program in addressing challenges related to adherence and retention in care (paper #3).

Option B+ presents a promising PMTCT strategy to accomplish global maternal and child health goals, namely to eliminate MTCT and keeping mothers living with HIV alive; however, attrition across PMTCT cascade, insufficient adherence and retention to care might undermine efforts and expected positive impacts of Option B+. While the impact of ART utilization on PMTCT and overall health of HIV-positive women during pregnancy and postpartum has been researched and documented, little is known about specific challenges related to the Option B+ PMTCT regimen and the best strategies to address them. The cMM strategy exemplifies UNAIDS recommendations for successful HIV-related interventions during pregnancy and postpartum in regards to task shifting utilizing the community and women living with HIV; however, this intervention is new and implemented on a small scale. We hypothesized that the cMM intervention would be an acceptable and effective strategy that may increase linkage, retention, and adherence to life-long ART treatment for pregnant HIV-positive women in Kenya. We also hypothesized that gaps in VL monitoring remain for pregnant/postpartum WLWH in these Kenyan settings and that many women were potentially not getting VL measurements at crucial times during pregnancy and breastfeeding, particularly those who were newly diagnosed with HIV at their first antenatal visit during the index pregnancy. We further hypothesized that women in vulnerable sub-groups (primigravida, younger women less than 25 years, and women newly diagnosed during pregnancy)

would be less likely to achieve sustained viral suppression during the observation period (pregnancy up to 12 months postpartum).

These dissertation projects aimed to address some of the gaps in the literature. The results will help us to understand specific challenges of Option B+ at the health facility level in the Kenyan setting, explore and improve understanding of how cMMs' support may impact HIV-positive pregnant women in the context of Option B+, and determine the role of viral load monitoring in effectively intervening within the PMTCT cascade to strengthen adherence and retention in ART care for pregnant and postpartum HIV-positive women.

THE HEALTH FACILITY CHALLENGES TO THE PROVISION OF OPTION B+ IN WESTERN KENYA: A QUALITATIVE STUDY

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Introduction

Among the estimated 1.5 million HIV-positive pregnant women globally, over 90% live in Sub-Saharan Africa (SSA). With no intervention, the mother-to-child transmission (MTCT) rate of HIV ranges from 15% to 45% [5]. The current World Health Organization guidance on prevention of MTCT (PMTCT) recommends life-long antiretroviral therapy (Option B+) for all pregnant and breastfeeding women in settings with generalized HIV epidemics (WHO 2012).[72] Option B+ represents a promising approach that is expected to substantially contribute towards goals set by the Joint United Nations Programme on HIV/AIDS Global Plan for the Elimination of New HIV Infections in Children (the Global Plan) [45].

Early results from the PROMISE study indicate that triple antiretroviral therapy (ART) therapy in pregnant women with high CD4 counts to be more effective in reducing MTCT during pregnancy than prophylaxis alone [16]. In addition to this outcome, Option B+ might also facilitate reduction in new HIV infections in sero-discordant couples and contribute to general improvement of mother's well-being [17, 18]. Immediate treatment versus deferred treatment until lower CD4 counts decreases likelihood of AIDS, serious non-AIDS illness, and mortality [19, 20]. Option B+ reduces logistical barriers by eliminating the need for CD4 testing (WHO 2013) and may be more cost-effective [22-24].

With rapid scale-up of ART services and lifelong ART treatment under the Option B+ regimen in SSA, retention in care and ART adherence will be critical. A meta-

analysis of 51 studies conducted in SSA showed that only 73.5% of pregnant women and 53% of postpartum women report adequate ART adherence prior to implementation of Option B+ [73]. Acceptability of Option B+ in Malawi among pregnant and breastfeeding women has been high; however, high rates of "non-starters" (women who default after their first visit) were reported and 20-30% of women were lost to follow-up in the first 3-6 months after ART initiation [25].

Kenya has been identified as one of the priority countries in the Global Plan for elimination of new HIV infections in children [5, 45]) with an HIV prevalence among adults of 5.6% (KAIS 2014) and an estimated 1.6 million people living with HIV (National AIDS Control Council of Kenya 2014).[74] Over 92% pregnant women in Kenya undergo routine HIV testing during antenatal care (ANC), yet, the MTCT rate remains high at approximately 14%[75, 76] of infants born to HIV-infected mothers. Nearly 80,000 HIV-infected pregnant women per year are in need of ART (National AIDS Control Council of Kenya 2014).[74] Current health guidelines of the Kenyan Ministry of Health support ART for all pregnant women where implementation is feasible [47]. While ART retention in the general population approaches 92%, only about 70% are retained in care after five years (National AIDS Control Council of Kenya 2014).[74]

The full benefit of Option B+ can only be realized if women are tested for HIV, initiated into treatment, retained in care, and adhere to treatment. However, barriers to successful implementation may occur at the individual, interpersonal, community, and

health care facility level [77]. Understanding these barriers is critical to the success of Option B+. In this study we explored health facility level challenges to Option B+ provision from the perspectives of health care providers and clients at low-resource health facilities in western Kenya.

Methods

Qualitative methods were utilized to achieve the study objectives. A total of forty individual gender-matched one-on-one in-depth interviews with HIV-positive pregnant or postpartum women (n=20) and male partners of such women (n=20), as well as four focus groups with a total of thirty health care providers, were conducted between September and November 2014 at four health facilities in Kisumu, Migori, and Homa Bay Counties (formerly Nyanza Province), Kenya. The four health facilities were selected from 20 facilities that are participating in the Mother Infant Visit Adherence and Treatment Engagement (MOTIVATE!) trial of interventions to support adherence and retention in the context of Option B+ rollout (Clinicaltrials.gov # 14-0331).

Setting

The former Nyanza Province in western Kenya accounts for nearly one third of all HIV infections in the country [40, 43] with county HIV prevalence rates ranging from 13.4% in Migori to 18.7% in Kisumu, and 27.1% in Homa Bay (National AIDS Control Council of Kenya 2014).[74] In these counties, high pregnancy rates (5.3%-9.0%), fertility rates (3.6-5.3), and underutilization of health care services (Kenya DHS 2014) [43] interact with high HIV prevalence resulting in increased infections, MTCT, and

delayed initiation into treatment for both women and infants [44]. Over 15,000 Kenyan women received maternal prophylaxis in 2013 with estimated 62-88% coverage (MOH Kenya 2014).[78] About half of women (58.7%) in Nyanza Province have four or more antenatal visits, 65% deliver with a skilled birth attendant, and 60% do not receive postnatal care. Only 35% of eligible infants are tested for HIV at six weeks (Kenya DHS 2014).[43]

Ethics

Ethical approval was obtained from the Kenya Medical Research Institute (KEMRI) Scientific and Ethical Review Unit (SERU), the University of Colorado, Denver Institutional Review Board, and the University of Alabama at Birmingham Institutional Review Board. All participants provided their written informed consent and were reimbursed for travel or other expenses related to study participation.

Data Collection Methods

Qualitative in-depth interview and focus group discussion guides were developed based on a review of the literature and prior studies on pregnancy and HIV in this setting [79, 80]. Both guides included topics related to the acceptability of Option B+, barriers and facilitators to adherence and retention in HIV care, and the acceptability of proposed interventions for the trial (community mentor mothers and text messaging). Experienced interviewers/moderators (one male, one female), fluent in English and the local languages, underwent additional training in qualitative research methods and the study topics prior to the initiation of the study.

Eligibility

Participants eligible for the study were: (1) HIV-infected pregnant/postpartum women (2) male partners of HIV-infected pregnant/postpartum women (3) health workers currently working/supervising at one of the study sites (4) aged 18 years or older.

Individual In-Depth-Interviews: A total of twenty in-depth interviews with pregnant/postpartum HIV-positive women, were conducted in the four selected study communities, five women per each community. Participants were identified from health care facilities providing Option B+ services during a routine ANC or MCH visit. Eligibility and interest in participating was determined during a short private session. Clear explanations were given to the participants that the study was separate from their regular medical care and that they had the option of refusing to participate in any part of the research. Pregnant/postpartum women who had previously disclosed their HIV status to their male partner were also asked if they would be willing to have their male partner contacted by a researcher regarding potential participation in an interview. Male partners were contacted through information provided by the woman and invited to participate in an interview. Half of males recruited were HIV-positive partners (concordant relationship) and half were HIV-negative partners (discordant relationship). Individual interviews were conducted in private settings in English, Dhuluo or Kiswahili language, depending on the preferences of the participant by gender-matched interviewers who identified themselves as members of an external research team. Participant characteristics were collected, including demographics, job characteristics, pregnancy and HIV-related information.

Focus Groups: Participants in focus groups were purposively selected for maximum variation in occupational characteristics, to ensure all types of health workers providing services to pregnant women were included. Potential participants were contacted in person by the research coordinator and asked to participate in a focus group located at their health facility. A total of thirty health care providers, 7-8 from each of the selected facilities participated in the four focus groups and included nurses, community health workers, health educators, mentor mothers, HIV counselors, laboratory technicians, facility in-charges, program technical advisors, and administrative staff. Participant characteristics were collected, including demographics and job characteristics.

Data Management and Analysis

Interviews and focus groups were digitally recorded, translated to English if applicable, and transcribed verbatim by professional transcriptionists, excluding any identifying information. All files were password-protected and stored in a secure location. Subsequently transcripts were coded by a team of three researchers using the Dedoose qualitative software program. Coding and analysis followed a thematic analysis approach [81, 82]. The coding framework was based on the literature, topics from interview guides, and emerging themes from transcripts. Transcripts were initially broad-coded by two individuals trained in qualitative coding. Consistency of coding between two individuals was established by initially coding the same transcripts and through frequent discussion between coders. Excerpts from broad codes were then fine-coded using an inductive approach. Major themes were refined and sub-themes identified.

Results

Participant Characteristics

Seventy participants, including twenty HIV-positive pregnant/postpartum women (mean age 24.7 years ±4.8), twenty male partners (mean age 33.5 years ±8.8), and thirty health care providers (mean age 32.2 years ±7.2) participated in the individual interviews or focus groups. The majority of participants were married (84%), currently living with their spouse (93%), and had at least 2 living children (66%). Seventy percent of women and male partners participating in individual interviews had not attained more than primary education. All health care providers in the study completed at least secondary education and 67% had worked in their current health/community services profession for at least 3 years. Forty-five percent of the interviewed female clients were housewives while the majority of male partners were either skilled workers (45%) or held a job in agriculture (45%). By study design, half of the individual interview participants were in HIV concordant and half were in HIV discordant relationships. Socio-demographic characteristics of participants are presented in Table 1.

Table 1
Socio-demographic and HIV-related characteristics

Characteristics	**Females N = 20**	**Males N = 20**	**Health workers N = 30**
Age: Mean (SD)	24.7 (4.8)	33.5 (8.8)	32.2 (7.2)
Participant education: N (%)			
Did not complete primary	11 (55.0)	6 (30.0)	0 (0)
Complete primary	5 (25.0)	6 (30.0)	0 (0)
Did not complete secondary	1 (5.0)	3 (15.0)	0 (0)
Complete secondary	3 (15.0)	5 (25.0)	10 (33.3)
Any college	0 (0)	0 (0)	20 (66.7)
Marital status: N (%)			
Monogamous marriage	16 (80.0)	18 (90.0)	20 (66.7)
Polygamous marriage	3 (15.0)	2 (10.0)	

Single	1 (5.0)	0 (0)	8 (26.7)
Widowed	0 (0)	0 (0)	2 (6.7)
Current occupation: N (%)			
Agriculture	3 (15.0)	9 (45.0)	0 (0)
Business/sales	5 (25.0)	2 (10.0)	0 (0)
Health/community services	0 (0)	0 (0)	30 (100.0)
Skilled worker	2 (10.0)	9 (45.0)	0 (0)
Housewife	9 (45.0)	0 (0)	0 (0)
None	1 (5.0)	0 (0)	0 (0)
Length of time in current occupation: Mean (SD)	Not asked	Not asked	4.7 (5.1)
Number of Living Children: Mean (SD)	2.2 (1.1)	3.2 (1.9)	1.8 (1.8)
Pregnant participants/partner: N (%)	12 (60.0)	12 (60.0)	Not asked
Postpartum participants/partner: N (%)	8 (40.0)	8 (40.0)	Not asked
Concordant HIV Partner Status: N (%)	10 (50.0)	10 (50.0)	Not asked

Qualitative Themes

Overall, our study showed high acceptability of Option B+ among all the different participant groups. The major advantages included elimination of CD4 assessment as a requirement for treatment initiation, easy administration due to the same regimen used during pregnancy, labor and delivery, and perceived effectiveness of PMTCT. High acceptability of Option B+ was also expressed in individual interviews with HIV-positive women and their male partners. The main motivation for women was expressed as protection of their child during pregnancy up to 18 months of age. However, health care providers warned that postpartum women may disengage from care after the child tests HIV-negative at 18 months. Importantly, perceived effectiveness of PMTCT seems to be increasing in the communities, as people are seeing more infants born without HIV and increasingly believe that adhering to treatment will result in a birth of HIV-negative infant.

Specific challenges to the success of Option B+ at the health facility level described by the participants fell under three major themes, including 1) Option B+ specific challenges, 2) resource constraints, and 3) lack of client-friendly services, as presented in Table 2.

Table 2
Identified Health Facility Challenges and Recommended Strategies

Themes	**Challenges**	**Recommended Strategies**
Option B+ specific challenges	• Same-day initiation into treatment • Health care providers unconvinced of the benefits of Option B+ • Insufficient training of health care providers on Option B+	<u>Individual level:</u> Continuous adherence counselling, tracing of clients lost to follow-up, text messages <u>Couples/groups:</u> Couple testing, assisted disclosure, treatment buddies, support groups <u>Community:</u> Reducing stigma, increased awareness, community mentor mothers, health educators <u>Changes in service provision:</u> Appropriate staff training on the Option B+ guidelines
Resource constraints	• Staff shortages • Drug shortages • Long queues • Space limitations	<u>Changes in service provision:</u> Private space for individual counselling, improved efficiency to decrease long waiting times, consistent drug supply, appropriate staff numbers
Lack of client-friendly services	• Scolding of patients for lack of retention and adherence • Inconvenient operation hours for patients • Lack of integration of services • Paperwork and other administrative requirements	<u>Changes in service provision:</u> Integration of ART with other services, more convenient clinic hours of operation, promotion of positive attitudes of health providers towards patients and Option B+, elimination of administrative requirements

Theme 1. Option B+ specific challenges

Same-day initiation into treatment

Possibly the most challenging aspect of Option B+ from the perspective of service providers is the practice of same-day initiation into treatment immediately after the woman tests HIV-positive. Providers expressed concern that pregnant women have little time to accept and disclose their HIV status when they are immediately initiated on treatment; which could potentially lead to stigma, conflict, domestic violence, or problems with retention to care. The providers expressed that women in discordant relationships in particular may have problems with initial acceptance of their HIV-positive status. Some women initially refuse to enroll into treatment and return after they have accepted the fact that they are HIV-positive.

> *"Put yourself in her shoes, you have come to the facility with a headache then you are sent for pregnancy test which turns positive then you are sent for ANC to start your clinic and at the same time you are required to start your drugs. You realize you have pain today, you realize you are pregnant today and that you are also HIV-positive and again you are required to start the HIV drugs immediately. It is too much and the patient hasn't even internalized her condition as HIV-positive." (Nurse, female, 26 years)*

However, many health care providers also related that through pre-initiation and ongoing counseling, education, and positive experiences with treatment, patients tend to gradually accept their status and develop more positive attitudes towards HIV treatment.

"When a client comes here you test them. Then counsel them. You see there is that part of crying and how did I get it then you tell the client that we want to initiate you because we want to protect you and we also want to protect your baby." (Clinical officer, female, 28 years)

Many health care providers expressed that women should be given some time to accept their HIV-positive status, disclose their status to their partners, and/or their family members prior to treatment initiation.

"Initially when a woman tested HIV-positive, they were given time to go think about it, consult. They give you Septrin [co-trimaxazole] for even three days then when you come back you can get enrolled, but now we are enrolling pap [immediately]." (Community and Clinical Health Assistant, female, 33 years)

Potential care recipients might be lost to follow-up due to the same-day initiation practice under the Option B+.

"It was very difficult before for the mothers because you are tested at the same time, you haven't disclosed your status to anybody and you are being told to go home with drugs, you don't even know how to go about it. Some were picking the drugs, they go home with them and you don't see them again". (Mentor mother, female, 26 years)

In contrast to providers' perspectives, same-day initiation as a challenge to Option B+ acceptance was rarely mentioned in the individual interviews with women and their male partners. This may be due to the fact that individuals were not probed on the immediate initiation aspect, but rather on the life-long therapy aspect of Option B+ since the importance of same-day initiation as a barrier emerged only during data analysis. In those few interviews where participants commented on same-day initiation, most agreed that for the sake of child and health of a woman immediate initiation into treatment is justified.

> *"P: There should not be a duration. She [pregnant woman] should start [ART] immediately she tests positive. […] So as to save the child in the womb". (postpartum female, concordant couple, 24 years)*

However, a few male participants did voice their concern about immediate initiation into treatment during individual interviews and expressed that women should be given some time to accept their HIV-positive status, disclose their status to their partners and involve them in decision-making regarding treatment.

> *"In case she is tested for HIV and advised to take the drugs immediately even before she experiences any signs of sickness, my advice would be that she gets counseled to understand why she needs to be initiated not that you just ambush her that you need to be initiated on HAART now for life. It is not an easy thing taking the drugs and she needs to be supported and counseled well until she*

accepts then she can be initiated on the drugs." (male partner, discordant couple, 38)

Health care providers unconvinced of the benefits of Option B+

Although most health care providers seem to favor Option B+, a few health care providers expressed doubts about the validity and effectiveness of Option B+, especially for women with high CD4 counts.

"The first disadvantage is that you find that a woman has a CD4 of 1000 and she will be given ARVs with other women whose CD4 is below 500. I am introduced on ART when my time is not yet, I start using it when my time is not yet reached." (Pharmaceutical technologist, female, 31 years)

"You know it will depend on the CD4, if the CD4 is low and the mother is going to get into the pregnancy and is down then we will put mother into Option B+, it is okay and in a situation where CD4 is high, I feel that option A should be used. So to me we should use two depending on our assessment of the client." (Nurse, male, 33 years)

Insufficient training of health care providers on Option B+

Some health care providers expressed the need for more training related to Option B+ and HIV care for pregnant and breastfeeding women due to frequent changes in guidelines and the need to provide consistent information to patients.

"Concerning the Option B+, the health care workers need to be trained so that they all speak the same thing when it comes to Option B+, because presently you find people are every conversant with it and others not so conversant." (Nurse, male, 27 years)

Need for additional training of staff is apparent from the experience of this study participant (client).

"I: You were never issued with drugs when you first came to the clinic?
P: No, they told me that my pregnancy was still not big enough.
I: How old was your pregnancy by then?
P: A month old. I just obliged and went home after they told me so. When I came back for the HIV clinic appointment, I was told to carry my card. The nurse I found on that day asked for the card but I told her I was to come with it in October. She overruled the other nurse's direction and told me that once a HIV-positive woman has conceived then she should immediately start taking the medication to protect the unborn child." (pregnant female, concordant couple, 25 years)

Theme 2. Resource constraints

Staff shortages

Several providers expressed concerns about staff shortages related to the additional work required to provide Option B+ including adherence/retention

interventions proposed to support Option B+. Staff shortages might undermine the quality of services provided and ultimately have negative impact on patients' adherence to medications and retention in care.

> *"There are times when the number of staff working at the facility is reduced, so the person attending to this client is having burn out so that information is not given correctly. Like giving medication without following how the client will use the medication." (HIV Testing Counsellor, female, 32 years)*

> *"Some people will keep you waiting on the bench. "Just wait for me. I am coming." This person is the only one who will handle those who are having antenatal clinic visits as well as those who are here for HIV treatment. He also needs to educate you. These guys have mixed everything up. One person wants to handle two different departments. Work will therefore be difficult." (male partner, discordant couple, 36 years)*

Drug shortages

Drugs shortages could result in inconsistent ART treatment and pose a barrier to adherence. One of the four clinics included in the study reported drug shortages. A few patients mentioned instances where drugs were not available the day of their clinic visit and were asked to return the following day.

"With Option B+ there is a new guideline with new regimen for drugs, then the challenge we have is that when we make phone calls to the higher authority in our case the XX sub-county hospital then they tell you that the drug is not available in fact they tell you not to initiate many people on it because the drug is still not available…" (Nurse, male, 27 years)

Long queues

Understaffing and high demand for HIV-related services increase waiting time and result in significant barriers when accessing HIV care. Long queues were discussed by many interviewed women and male partners, especially in the context of required monthly visits for the rest of her life under the Option B+.

"Getting the drugs from the clinic is a major difficulty. They try because people are many and sometimes I am number eighty something. And I have to be seen. So I am forced to be there until when my wife goes back home. When I come with her it is usually easier because I see them jump the queue for us … When we come with her they jump the queue for us but when she is alone she has to queue." (male partner, discordant couple, 49 years)

"They [patients] are just kept waiting endlessly and that discourages. […] you are just there and no one is attending to you or telling you anything." (pregnant female, concordant couple, 26 years)

Space limitations

Limited space available in clinics precludes privacy, resulting in increased risk of inadvertent disclosure and stigmatization of HIV patients. Some participants discussed the need to integrate HIV services in the same space with other services to reduce stigma but provide individual services in a private space.

> *"One is privacy. You need to get a private place. Don't shout. "We want those who came for HIV treatment." You will get into the clinic without anyone knowing the reason of your visit. They don't know whether you are sick or whether you have come to visit a patient. They will serve you and then you leave. But sometimes you get people are being isolated. They say that the sick will be educated separately. Someone will see the group and ask, "Who are they?" "Those are people suffering from HIV. He is a member of the group that is being educated there." These are some of the things that might prevent people from coming for such lessons which are very important. If you can educate someone alone-like the way we are seated here today-no one will know what I am doing in this room." (male partner, discordant couple, 36 years)*

Theme 3. Lack of client-friendly services

Scolding of patients for lack of retention and adherence

The health workers reported that most women adhere to the scheduled appointments or provide valid reason for missing an appointment. However, it was mentioned across interviews and focus groups that in some facilities if someone doesn't

adhere to their clinic appointments, she is subject to scolding and punishment from health care providers. In many cases, this may be driven by established belief among health workers that this approach is in the best interest of the patient and will result in improved adherence and retention to care.

> *"Here we don't punish them; we tell them to attend the retention class where we talk to them and tell them that it is very, very important for them to keep their scheduled clinic visits and you have to tell them that very firmly!" (Nurse, male, 58 years)*

Many patients expressed their feelings and emotions related to negative attitudes of health care providers, especially when they miss their appointments. They frequently mentioned questioning about reasons for missed appointments, quarreling, and applying various forms of punishment, including retention classes, counseling, more frequently scheduled visits, transfer to the end of queue, declining of care or not receiving medications.

> *"P: So you may be told either to go back or they make you be the last person on the queue even if you came very early in the morning just because you had missed your scheduled visit. […]They feel that you are undisciplined so they punish you. I: You go back home without your drugs? P: Yes. I: Then what do you do? They ask you come back another day?*
>
> *P: Yes. That day they are busy with the people that came on their appointed dates.*

I: Okay. What do you do when you drugs get finished?

P: That is why some people beg them and they end up giving them. Sometimes I would see someone give a bribe so that they are given drugs because he missed his visit."(postpartum female, discordant couple, 20 years)

However, in some instances, patients believed that scolding and punishments are justified.

"They told me I had come late, past working hours and that I should go back and come the next day and mark you it was so early but because I had wronged them by missing my appointment I understood their anger." (male partner, concordant couple, 28 years)

Importantly, some participants mentioned how scolding and other negative provider attitudes at the clinic may result in poor retention or defaulting.

I: How did you feel when you were quarreled?

P: I felt bad because that is being disrespectful to patients. I felt they didn't know how to counsel patients.

I: How did that make you feel about taking the ARVs, when they subjected you to humiliation yet it's human nature to forget?

P: At first I thought of not going for the medicine then I later told myself that if I fail to go it would be my health and life that will be at risk." (pregnant female, discordant couple, 22 years)

"For example if I miss to go to the clinic and I am called to find out why I didn't come, I shouldn't be talked to or shouted at in a humiliating way, telling you things like it is your health and it's up to you if you don't want to come. Some just talk to you carelessly and that may offend and discourage someone." (pregnant female, discordant couple, 21 years)

Inconvenient operation hours for patients

Some health care providers and participants mentioned the need for more convenient operation hours of the clinic. For some women it's a challenge to ask their employer for permission to attend clinic every month for the fear of losing their jobs. Inadvertent disclosure and stigma was another reason cited for non-traditional clinic operation hours, e.g. late evening or weekend hours. Several patients mentioned that sometimes they have difficulty reaching the clinic in time due to distance, inclement weather, or access ability of clinic.

"Some fear asking for permission from their employers each and every time they are asked to come to the clinic for example if they have bad employers […] and maybe they haven't disclosed because they fear losing their jobs. Some even come over lunch break and they want to be attended to very fast so that they go back to

work so if you can't meet their demands then they simply default." (health care provider)

"The challenging part about this is when it comes to transportation, then after arriving you find so many people waiting to be attended to also. Mostly the clinic opens at 7:00 in the morning and normally by 6:00 AM people will be here already so if one makes a mistake and delays a bit then the hospital will be swarming with people, if 2:00 PM finds you outside the hospital then from 3:00 they start locking the place." (male partner, concordant couple, 28 years)

Lack of integration of services (separate appointments for antenatal and HIV clinics)

Although the majority of women indicated that their antenatal clinic and HIV clinic visits are integrated, some said that they still have separate visits creating additional barrier for women when accessing care.

"It did give me hard time of walking all the time. When it is divided you may end up being committed [busy] and they are put together it is very easy." (postpartum female, discordant couple, 20 years)

Difficulties related to separate visits included demands related to increased frequency of visits to clinics once woman becomes pregnant, distance, time, and costs.

"[…] challenge is distance, one might go to this hospital this week the next time she is required to go to another hospital, and mark you they are all far from home, the next month they are expected to visit another hospital, after two weeks again another clinic, she heads there and you know walking is a challenge when one is expectant." (male partner, concordant couple, 28 years)

Paperwork and other administrative requirements

Examples of administrative issues resulting in challenges when accessing HIV care included requirement of a transfer letter when changing clinics and complex documentation when enrolling into Option B+.

"First, they told me they won't give me any drug without the transfer letter. I asked them if I should miss my drugs because of the transfer letter. They wondered how they could assist me because you must have the letter with you. I wondered how I could walk everywhere with the whole file. I told them to give me the drug because I can go pick the transfer letter when I have money. They said that they won't give me the drug without the letter. I begged them and they later gave me the drugs. They told me to come with the letter next time when I come to pick my drugs." (postpartum female, concordant couple, 21 years)

"I: After testing positive for HIV were you initiated on HIV medications immediately?

P: I wasn't initiated immediately because there were many issues, there were some forms to be filled and I also had to consult. […] It was already evening and I also needed to go back home early, my husband was also rushing to go to work and they still wanted to talk to us. There was no time to take us through the entire enrollment process at that time." (pregnant female, discordant couple, 18 years)

Discussion

The results of our study suggest high acceptability of Option B+ in rural western Kenya among both patients and health care providers. Despite this finding, we found that health facilities are facing many challenges while implementing Option B+, some of which have likely persisted a long time in this setting as well as others that may be specific to this guideline. Overcoming these challenges will be crucial for success of Option B+ in Kenya. Our study highlights the perspectives of HIV-positive pregnant and postpartum women, male partners, and health care providers on the health facility challenges to the provision of Option B+ in this setting.

While health care providers highlighted same-day initiation as possibly the most substantial challenge related to Option B+, individual clients did not identify this as an issue, with the exception of a few individuals. Same-day initiation has been identified as a major challenge by countries implementing Option B+ [83-85] who report concerns similar to our study, including fear that women do not have time to internalize their

status, disclose to partners, experience peer and staff pressure to initiate ART, and are at increased risk for attrition. In a few reports, women had few problems with same day initiation, especially if they were already aware of their status and had disclosed it. However, it is uncertain if non-initiation and high rates of loss to follow-up seen in some settings may be related to same-day initiation. These studies reveal the mixed views on the risks and benefits of same day initiation. Consensus seems to be that under the same day initiation procedures, women are more likely to initiate treatment and initiate treatment in earlier stages. This may outweigh risks of attrition, but same-day initiation needs to be supported by proper counselling and follow-up [83-86].

Another significant barrier at health-facility level is shortage of staff, which is compounded by increasing workforce demands with the provision of Option B+. In response to staff shortages during scale up under Option B+, several countries in SSA have responded with extensive hiring and training of health care staff, as well as task shifting among health care cadres [83]. Similar to our study, previous reports suggest that training is insufficient and staff often don't feel comfortable implementing Option B+. Several studies suggest that insufficient training led to confusion, delays, or incorrect implementation of WHO guidelines on Option B+ [87, 88]. Importantly, results of our study revealed that some health care providers are still unconvinced of the benefits of Option B+ over other regimens, especially for women with higher CD4 counts. Lack of space at the clinics for counselling, testing, ART treatment, and drug storage is well-known but more prominent challenge for HIV health care facilities under Option B+ in Kenya and elsewhere (WHO 2014).[88] Combination of high demands on the health care

system under Option B+, lack of space, and staff shortage leads to long queues, often creating frustration of both patients and health care providers. Additionally, inconvenient operation hours for patients create barriers when accessing care, especially among employed patients. Patients often fear inadvertent disclosure of HIV status at the clinic [89]. However, integration with antenatal care and/or infant testing substantially increases likelihood of ART initiation and retention to care [88-90]. More convenient operation hours for patients might not be possible due to prevalent staff shortage and confidentiality in integrated clinics might be compromised by a lack of space.

In concordance with previous research, participants in our study revealed a common problem of scolding and various forms of punishment of patients for lack of retention and ART adherence that represent major barriers to access of care [90-94]. It has been suggested that they are result of frustration of health care providers with high demands of HIV services and based on the beliefs that this often harsh treatment of patients helps to increase adherence and retention to care. Despite this common belief, growing evidence links poor treatment of patients in HIV care and negative patient-health care provider interaction to lowered uptake and retention to care [77, 91, 95]. Importantly, long-standing customer service issues and weak patient-provider relationships may result in lower effectiveness of interventions targeting adherence and retention in care in the context of Option B+ (Gourlay et al. 2013).

Multi-level strategies to overcome these challenges have been suggested by our participants to ensure successful implementation of Option B+. These strategies are

summarized in Table 2 and are supported by the findings in recent reviews [77, 89]. At the individual client level suggested strategies included continuous adherence counseling, tracing of clients lost to follow-up, text messages, and incentive programs. Couple/group strategies discussed included couple testing, assisted disclosure, treatment buddies, and support groups. Community strategies included reduction of stigma, community mentor mothers, health education, and increased awareness. Potential changes in service provision discussed included integration of ART with other services, privacy for individual counselling, more convenient clinic hours, efficiency to decrease long waiting times, appropriate staff training and staff numbers, elimination of administrative barriers, consistent drug supply, and promotion of positive patient-provider relationships.

Strengths and Limitations

Our study is one of the first to explore barriers at the heath care facility level in the context of Option B+ in Kenya. This study includes perspectives of health care providers, pregnant and postpartum women, and their male partners using qualitative in-depth interviews and focus groups. Despite these strengths, this study has some limitations. Perceived acceptability of same-day initiation among patients based on individual interviews in our study must be considered with caution. Female client participants in this study had agreed to HIV testing and disclosure of HIV status to their partner. Thus, their perception might be inherently different from women who were not tested, women who have not disclosed their status, women who have not utilized antenatal/postnatal care, or are categorized as non-starters. Other possible biases include recall bias and social

desirability bias. This study represents three counties in western Kenya and results might not be generalizable to other communities.

Conclusions

This study highlights important challenges at the health facility level related to Option B+ rollout in western Kenya. Addressing the identified challenges using some of the suggested strategies may increase linkage, retention and adherence to life-long treatment for pregnant women in Kenya, contribute towards elimination of mother-to-child HIV transmission, and improve maternal and child outcomes.

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GAPS IN VIRAL LOAD MONITORING AND PREDICTORS OF VIRAL SUPPRESSION IN A COHORT OF PREGNANT WOMEN WITH HIV IN SOUTHWESTERN KENYA

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Abstract

Background: Achieving and sustaining viral suppression among pregnant and breastfeeding women living with HIV (PWLWH) is critical to prevent mother-to-child transmission of HIV and optimize the health of women and infants. We examined the timing, frequency, predictors, and outcomes of routine VL testing at 24 government clinics among PWLWH enrolled in large cluster-randomized trial (MOTIVATE!), which aimed to enhance antiretroviral therapy (ART) adherence and engagement in HIV care in three high burden counties of southwestern Kenya.

Methods: In the MOTIVATE! Trial, PWLWH were enrolled at antenatal clinics during pregnancy between 2015-2018 and were followed until at least 12 months postpartum. VL testing was carried out as part of routine clinical care as per national guidelines at confirmation of pregnancy if already on ART, or six months after ART initiation if newly initiating, and then every six months thereafter until cessation of breastfeeding. Longitudinal data on VL were routinely abstracted from medical records and the Kenyan national VL database. We examined timing and trends in VL measurement by stage of pregnancy/postpartum and relative to the date of ART initiation. VL non-suppression was defined as 1) more than 1,000 copies/ml (as per current Kenyan standards during the study period) or 2) detectable VL (>0 copies/ml) versus undetectable. Cluster-adjusted multivariate logistic regression with Generalized Estimating Equation (GEE) was used to examine factors associated with VL supression at 12 months postpartum, as well as sustained VL suppression during the study period. **A**nalyses were performed using Stata 16.

Results: Of the 1330 PWLWH enrolled in the trial, 19.1% were newly diagnosed during pregnancy, while the remainder had been diagnosed prior to the current pregnancy. Of this sample 1165 (87.6%) women were retained in the study. Of these, 1113 women (95.5%) had at least one VL measurement at some point during study period. The mean number of VL measurements during the study period was 2.3 (range 0-5, SD±1.02). About one out of three women had a VL measurement during the first trimester of pregnancy (27.7%), which was similar to the proportion of those with VL in the second (32.3%), and third (34.2%) trimesters. Significantly fewer newly diagnosed PWLWH had a VL test performed during pregnancy (20.6%) compared to women diagnosed with HIV prior to the index pregnancy (77.8%, p=0.000). Approximately 22.0% of women had one or more non-suppressed VL during the study period, and 39.7% had at least one detectable VL. Over 60% of women achieved sustained undetectable VL, and 78% achieved sustained viral suppression during the observation period from pregnancy up to 12 months postpartum. In multivariable analysis, predictors of sustained undetectable VL included having ≥3 VL measurements (ARR=1.609, p=0.006), VL measurement in the 1st trimester (ARR=1.508, p=0.001), fidelity to the national VL testing guidelines (ARR=1.511, p=0.011), being on a nucleoside reverse transcriptase inhibitor-based ART regimen (ARR=1.774, p=0.037), and being ≥25 years old (ARR=1.546, p=0.009). Additionally, PWLWH with a detectable VL or who were not virally suppressed at baseline had significantly lower chance of achieving undetectable VL at 12 months postpartum (ARR=0.399, p=0.001/ARR=0.205, p=0.000).

Conclusion: Although VL monitoring has been scaled up in this region of Kenya, significant gaps still remain for pregnant/postpartum women with HIV. Large proportions

of women are not getting VL measurements at crucial times during pregnancy and breastfeeding, and did not have VL testing according to current Kenyan guidelines. Improved follow up of women with virologic failure during pregnancy or breastfeeding is urgently needed. Risk factors for suboptimal VL outcomes in PWLWH included history of viremia, less VL monitoring (fewer VL tests, no test in 1st trimester), being on a second-line ART regimen, and younger age.

Introduction

Prevention of mother-to-child transmission (PMTCT) programs in high HIV-prevalence settings, such as southwestern Kenya, are a unique opportunity to make substantial gains toward achieving The Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets.[2] Approximately 57,500 Kenyan women received PMTCT interventions in 2018, with estimated 91% coverage.[38] However, only 67.3% of HIV-exposed infants underwent early infant diagnosis before eight weeks of age[38], indicating continued challenges in retention across the full continuum of care. Kenya rolled out universal, lifelong antiretroviral therapy (ART) for pregnant and breastfeeding women with HIV (PWLWH) ("Option B+") in 2013.[96] This approach holds promise for improving maternal and child health, but gaps in the PMTCT continuum (HIV testing, linkage to ART treatment, initiation, adherence, and retention) could undermine the expected positive impact of Option B+ in Kenya.[26]

The last 90 of the 90-90-90 goals aims for 90% of all people receiving ART to achieve viral suppression. Viral Load (VL) testing is a key monitoring measure of the

effectiveness of ART and patient adherence.[4] Literature shows that with good adherence, patients who are ART naïve normally achieve viral suppression within 4-8 weeks of initiation of ART initiation.[29, 30] Despite the rapid increase in VL testing in many sub-Saharan African (SSA) countries, slow turn around for results of VL testing poses problems with timely clinical response.[32] In 2013, the World Health Organization (WHO) recommended that countries introduce targeted VL monitoring for pregnant and postpartum women.[33] The demands on national HIV programs and healthcare systems worldwide have further increased with 2016 WHO consolidated guidelines, recommending the Test & Treat all approach, scale-up of VL testing, and the use of pre-exposure prophylaxis (PrEP) for populations at risk.[4]

With the increasing demands on healthcare and laboratory systems[32, 34], it is pertinent to ensure that VL testing for pregnant, postpartum, and breastfeeding women is not neglected. These women have limited time for response to an elevated VL during pregnancy/postpartum in time to decrease the risk of vertical transmission.[35, 36] Sustained viral suppression during the pregnancy and the postpartum/breastfeeding periods is crucial; however, lack of uptake of VL testing and long turnaround times for test results limit options for timely clinical decisions and interventions.[32] ART naïve pregnant women (those newly initiating ART during pregnancy) are particularly vulnerable during this period.[4] Sub-Saharan African countries have consistently found that women who test and newly initiate ART during the index pregnancy, are less likely to achieve viral suppression by the time of their delivery.[97] Thus it is important to

examine and compare VL monitoring and outcomes for newly diagnosed and known-positive pregnant women.

The national VL testing guidelines in Kenya were initiated in 2012 with rapid scale-up of services over the subsequent years.[34] VL testing is available at no cost for qualifying patients on ART at all public health facilities. The standard VL monitoring for PLWH requires VL tests at 6 and 12 months after ART initiation, then annually thereafter, and more frequently if results show viremic failure (≥1,000 copies/ml). The guidelines require VL testing every 6 months for those 0-24 years, for all during the first year of ART initiation, and for special populations, e.g., pregnant and breastfeeding women.[48] According to national guidelines in Kenya, pregnant women living with HIV should receive viral load monitoring at confirmation of pregnancy (if already on ART) or 6 months after ART initiation, and then every 6 months thereafter until the complete cessation of breastfeeding.[48] In accordance with national guidelines, and based on the timing of the first antenatal visit, HIV testing (if HIV status is unknown), and ART initiation, the first VL test might not occur until after the baby is born. VL suppression might, therefore, not be accomplished by the time of labor/delivery and early breastfeeding, increasing the probability of mother-to-child transmission (MTCT). Kenya and many other countries are moving towards using lower VL cutoffs to indicate viremia, with an aim towards making sure that all clients have undetectable VLs.[4, 48, 98] The 2018 Kenya guidelines treat low-level viremia (VL $\underline{\geq}$ 400 copies/ml) and virologic failure similarly. Clinically, however, 1,000 copies/ml is still important for determining the risk

of transmission to the infant and detectable VL during pregnancy or breastfeeding at any level can pose a risk for transmission.[99]

The goals of this study were to 1) examine timing and frequency of viral load testing among pregnant and postpartum women living with HIV enrolled in the Mother Infant Visit Adherence and Treatment Engagement (MOTIVATE!) study in terms of stage of pregnancy/postpartum, as well as relative to the date of ART initiation (newly diagnosed during pregnancy versus known positive women), and 2) to examine possible predictors of viral load suppression in this cohort.

Methods

Study design

The current study is a secondary analysis of longitudinal data conducted in the context of a larger randomized control trial (MOTIVATE!; R01HD0808477; Multiple Principal Ivestigators: Abuogi and Turan). The MOTIVATE! study utilized a 2x2 cluster-randomized factorial research design. The individual and combined effects of two interventions, community mother mentors (cMMs) and text messaging (alone and combined), on ART adherence and postpartum retention in care were examined against standard care. MOTIVATE! Study participants were pregnant women with HIV who were 18 years and older accessing care at one of the 24 government antenatal clinics that had been randomized into one of the four study arms. Three high-burden counties within southwestern Kenya were included: Homa Bay, Migori, and Kisumu. Study participants

were enrolled during pregnancy during 2015-2018 and followed until at least 12 months postpartum. More details on the parent study are published elsewhere.[100]

Setting

The counties included in this study have some of the highest reported HIV prevalence rates in Kenya: Kisumu County (16.3%), Homa Bay County (20.7%), and Migori County (13.3%).[41] This region represents 54% of the country's new infant HIV infections and 45% of its need for PMTCT services.[42] The ART coverage in adults in these counties is 90% in Kisumu, 79% in Homa Bay, and 83% in Migori.[38] In these counties, high total fertility rates (3.6-5.3) and underutilization of healthcare services (Kenya DHS 2014)[43] among women age 15-49 interact with high HIV prevalence resulting in increased MTCT and delayed initiation into treatment for both women and infants [44].

Data collection methods

VL test results and other study indicators were routinely abstracted from medical records by study data clerks, with confirmation and supplementation from the national VL database. The National AIDS & STI Control Programme (NASCOP) of the Ministry of Health in Kenya established a national Kenya Viral Load Dashboard online, containing patient-level VL test results, and information on monthly viral load testing trends and outcomes by age, gender, county, regimen, facility type, and implementing partner outcomes, as well as lab performance statistics for national viral load testing,

sample type, the reason for testing, and turnaround times.[101] Data were abstracted for the period from study enrollment (in pregnancy) up to 12 months after the birth.

Measures

We first examined the timing and frequency of routine VL testing among pregnant and postpartum women enrolled in the MOTIVATE! Study during pregnancy and up to 12 months postpartum. The baseline sociodemographic and clinical characteristics were abstracted at the time of study enrollment during the index pregnancy.

Measures of VL timing and frequency

We assessed the number of VL measurements in pregnancy, in the postpartum (PP) period up to 12 months after the birth, and the overall number of VL measurements during the observation period (pregnancy through 12 months PP). This was then categorized into binary variables for the analysis. A low number of measurements (0-1 VL measurements during pregnancy/postpartum, and ≥2 measurements during the whole observation period) was coded as 0, and a higher number of VL measurements (≥2 during pregnancy/postpartum, or ≥3 during the observation period) was coded as 1.

The frequency of VL testing was defined as the mean time between the baseline VL measurement to the next VL measurement during pregnancy and up to 12 months postpartum. This variable was then categorized into no VL measurements after baseline, <3 months, 3-5.99 months, 6-8.99 months, 9-11.99 months, and >12 months. To explore the timing of VL measurements in pregnancy and postpartum, VL measurements were

also categorized into seven time periods relative to pregnancy and the birth: first trimester, second trimester, third trimester, 0-3 months postpartum, 4-6 months postpartum, 7-9 months postpartum, and 10-12 months postpartum.

VL monitoring according to guidelines[48] was captured as a binary variable (1=yes, 0=no). For women newly tested and initiated on ART during this pregnancy, this was defined as VL testing 6 months (+/-1 month) after ART initiation and then VL testing 6 months later (+/-1 month); i.e., ~ 12 months after ART initiation. For those who were known-positive prior to pregnancy, it was defined as VL testing conducted immediately after the initiation of antenatal care (+/-1 month) and then every 6 months (+/-1 month) after that.

For the descriptive part of the study, we also assessed two other combined measurements: 1) viral load monitoring done according to guidelines & achieved sustained undetectable viral load and 2) viral load monitoring done according to guidelines & achieved sustained viral suppression.

Measures of viral suppression

In the second part of this manuscript, we explored predictors of four measures of viral suppression: (1) viral suppression defined as VL <1000 copies/ml (as per Kenyan guidelines at the time of the study) at +/- 90 days of the 12-month postpartum date; (2) undetectable viral load (0 copies/mL) at at +/- 90 days of the 12-month postpartum date; (3) sustained viral suppression (VL < 1000 copies/ml) over the observation period (baseline to 12 months postpartum) for those with at least 2 VL measurements during the study period; and (4) sustained undetectable viral load (0 copies/ml) during the

observation period for those with at least 2 VL measurements during the study period. These outcomes were all coded as binary variables (1=yes, 0=no).

Primary independent variables included in these analyses as potential predictors included measures of VL monitoring, including the number of VL measurements in pregnancy & postpartum, the time between VL measurements, the timing of VL measurements in pregnancy/postpartum, VL tests done according to the guidelines, and available sociodemographic and clinical baseline characteristics. Baseline sociodemographic and clinical characteristics (abstracted from medical records) were compared by initial HIV status (women newly diagnosed with HIV at an antenatal visit vs. known positive prior to the current pregnancy) and include age (categorized into <25 years, 25-28 years, 29-32 years, and ≥33 years), marital status (married vs. not), county of the clinic (Homa Bay, Kisumu, Migori), gravida (primigravid vs. 2 or more pregnancies), advanced gestational age at the first antenatal visit during this pregnancy (≤28 weeks vs. >28 weeks), initial ART regimen [azidothymidine (AZT) vs. tenofovir (TDF) based, and protease inhibitor (PI)-based vs. nucleoside reverse transcriptase inhibitor (NNRTI)-based], study arm (cMM, text, cMM+text, standard care), and study enrollment viral load taken ±90 days of study enrollment during the index pregnancy (undetectable, suppressed, not suppressed).

Statistical analyses

Analyses were performed using Stata 16 (StataCorp, College Station, Texas, USA). Baseline sociodemographic and clinical characteristics were described and were

tested for differences between women newly diagnosed with HIV and known positives, using the chi-square test for categorical and t-test for continuous variables.

Bivariate and multivariable logistic regression models with robust variance for clustering by site were used to assess the statistical association between independent variables (number, frequency, and timing of viral load measurements up to 12 months postpartum, a measure indicating whether the viral load measurements have been done according to the guidelines, and selected sociodemographic and patient baseline variables) and outcomes (viral suppression & undetectable VL at 12 months postpartum, and sustained viral suppression & sustained undetectable VL at 12 months postpartum). See Figure 1 for a summary of variables and relationships.

Variables were tested for multicollinearity, and strongly correlated variables ($r \geq 0.60$) were excluded from the model. Covariates with a p-value of <0.20 in bivariate analyses were considered for inclusion in multivariable models. Both bivariate and multivariable models are presented. Given the clustered study design of the MOTIVATE! Study (24 study sites), Generalized Estimating Equation (GEE) models were used to test for differences of interest in univariate and multivariable models, adjusted for relevant covariates, and accounting for clustering by site. Results were summarized as relative risks for models based on binary responses. Relative risk estimates were selected instead of the odds ratios as a more accurate measure, given the prospective nature of the data and high prevalence of the outcome measures. Statistical significance, set at a two-sided $p<0.05$, was also reported based on the robust variance estimates from the GEE models.

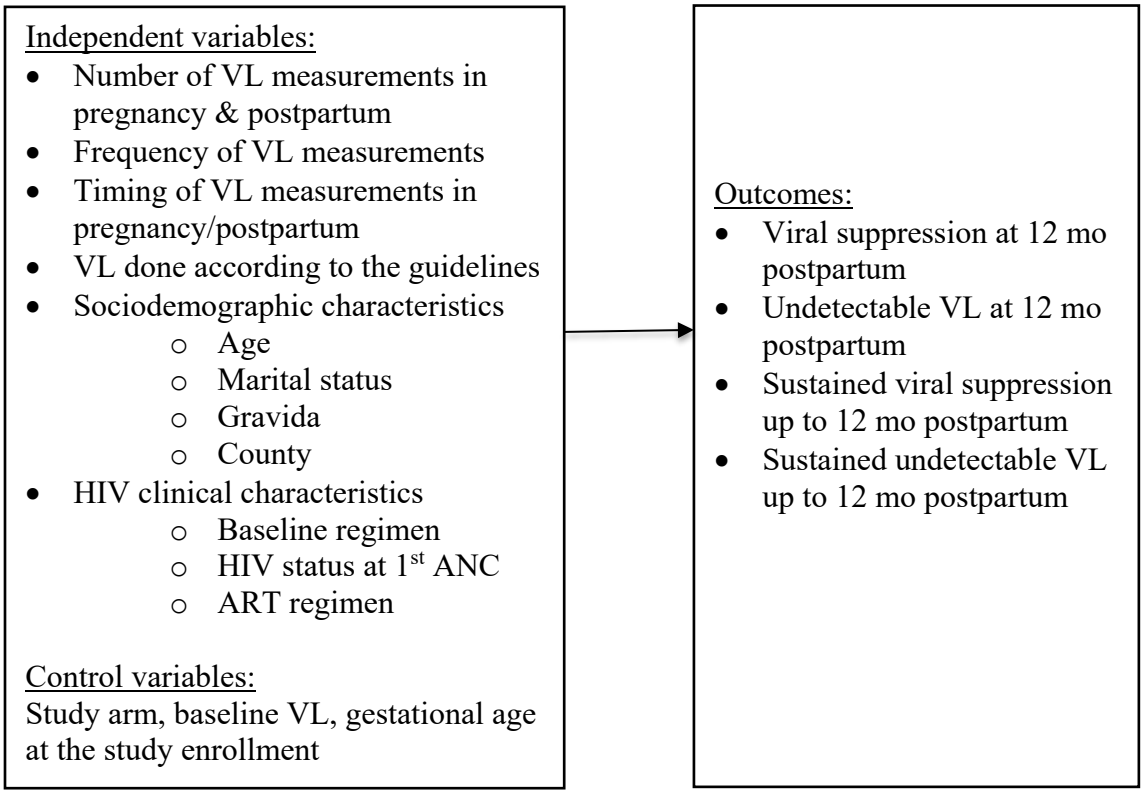

Figure 1. Analytical model[a]
[a]Abbreviations: antenatal care (ANC), antiretroviral therapy (ART), viral load (VL)

We hypothesized that gaps in VL monitoring remain for PWLWH in these Kenyan settings and that many women were potentially not getting VL measurements at crucial times during pregnancy and breastfeeding, particularly those who were newly diagnosed with HIV at their first antenatal visit during the index pregnancy. We further hypothesized that women in vulnerable sub-groups (primigravida, younger women less than 25 years, and women newly diagnosed during pregnancy) would be less likely to achieve sustained viral suppression during the observation period (pregnancy up to 12 months postpartum).

Results

Of the 1330 pregnant women enrolled in the MOTIVATE! study, 165 (12.4%) were discontinued from the study or lost to follow-up. Of the 1165 (87.6%) women retained in the trial and included in this analysis, 223 (19.1%) were newly diagnosed with HIV at first antenatal visit during this pregnancy. Sociodemographic characteristics of these women by initial HIV status at study enrollment are presented in Table 1. Most women (92.7%) were married, relatively young (76.0% were younger than 33 years), and had been pregnant before (92.8%). Women newly diagnosed with HIV in this pregnancy were significantly younger (25.6 years vs. 29.7 years, $p<0.000$) and more likely to be experiencing their first pregnancy (15.7% vs. 5.2%, $p<0.000$), as compared to women known to be living with HIV prior to pregnancy. Most women were enrolled in Migori County (43.1%), followed by Kisumu (35.8%) and Homa Bay (21.1%), and this did not differ significantly between new and known HIV-positive women. Newly diagnosed women were more likely to enroll in the study later in the pregnancy (average gestational age: 25.3 vs. 24.3 weeks, $p=0.034$), were less likely to be randomized into one of the intervention study arms (73.5% vs. 75.9%, $p=0.005$), particularly the combined cMM and text messaging arm (16.1% vs. 27.7%). All (100%) newly diagnosed vs. 93.7% of known positive women were on an NNRTI-based ART regimen at baseline ($p<0.000$), and newly diagnosed women were more likely to be on a TDF-containing vs. AZT-containing ART regimen (99.1% vs. 86.7%, $p<0.000$).

Table 1.

Baseline sociodemographic and HIV-related participant characteristics[a]

Variable/HIV status at 1st ANC visit	Women known HIV-positive (n=942; 80.9%)	Women newly diagnosed with HIV (n=223; 19.1%)	Total HIV-positive women enrolled in the study (n=1165)	p-value (Chi-square)
Age at enrollment (years)	29.7 ±5.4	25.6 ±4.8	28.91 ±5.5	**0.000**
<25years	201 (21.3%)	120 (53.8%)	321 (27.6%)	(110.3)
25-28 years	217 (23.0%)	52 (23.3%)	269 (23.1%)	
29-32 years	262 (27.8%)	33 (14.8%)	295 (25.3%)	
≥33 years	262 (27.8%)	18 (8.1%)	280 (24.0%)	
Marital status				
Married	876 (93.0%)	204 (91.5%)	1080 (92.7%)	0.434
Not married	66 (7.0%)	19 (8.5%)	85 (7.3%)	(0.6)
County				0.581
Homa Bay	203 (21.6%)	43 (19.3%)	246 (21.1%)	(1.1)
Kisumu	331 (35.1%)	86 (38.6%)	417 (35.8%)	
Migori	408 (43.3%)	94 (42.2%)	502 (43.1%)	
Gravida	2.7 ±1.4	3.7 ±1.6	3.5 ±1.6	**0.000**
Primigravid	49 (5.2%)	35 (15.70%)	84 (7.2%)	(29.7)
≥ 2	893 (94.8%)	188 (84.30%)	1081 (92.8%)	
Gestational age at the study enrollment (weeks)	24.28 ±7.6	25.3 ±7.8	24.5 ±7.6	**0.034** (4.5)
≤ 28 weeks	680 (72.2%)	145 (65.0%)	825 (70.8%)	
>28 weeks	262 (27.8%)	78 (35.0%)	340 (29.2%)	
Study arm				**0.005**
Standard care (control)	227 (24.1%)	59 (26.5%)	286 (24.5%)	(13.0)
cMM intervention	226 (24.0%)	65 (29.2%)	291 (25.0%)	
text messages intervention	228 (24.2%)	63 (28.3%)	291 (25.0%)	
cMM + text messages	261 (27.7%)	36 (16.1%)	297 (25.5%)	
ART regimen at baseline[b]				**0.000**
AZT-containing	125 (13.3%)	2 (0.9%)	127 (10.9%)	(28.4)
TDF-containing	817 (86.7%)	221 (99.1%)	1038 (89.1%)	

ART regimen at baseline[b]	59 (6.3%)	0 (0%)	59 (5.1%)	**0.000**
PI-based	883 (93.7%)	223 (100%)	1106 (94.9%)	(14.7)
NNRTI-based				

[a]Abbreviations: antenatal care (ANC), antiretroviral therapy (ART), viral load (VL), community-based mentor mothers (cMM) [b]ART regimen: azidothymidine (AZT), tenofovir (TDF), nucleoside reverse transcriptase inhibitor (NNRTI; first-line regimen), protease inhibitor (PI; second-line regimen)

Timing and frequency of routine viral load measurements

Table 2 presents viral load measurement and viral load outcomes by new versus known positive status (n=1165). Overall, only 76.7% of newly diagnosed vs. 93.2% of known positives had a VL measurement at +/- 90 days of study enrollment (p=0.000). Of those with baseline VL measurement (n=1049; p=0.151), 10.8% of newly diagnosed women vs. 14.6% of known positives were not virally suppressed (p=0.153), and 66.1% vs. 64.2% had an undetectable viral load (p=0.645). The mean number of VL measurements during the period of observation was 2.3 (range 0-5, SD±1.02). While 97.1% of women with known HIV-status prior to the current pregnancy had at least one viral load measurement during the study period, fewer (88.8%) newly diagnosed women had at least one VL measurement (p=0.000). Newly diagnosed women were also more likely to not have any measurements in pregnancy compared to known positive women (79.4% vs. 22.2%, p=0.000) or from birth up to 12 months after the birth (14.4% vs. 8.5%, p=0.030).

More than one out of five women (22.0%) had one or more non-suppressed VL measurements during the period of observation, and 39.7% had at least one detectable VL measurement. At 12 months after the birth, a similar proportion of known positives (93.9%) and newly diagnosed women (92.8%) were virally suppressed (p=0.914); however, a higher proportion of newly diagnosed women (74.8%) achieved an undetectable viral load by 12 months after the birth compared to 68.2% of known positives, although the difference is not statistically significant (p=0.085). Overall, among women retained in the study, 8 infants had an HIV-positive test result during the 12-month postpartum observation period.

Table 2

VL measurement and outcomes during the study period[a]

Variable/HIV status at 1st ANC visit	**Known HIV-positive (n=942; 80.86%)**	**Newly diagnosed with HIV at first ANC visit (n=223; 19.14%)**	**Total HIV-positive women enrolled in the study (n=1,165)**	**p-value (Chi-sqaure)**
Study enrollment viral load[b]	N=878	N=171	N=1,049	0.151
Undetectable	564 (64.2%)	113 (66.1%)	677 (64.5%)	(3.8)
Viral suppression	219 (24.9%)	33 (19.3%)	252 (24.0%)	
Not virally suppressed	95 (10.8%)	25 (14.6%)	120 (11.4%)	
Number of VL measurements in pregnancy	0.97 (±0.7)	0.23 (±0.5)	0.83 (±0.7)	**0.000**
0	209 (22.2%)	177 (79.4%)	386 (33.1%)	(267.6)
1	563 (59.8%)	41 (18.4%)	604 (51.9%)	
2	159 (16.9%)	5 (2.2%)	164 (14.1%)	
3	11 (1.2%)	0 (0.0%)	11 (0.9%)	
Number of VL measurements birth - 12 months postpartum	1.49 (±0.7)	1.43 (±0.9)	1.48 (±0.8)	**0.030** (9.0)
0	80 (8.5%)	32 (14.4%)	112 (9.6%)	
1	379 (40.2%)	83 (37.2%)	462 (39.7%)	
2	426 (45.2%)	90 (40.4%)	516 (44.3%)	
3	57 (6.0%)	18 (8.1%)	75 (6.4%)	
Number of total VL measurements in pregnancy & up to 12 months postpartum	2.46 (±1.0)	1.65 (±0.90)	2.31 (±1.0)	**0.000** (116.8)
0	27 (2.9%)	25 (11.2%)	52 (4.5%)	
1	117 (12.4%)	64 (28.7%)	181 (15.5%)	
2	329 (34.9%)	100 (44.8%)	429 (36.8%)	
3	338 (35.9%)	32 (14.4%)	370 (31.8%)	
4	127 (13.5%)	2 (0.9%)	129 (11.1%)	
5	4 (0.4%)	0 (0.0%)	4 (0.3%)	

Time between VL measurements				**0.000**
No VL at/after baseline	372 (39.5%)	187 (83.9%)	559 (48.0%)	(142.9)
<3 months	35 (3.7%)	1 (0.5%)	36 (3.1%)	
3-5.99 months	133 (14.1%)	11 (4.9%)	144 (12.4%)	
6-8.99 months	240 (25.5%)	16 (7.2%)	256 (22.0%)	
9-11.99 months	95 (10.1%)	5 (2.2%)	100 (8.6%)	
≥12 months	67 (7.1%)	3 (1.4%)	70 (6.0%)	
VL done according to the guidelines [c]				
Yes	321 (34.1%)	42 (18.8%)	363 (31.2%)	**0.000**
No	621 (65.9%)	181 (81.2%)	802 (68.6%)	(19.5)
Undetectable VL at 12 months postpartum[b]	N=575	N=111	N=686	
Yes	392 (68.2%)	83 (74.8%)	475 (69.2%)	0.168
No	183 (31.8%)	28 (25.2%)	211 (30.8%)	(1.9)
Viral suppression at 12 months postpartum [b]	N=575	N=111	N=686	
Yes	540 (93.9%)	103 (92.8%)	643 (93.7%)	0.656
No	35 (6.1%)	8 (7.2%)	43 (6.3%)	(0.2)
Sustained undetectable VL[d]	N=915	N=198	N=1113	
Yes	573 (62.6%)	98 (49.5%)	671 (60.3%)	**0.001**
No	342 (37.4%)	100 (50.5%)	442 (39.7%)	(11.7)
Sustained viral suppression[e]	N=915	N=198	N=1113	
Yes	746 (81.5%)	122 (61.6%)	868 (78.0%)	**0.000**
No	169 (18.5%)	76 (38.4%)	245 (22.0%)	(37.6)
Optimal outcome: VL monitoring & sustained undetectable VL over the study period				
Yes	218 (23.1%)	32 (14.3%)	250 (21.5%)	**0.004**
No	724 (76.9%)	191 (85.7%)	915 (78.5%)	(8.3)

[a]Abbreviations: antenatal care (ANC), antiretroviral therapy (ART), viral load (VL)

[b] Undetectable VL =0 copies/ml, viral suppression between 0 and ≤1000 copies/ml, not virally suppressed>1000 copies/ml

[c] For women newly tested and initiated on ART during this pregnancy, this was defined as VL testing 6 months (+/-1 month) after ART initiation and then VL testing 6 months later (+/-1 month); i.e., ~ 12 months after ART initiation. For those who were known-positive prior to pregnancy, it was defined as VL testing conducted immediately after the initiation of antenatal care (+/-1 month) and then every 6 months (+/-1 month) after that.

[d] Sustained viral suppression (VL < 1000 copies/ml) over the observation period (baseline to 12 months postpartum) for those with at least 2 VL measurements during the study period.

[e]Sustained undetectable viral load (0 copies/ml) during the observation period for those with at least 2 VL measurements during the study period.

Timing of VL measurements

Among the 1165 women retained, 22.9% had a VL measurement during the first trimester of pregnancy, 26.9% during the second trimester, and 30.7% during the third trimester. Significantly fewer newly diagnosed women had a VL test performed during pregnancy (22.9%) compared to women diagnosed prior to the index pregnancy (94.2%) (p=0.000). Figure 2 shows that women whose HIV status was known prior to the index pregnancy had VL tests conducted starting in the first trimester and proportionately distributed across the 3-month increments during the pregnancy and up to 12 months postpartum. As per the Kenyan VL testing guidelines, only a few women who were newly diagnosed with HIV during the index pregnancy had VL measurements done during their pregnancy, and the majority of these were done in the third trimester.

Frequncy of VL Testing

To examine the frequency of VL testing in our study, we looked at the amount of time between the woman's baseline VL test and her next test during the study period. Overall, 48.0% of women did not have subsequent VL measurements after the VL around the time of study enrollment (+- 90 days) during the remaining study period, with 83.9% new positives and 39.5% of known positives with only a study enrollment VL test. Approximately 15.5% of women underwent VL monitoring within 6 months after the baseline measurement, 5.4% newly positives, and 17.8% known positive women. A small portion of women (6.0%) had a VL test performed 12 or more months after the baseline, 1.4% of newly positives, and 7.1% of known positives. Time between VL

measurements statistically differed between known and newly HIV-positive women (p=0.000).

The VL testing according to the Kenyan guidelines appears to have been followed for about 31.2% of the participants overall. Only a small portion (18.8%) of women newly diagnosed with HIV during antenatal care had a viral load measurement 6 months after

ART initiation (+/- 1 month) and the next viral load measurement 6 months later (12 months +/- 1 month). About 34.1% of known positive women in our sample underwent VL testing according to these guidelines, i.e., had viral load monitoring at confirmation of pregnancy or 6 months after ART initiation, and then every 6 months thereafter until 12 months postpartum. The VL testing protocol was more likely followed for women with known HIV status (34.1% vs. 18.8%, p=0.000). Overall, 21.5% of women achieved an optimal VL outcome (VL monitoring according to guidelines as well as sustained undetectable VL over the study period). Women with known HIV status were more likely to achieve the optimal outcome compared to women newly diagnosed during this pregnancy (23.1% vs. 14.3%, p=0.004).

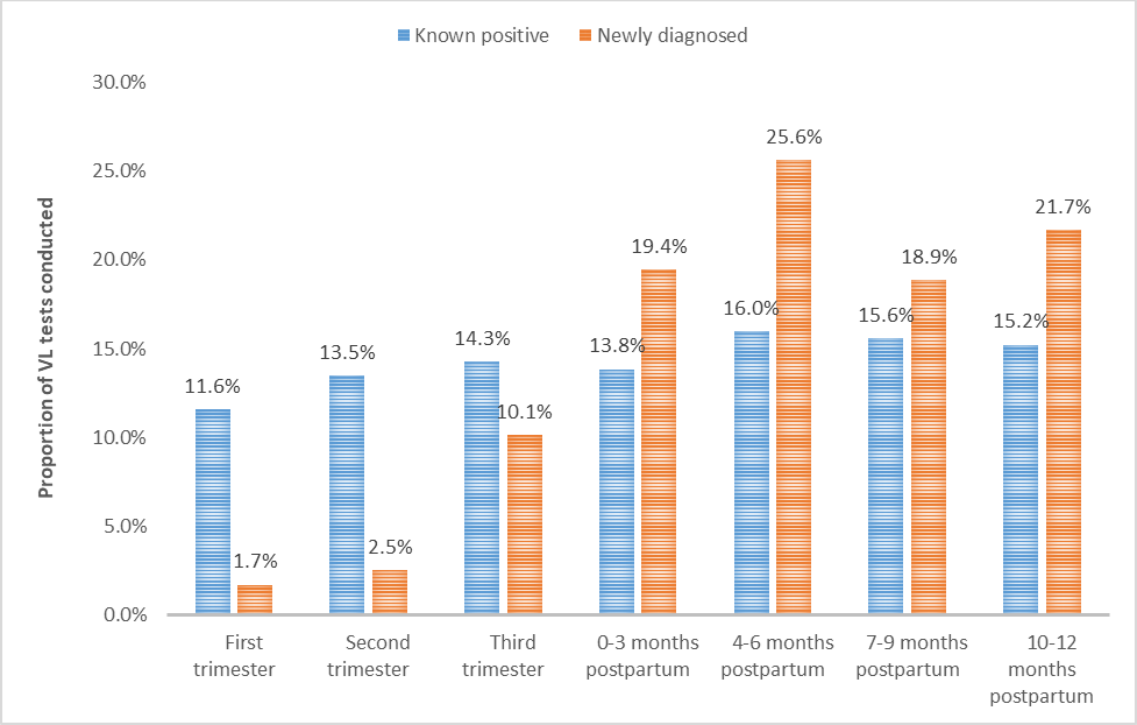

Figure 2. Distribution of VL tests conducted for 1,165 women with HIV during pregnancy and up to 12 months postpartum (N=2,608 VL tests)

Predictors of Viral Suppression

The results of bivariate analyses are presented in Table 3. The likelihood of not achieving viral suppression at 12 months postpartum was predicted by baseline VL status. Specifically, viral non-suppression at study baseline (RR=0.134, p=0.000) and detectable VL at study baseline (RR=0.298, p=0.036), as well as having a VL measurement between 7-9 months postpartum (RR=0.466, p=0.016) predicted a lower likelihood of viral suppresion at 12-months postpartum.

Undetectable VL at 12 months postpartum was positively predicted by residing in Migori County compared to Homa Bay County (RR=2.763, p=0.012), and negatively associated with 3 or more VL measurements during the study period (RR=0.878, p=0.036), having VL measurements in 2nd trimester (RR=0.667, p=0.046) and 0-3

months after birth (RR=0.663, p=0.041) compared to those who did not have measurements during this period, non-supressed VL status at study baseline (RR=0.404, p=0.000), and detectable VL at study baseline (RR=0.243, p=0.000).

Predictors of sustained viral suppression included ≥2 VL measurements in the postpartum period (RR=1.102, p=0.000), ≥3 during the whole study observation period (RR=1.373, p=0.000), a subsequent VL measurement ≥6 months after the baseline (RR=2.799, p=0.000); having a VL measurement during the first trimester (RR=1.864, p=0.000) and during the 10-12 month postpartum period (RR=1.740, p=0.000), having VL monitoring done according to Kenyan guidelines (RR=1.428, p=0.008), and being 25 years or older compared to those less than 25 (RR=1.460, p=0.000). Women newly diagnosed were at a higher risk of not being able to achieve sustained suppression (RR=0.866, p=0.000).

Predictors of sustained undetectable VL included ≥2 VL measurements in the postpartum period (RR=1.106, p=0.003), ≥3 during the study period (RR=1.335, p=0.000), subsequent VL measurement ≥6 months after the baseline (RR=1.409, p=0.025), VL measurement during the first trimester (RR=1.279, p=0.008) and during the 10-12 month postpartum period (RR=1.266, p=0.030) compared to those with no measurements during the given period, being 25 years or older compared to those less than 25 (RR=1.283, p=0.014), and residing in Kisumu and Migori Counties compared to Homa Bay County (RR=1.675, p=0.027/RR=1.920, p=0.002, respectively). Women newly diagnosed were at a higher risk of not being able to achieve sustained undetectable VL (RR=0.866, p=0.000) or sustained undetectable VL (RR=0.891, p=0.043).

Marital status, gravida, gestational age, study arm, ART regimen (TDF vs. AZT or NNRTI vs. PI), and number of VL measurements in pregnancy were not significantly associated with any of the outcomes in bivariate analyses.

Table 3

Bivariate analyses of predictors of viral load suppression and undetectable viral load[a]

VARIABLE	Viral suppression at 12m postpartum (N=686)		Undetectable VL at 12m postpartum (N=686)		Sustained viral[b] suppression (N=1113)		Sustained undetectable[b] VL (N=1113)	
RR (95% CI), p-value (Chi-square: χ^2)	**RR (95% CI)**	**p-value (χ^2)**	**RR (95% CI)**	**p-value (χ^2)**	**RR (95% CI)**	**p-value (χ^2)**	**RR (95% CI)**	**p-value (χ^2)**
Number of VLs in pregnancy								
≤1	ref.	0.716	ref.	0.095	ref.	0.626	ref.	0.055
≥2	0.990 (0.94-1.05)	(0.1)	0.880 (0.76-1.02)	(2.8)	1.014 (0.96-1.07)	(0.2)	0.915 (0.84-1.00)	(3.7))
Number of VLs birth - 12m postpartum								
≤1	ref.	0.661	ref.	0.784	ref.	**0.000**	ref.	**0.003**
≥2	0.987 (0.93-1.04)	(0.2)	1.021 (0.88-1.18)	(<0.1)	1.102 (1.06-1.15)	(19.6)	1.106 (1.03-1.18)	(8.8)
Number of total VLs								
≤2	ref.	0.259	ref.	**0.036**	ref.	**0.000**	ref.	**0.000**
≥3	0.978 (0.94-1.02)	(1.3)	0.878 (0.78-0.99)	(4.4)	1.373 (1.25-1.51)	(40.8)	1.335 (1.19-1.50)	(24.7)
Time between VLs								
No VL after study enrollment VL	ref.	(3.2)	ref.	(2.7)	ref.	(27.7)	ref.	(22.7)
<6 months	0.639 (0.25-1.64)	0.352	0.584 (0.30-1.14)	0.116	1.274 (0.85-1.90)	0.237	0.774 (0.60-1.00)	0.054
≥6 months	1.521 (0.71-3.24)	0.278	0.805 (0.55-1.17)	0.255	2.799 (1.83-4.29)	**0.000**	1.409 (1.04-1.90)	**0.025**
Timing of VL (ref is no measurement in the given period)								
1st trim	1.470 (0.67-3.22)	0.335 (0.9)	1.120 (0.75-1.68)	0.584 (0.3)	1.864 (1.33-2.61)	**0.000** (13.1)	1.279 (1.06-1.54)	**0.008** (6.9)
2nd trim	0.933 (0.51-1.69)	0.819 (<0.1)	0.667 (0.45-0.99)	**0.046** (4.0)	1.345 (0.98-1.85)	0.066 (3.4)	0.893 (0.75-1.06)	0.188 (1.7)
3rd trim	1.166 (0.63-2.17)	0.627	0.929 (0.68-1.26)	0.634	1.103 (0.82-1.48)	0.516	0.959 (0.78-1.18)	0.692

		(0.2)		(0.2)		(0.4)		(0.2)
0-3m pp	0.893 (0.50-1.58)	0.696	0.663 (0.45-0.98)	**0.041**	1.191 (0.93-1.53)	0.168	1.066 (0.88-1.30)	0.526
		(0.2)		(4.2)		(1.9)		(0.4)
4-6m pp	1.406 (0.92-2.16)	0.118	1.247 (0.95-1.64)	0.111	1.133 (0.95-1.36)	0.172	1.014 (0.90-1.15)	0.831
		(2.4)		(2.5)		(1.9)		(<0.1)
7-9m pp	0.466 (0.25-0.87)	**0.016**	0.727 (0.51-1.03)	0.077	1.041 (0.81-1.34)	0.755	0.952 (0.78-1.16)	0.630
		(5.8)		(3.1)		(0.1)		(0.2)
10-12m pp	1.203 (0.63-2.28)	0.572	1.295 (0.90-1.87)	0.164	1.740 (1.31-2.32)	**0.000**	1.266 (1.02-1.57)	**0.030**
		(0.3)		(1.9)		(14.3)		(4.7)
VL done according to the guidelines[c]								
Yes	1.073 (0.56-2.07)	0.833	0.957 (0.67-1.37)	0.809	1.428 (1.10-1.86)	**0.008**	1.024 (0.79-1.32)	0.852
No	ref	(<0.1)	ref	(<0.1)	ref	(7.1)	ref	(<0.1)
Age								
<25yrs	ref	0.894	ref	0.358	ref	**0.000**	ref	**0.014**
≥25 yrs	1.055 (0.48-2.31)	(<0.1)	0.851 (0.60-1.20)	(0.8)	1.460 (1.22-1.75)	(17.2)	1.283 (1.05-1.57)	(6.0)
Marital status								
Married	1.008 (0.93-1.09)	0.853	0.998 (0.81-1.23)	0.986	1.049 (0.98-1.12)	0.140	1.039 (0.96-1.13)	0.366
Not married	ref	(<0.1)	ref	(<0.1)	ref	(2.2)	ref	(0.8)
Gravida								
Primigravid	ref	0.439	ref	0.491	ref	0.287	ref	0.441
≥2	1.057 (0.92-1.22)	(0.6)	0.924 (0.74-1.16)	(0.5)	1.027 (0.98-1.08)	(1.1)	1.037 (0.94-1.14)	(0.6)
Gestational age at the study enrollment								
≤ 28 weeks	ref	0.101	ref	0.182	ref	0.052	ref	0.910
>28 weeks	0.962 (0.92-1.01)	(2.7)	1.110 (0.95-1.29)	(1.8)	0.967 (0.93-1.00)	(3.8)	0.996 (0.94-1.06)	(<0.1)
HIV status at 1st ANC visit								
Newly positive	0.997 (0.95-1.04)	0.914	1.121 (0.98-1.28)	0.085	0.866 (0.82-0.92)	**0.000**	0.891 (0.80-0.99)	**0.043**
Known positive	ref	(<0.1)	ref	(3.0)	ref	(21.6)	ref	(4.1)
ART regimen[d]								
AZT -containing	ref	0.564	ref	0.579	ref	0.973	ref	(<0.1)
TDF based	0.979 (0.91-1.05)	(0.3)	0.967 (0.86-1.09)	(0.3)	1.000 (0.97-1.03)	(<0.1)	1.005 (0.94-1.08)	0.896

ART regimen[e]								
PI-based	ref	0.361	ref	0.078	ref	0.734	ref	0.098
NNRTI-based	1.041 (0.95-1.14)	(0.8)	1.272 (0.97-1.66)	(3.1)	1.008 (0.96-1.06)	(0.1)	1.104 (0.98-1.24)	(2.8)
County								
Homa Bay	ref	(2.7)	ref	(7.0)	ref	(15.1)	ref	(9.6)
Kisumu	2.670 (0.82-8.67)	0.102	1.667 (0.62-4.52)	0.315	1.542 (0.87-2.75)	0.142	1.675 (1.06-2.65)	**0.027**
Migori	2.302 (0.66-8.02)	0.190	2.763 (1.25-6.08)	**0.012**	0.813 (0.44-1.49)	0.502	1.920	**0.002**
Study Enrollment VL[e]								
Undetectable	ref	(14.4)	ref	(20.2)	--	--	--	--
Viral suppression	0.298 (0.10-0.92)	**0.036**	0.404 (0.26-0.64)	**0.000**				
Not virally suppr.	0.134 (0.05-0.38)	**0.000**	0.243 (0.12-0.51)	**0.000**				

[a]Abbreviations: antenatal care (ANC), antiretroviral therapy (ART), viral load (VL)

[b] Sustained viral suppression (VL < 1000 copies/ml) over the observation period (baseline to 12 months postpartum) for those with at least 2 VL measurements during the study period. Sustained undetectable viral load (0 copies/ml) during the observation period for those with at least 2 VL measurements during the study period.

[c] For women newly tested and initiated on ART during this pregnancy, this was defined as VL testing 6 months (+/-1 month) after ART initiation and then VL testing 6 months later (+/-1 month); i.e., ~ 12 months after ART initiation. For those who were known-positive prior to pregnancy, it was defined as VL testing conducted immediately after the initiation of antenatal care (+/-1 month) and then every 6 months (+/-1 month) after that.

[d]ART regimen: azidothymidine (AZT), tenofovir (TDF), nucleoside reverse transcriptase inhibitor (NNRTI; first-line regimen), protease inhibitor (PI; second-line regimen)

[e] Undetectable VL =0 copies/ml, viral suppression between 0 and ≤1000 copies/ml, not virally suppressed>1000 copies/ml. Baseline VL was not considered in sustained-outcomes analyses as this measurement was incorporated within the sustained outcome variable.

In multivariable analyses, we controlled for gestational age and study arm in all models, and baseline VL in the 12-month postpartum outcomes (viral suppression and undetectable VL at 12-month postpartum). The VL at baseline was not considered in sustained-outcomes analyses as this measurement was incorporated within the sustained outcome variable. Results of multivariable analyses are presented in Table 4. In adjusted analyses, women who were non-suppressed at study baseline were less likely to achieve viral suppression at 12 months postpartum (ARR=0.091, p=0.000). The baseline VL status also predicted undetectable VL at 12 months postpartum. Women not virally suppressed at baseline (ARR=0.205, p=0.000) and women with detectable VL at baseline were less likely to achieve undetectable VL at 12 months postpartum (ARR=0.399, p=0.001). Additionally, undetectable VL at 12 months postpartum was more likely for women enrolled in the study after 28 weeks of gestation (ARR=1.800, p=0.040) and those on an NNRTI-based ART regimen (ARR=3.082, p=0.008).

The predictors of sustained viral suppression in multivariable analysis included having ≥3 VL measurements during the study period (ARR=3.595, p=0.000), VL taken in the first trimester of the index pregnancy (ARR=2.217, p=0.002), and VL monitoring done according to guidelines (ARR=2.353, p=0.000). Sustained undetectable VL in multivariable analyses was predicted by 3 or more VL measurements during the study period (ARR=1.609, p=0.006), VL taken in the first trimester of the index pregnancy (ARR=1.508, p=0.001), and VL monitoring done according to guidelines (ARR=1.511, p=0.011). Additionally, women ≥25 yrs (ARR=1.546, p=0.009), those on the NNRTI-based ART regimen (ARR=1.774, p=0.037), and women residing in Kisumu vs. in Homa

Bay County (ARR=2.136, p=0.027) were more likely to achieve a sustained undetectable VL during the study period.

Table 4

Multivariable analyses of predictors of viral load suppression and undetectable viral load[a]

VARIABLE	Viral suppression at 12m postpartum		Undetectable VL at 12m postpartum		Sustained viral suppression[b]		Sustained undetectable VL[b]	
	Adjusted RR (95% CI)	**p-value**	**Adjusted RR (95% CI)**	**p-value**	**Adjusted RR (95% CI)**	**p-value**	**Adjusted RR (95% CI)**	**p-value**
Number of total VLs								
≤2	ref		ref		ref		ref	
≥3	0.645 (0.22-1.87)	0.420	0.933 (0.49-1.77)	0.831	3.595 (2.46-5.26)	**0.000**	1.609 (1.15-2.26)	**0.006**
Timing of VL								
No VL measurem.	ref		ref		ref		ref	
1st trim	1.445 (0.56-3.71)	0.445	1.029 (0.69-1.54)	0.891	2.217 (1.34-3.67)	**0.002**	1.508 (1.18-1.92)	**0.001**
Timing of VL								
No VL measurem.	ref		ref		ref		ref	
10-12m pp	--		0.688 (0.40-1.19)	0.182	1.323 (0.91-1.92)	0.142	1.100 (0.83-1.47)	0.515
VL done according to the guidelines[c]								
Yes	1.186 (0.45-3.16)	0.733	1.384 (0.91-2.10)	0.128	2.353 (1.50-3.68)	**0.000**	1.511 (1.10-2.08)	**0.011**
No	ref		ref		ref		Ref	
Age								
<25yrs	ref		ref		ref		ref	
≥25 yrs	1.515 (0.75-3.06)	0.248	0.761 (0.53-1.10)	0.141	1.296 (0.95-1.77)	0.100	1.546 (1.11-2.14)	**0.009**
Gestational age at study enrollment								
≤ 28 weeks	ref		ref		ref		ref	
>28 weeks	0.503 (0.21-1.19)	0.116	1.800 (1.03-1.16)	**0.040**	0.974 (0.64-1.49)	0.904	0.889 (0.62-1.28)	0.525
HIV status at 1st ANC visit								
Newly positive	1.138 (0.36-3.57)	0.825	1.126 (0.40-3.19)	0.823	0.654 (0.41-1.04)	0.074	0.862 (0.49-1.51)	0.602
Known positive	ref		ref		ref		ref	

ART regimen[d]								**0.037**
PI-based	ref	0.244	ref	**0.008**	ref	0.453	ref	
NNRTI-based	2.110 (0.60-7.40)		3.082 (1.35-7.06)		1.281 (0.67-2.44)		1.774 (1.03-3.04)	
County								
Homa Bay	ref		ref		ref		ref	
Kisumu	3.704 (0.45-0.81)	0.226	1.265 (0.48-3.32)	0.633	1.492 (0.66-3.35)	0.334	2.136 (1.09-4.19)	**0.027**
Migori	4.033 (0.59-7.53)	0.155	3.622(1.40-9.34)	**0.008**	0.716 (0.36-1.43)	0.342	1.640 (0.94-2.87)	0.083
Baseline VL[e]								
Undetectable	ref		ref					
Viral suppression	0.408 (0.12-1.41)	0.155	0.399 (0.23-0.70)	**0.001**	--		--	
Study Enrollment VL[e]	ref		ref					
Undetectable	0.091 (0.03-0.25)	**0.000**	0.205 (0.08-0.50)	**0.000**	--		--	
Not virally suppress.								
Wald chi-square		791.6		73.5		227.9		180.1

[a]Abbreviations: antenatal care (ANC), antiretroviral therapy (ART), viral load (VL)

[b] Sustained viral suppression (VL < 1000 copies/ml) over the observation period (baseline to 12 months postpartum) for those with at least 2 VL measurements during the study period. Sustained undetectable viral load (0 copies/ml) during the observation period for those with at least 2 VL measurements during the study period.

[c] For women newly tested and initiated on ART during this pregnancy, this was defined as VL testing 6 months (+/-1 month) after ART initiation and then VL testing 6 months later (+/-1 month); i.e., ~ 12 months after ART initiation. For those who were known-positive prior to pregnancy, it was defined as VL testing conducted immediately after the initiation of antenatal care (+/-1 month) and then every 6 months (+/-1 month) after that.

[d]ART regimen: azidothymidine (AZT), tenofovir (TDF), nucleoside reverse transcriptase inhibitor (NNRTI; first-line regimen), protease inhibitor (PI; second-line regimen)

[e] Undetectable VL =0 copies/ml, viral suppression between 0 and ≤1000 copies/ml, not virally suppressed>1000 copies/ml. Baseline VL was not considered in sustained-outcomes analyses as this measurement was incorporated within the sustained outcome variable.

Discussion

Pregnant and breastfeeding women in sub-Saharan Africa are priority population for VL monitoring.[36] The goal of this study was to examine the timing and frequency of viral load testing among pregnant/postpartum women living with HIV enrolled in the MOTIVATE! study as well as predictors of viral suppression at 12 months postpartum and during the entire period of observation (starting at study enrollment in pregnancy and up to 12 months postpartum). We found that viral load monitoring of pregnant women in this setting was sub-optimal, putting substantial numbers of women at risk of MTCT during crucial periods. We also found that certain sub-groups of women were less likely to achieve sustained VL suppression during pregnancy and postpartum, particularly women newly diagnosed during the index pregnancy, younger women, and those residing in rural areas.

While most women with known HIV status prior to the pregnancy underwent VL testing at their first antenatal visit and then had additional measurements later in the pregnancy, women newly diagnosed with HIV during this pregnancy often had not initiated ART in sufficient time to have a VL measurement within the recommended eight weeks prior to the delivery. This is not surprising given that according to the current guidelines in most countries, including Kenya, women must be on ART for at least six months prior to having an initial VL measurement. In order to meet this guideline, newly initiating women would have to start ART by 16 weeks of pregnancy, while the majority of women in our study and in many SSA settings do not seek antenatal care until around 20 weeks or later.[48, 102] Research has found that women newly diagnosed with HIV during the pregnancy are at higher risk of not

achieving viral suppression at 12 months after the birth compared to the women with a known HIV status and have a higher risk of MTCT.[4] Other studies have found that pregnant women newly diagnosed with HIV at the entry into antenatal services are more likely to have no VL measurements at all during pregnancy[103]. So late presentation for antenatal care at the time of initial HIV diagnosis results in few women being able to have VL monitoring prior to the birth of the baby.

Consistent with other research, women younger than 25 years in this cohort were less likely to achieve sustained undetectable VL. In other studies, younger women presented to antenatal care later compared to their older counterparts and were less likely to achieve viral suppression compared to their older counterparts.[34, 97, 104] In this study, being primigravid and newly diagnosed with HIV during the index pregnancy, were not statistically associated with achieving sustained undetectable VL, and were not been collinear with the age variable. However, it is possible that there might be some undetected synergies between being younger than 25 years, primigravid, and newly diagnosed with HIV. Geographical differences also play a role in health care access. In our study, women residing in Kisumu, the most urbanized and possibly most accessible of the three counties included in the study, were more likely to achieve sustained undetectable VL during pregnancy and up to 12 months postpartum compared to Homa Bay County, which is more rural and less developed. Lack of access and utilization of health care and delayed initiation of antenatal care and ART could undermine the successful achievement of viral suppression to prevent MTCT.[105]

Clinically, we found that in this cohort, increased number of VL measurements, early pregnancy VL testing, adherence to testing guidelines, being on an NNRTI-based ART regimen, and a suppressed VL at study enrollment in pregnancy were important predictors of viral load suppression and undetectable viral load in a late postpartum period. Viral suppression rates in many pregnant/postpartum women across SSA remain insufficient at approximately 80% (range 30%-98%).[35] In our study, 22% of women had one or more non-suppressed VL during the period of observation, and 40% had at least one detectable VL. The results are consistent with many other SSA settings.

Notably, PWLWH in this study were more likely to achieve sustained suppression if they had repeated VL monitoring. The literature shows that retention in care and VL monitoring at critical time points of the PMTCT cascade, i.e., first trimester, birth, early postpartum, and at 12-18 months after the delivery until the cessation of breastfeeding, now recommended until 24 months after the birth[106], are particularly crucial in PMTCT efforts.[35, 102, 107-110] In this cohort, initial adherence to treatment and treatment effectiveness, indicated by viral load status around the time of study enrollment, was a significant predictor of viral load status at 12 months postpartum. Thus, those who started off as unsuppressed were less likely to achieve and sustain undetectable VL status at 12 months postpartum. However, some research shows that even if a woman is virally suppressed at an antenatal visit, she might be viremic later on, particularly in the early postpartum period.[110] Adherence to HIV care often decreases in a late postpartum period and, in turn, is

associated with viremic failure.[103] Therefore, frequent VL monitoring during pregnancy and postpartum is important for timely clinical interventions.

In this cohort, over 70% of women started antenatal care prior to their third trimester, and thus were tested, and placed on ART earlier than in many countries in this region. Across SSA, VL testing uptake among pregnant women on ART is low.[111] A study conducted in South Africa showed that women who present to the antenatal care during the third trimester, have a lower number of antenatal visits, and delay initiation of ART, have lower odds of achieving viral suppression by third trimester.[97] Women who are on ART for less than eight weeks prior to the delivery and those who are not suppressed by 32 weeks of gestation, are more likely to transmit HIV to their infant.[4] In our study, although over 70% of women overall initiated antenatal services prior to the third trimester, newly known HIV-positive women were more likely to start antenatal check up after 28 weeks gestation; thus delaying initiation on ART and further shortening the window for the viral suppression by the time of delivery.

Study particpants on NNRTI-based versus those on the PI-based ART regimens were more likely to achieve sustained undetectable VL and undetectable VL at 12 months postpartum. This finding is even more interesting since NNRTI resistance is high [112, 113] and it is possible women had prior exposure during prior pregnancies. Also, all newly diagnosed HIV-positive study participants were on NNRTI-based ART compared to 93.7% of known positive women in the sample. This is consistent with the Kenyan guidelines that direct NNRTI-based regimens as first-line since 2011. NNRTI is considered the first-line regimen in many countries

worldwide.[4, 36] Studies show that patients are expected to be suppressed within within 4-8 weeks of initiation of being on ART.[29, 30] Also, in a study from South Africa, 71% of known positive versus 59.3% of newly initiated pregnant women achieved viral suppression by their third trimester.[97] The guidelines also recommend minimal changes to the ART regimen during the pregnancy. PI-based ART is a preferred second-line regimen and are more likely to result in viral suppression if PLWH adhere to treatment compared to NNRTI; however, it is associated with more adverse side effects (low birth weight, preterm birth, as well as gastrointestinal complications, including vomiting/diarrhea) and an increased pill burden as well as twice daily vs once daily dosing for patients..[36, 114, 115] Being on PI-based regimens might thus suggest a prior history of treatment failure of the first-line NNRTI-based regimen, the potential for higher VL during pregnancy, and possibly more severe HIV-related morbidity. Newly introduced integrase strand transfer inhibitor (INSTI)-based ART shows promising effects on HIV transmission and viral suppression compared to non-INSTI-based regimen, and could be recommended to those experiencing virologic failure.[116-118]

Implications for policy and practice

Although VL monitoring has been scaled up in this region of Kenya, significant gaps still remain for pregnant and postpartum women living with HIV. Large proportions of women are not getting VL measurements at crucial times during pregnancy and breastfeeding and did not have VL testing according to current Kenyan guidelines. Improved follow up of women for virologic failure during

pregnancy or breastfeeding is urgently needed. Early detection of treatment failure is crucial to PMTCT. Some ideas proposed 1) include point-of-care VL testing at facilities with results available within hours, 2) intensified (more frequent) schedules of VL monitoring, particularly if facilities face long turnaround times for VL results, and 3) testing pregnant women earlier in the pregnancy, even if they have not been on ART for 6 months. Some authors suggest requiring VL measurement at certain gestational ages, e.g., 4 weeks prior to the due date.[36] This seems logical, given that recent data show that a majority of women will achieve viral suppression on current first line NNRTI-based regimens within 4-8 weeks of initiation.[29, 30]

Thus, policy makers should consider revising the current VL testing guidelines to ensure VL suppression of PWLWH is assessed and achieved prior to delivery. Focusing on VL monitoring at critical time points in sub-groups at the highest risk of viremic failure (younger women, newly HIV-positive, rural areas) appears to be critical for PMTCT efforts and for the achievement of the 90-90-90 targets.

Strengths and Limitations

This study contributes to our understanding of the timing, frequency of viral load testing, as well as predictors of sustainable undetectable VL among pregnant and postpartum women living with HIV in Kenya. The robustness and extrapolation of the study results to a similar setting across SSA was strengthened by a large sample size consisting of longitudinal data for both women on ART prior to the index pregnancy and newly diagnosed HIV-positive women, recruitment from 24 clinics in

three counties in Western Kenya, and longitudinally observed cohort throughout the pregnancy and up to 12 months postpartum.

The study results are subject to some limitations and possible biases. The study recruited pregnant women visiting antenatal clinics who meet additional eligibility criteria for the trial (≥18 years, have access to a mobile phone and have disclosed their HIV status to any person sharing the phone, and are willing to have home visits). Thus, women enrolled in the study might be inherently different from women who do not utilize antenatal care or did not meet these eligibility criteria. This geographic area is predominantly rural and low-resource health facilities were not always able to achieve sufficient VL monitoring for many women at key time points (around 12 months postpartum), resulting in missing data. Data were abstracted from medical records that lack detailed sociodemographics and psychosocial determinants that might play a role in adherence and VL suppression (e.g., poverty, mental health issues, intimate partner violence, other medical conditions). Additionally, the study was conducted in the context of frequent changes to policies and standard care provision.

Conclusions

Improved follow up of women with virologic failure during pregnancy and until the cessation of breastfeeding is urgently needed to succeed in PMTCT and efforts to reduce horizontal transmission of HIV, reduce maternal mortality/morbidity, and sustain family health. The most optimal and cost-effective timing and frequency of VL monitoring in this target population in SSA needs to be

determined in the context of a resource-limited setting and the 'Test & Treat All' approach.[36]

Acknowledgments

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Ethical Approvals

The study was approved by ethical committees at KEMRI, the University of Colorado Denver, and the University of Alabama at Birmingham. Informed consent was obtained from each study participant prior to the study enrollment.

EXPERIENCES, PERCEPTIONS, AND POTENTIAL IMPACT OF COMMUNITY-BASED MENTOR MOTHERS (cMMs) IN SUPPORTING HIV-POSITIVE PREGNANT WOMEN IN KENYA: A MIXED-METHODS STUDY

by

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Abstract

Background: Community-based mentor mothers (cMM) are women living with HIV (WLWH) who provide peer support to pregnant/postpartum (PP) WLWH (PWLWH) in the community to enhance lifelong antiretroviral therapy (ART) adherence and retention in care, and prevent mother-to-child transmission of HIV. Methods: We conducted a prospective, mixed-methods study utilizing a convergent parallel study design in southwestern Kenya. In the qualitative phase, we completed 24 in-depth interviews with cMMs between April-May 2016 to explore their perceptions of their role in supporting PWLWH. Transcripts were coded using a coding framework based on the literature, interview guides, and emerging themes from transcripts, and fine-coded using an inductive approach. In the quantitative phase, we extracted data from medical records of 589 PWLWH on ART and their infants randomized into a cMM intervention arm of the Mother Infant Visit Adherence and Treatment Engagement (MOTIVATE!) trial during 2015-2018. The goal of this phase was to examine if cMMs' support and home visits impact the prevention of mother-to-child (PMTCT) behaviors of WLWH. The composite outcome consisted of facility delivery, infant HIV testing, good ART adherence, and undetectable VL at 6 weeks PP. We used cluster-adjusted generalized estimating equation models, adjusted for weeks of pregnancy at the start of the study and other predictors. Results from the qualitative and quantitative data were integrated in the final phase of this study, and major themes were summarized in a side-by-side matrix. Results: Integrated results revealed three main themes related to the impact of cMMs in supporting PWLWH: (1) The cMM intervention was utilized and was highly

acceptable to women and the community. WLWH in our study received, on average, 6.2 home visits, and nearly a third received the planned full dose of 8 home visits (4 in pregnancy & 4 in PP). cMMs reported serving as role models/confidantes, supporting acceptance of HIV status, providing messages about the potential of having an HIV-negative child, assisting with male partner disclosure/communication, and providing tangible support. (2) cMM visits support adherence to PMTCT behaviors by WLWH. During home visits, cMMs described the provision of health education, making linkages to HIV care, PMTCT/maternal and child health (MCH) services, and having a positive impact on increased ART adherence and retention in care among WLWH. CMMs also described personal benefit through self-empowerment and increased income. Consistently, having ≥4 cMM home visits pregnancy and up to 6 weeks PP, as compared to < 4 visits, was associated with improved composite outcome for PMTCT behaviors, (ARR=1.414, p=0.045). (3) Assistance with disclosure of HIV status to a male partner might be a pathway through which the cMM intervention leads to improved PMTCT behaviors. In interviews, cMM emphasized their role in male partner status disclosure as one of their most important ways of supporting WLWH. However, the quantitative analyses did not reveal a significant association between disclosure to the male partner by the time of the birth and good PMTCT behaviors.

Conclusions: Kenya, similar to other countries, is in need of innovative approaches to overcome challenges associated with the scale-up of lifelong ART services. This study suggests that a cMM strategy may play an important role in enhancing PMTCT

behaviors in the crucial early postpartum period, and may also have positive effects on the cMMs themselves.

Introduction

As of 2018, the national HIV prevalence in Kenya was 4.9%, 1.6 million Kenyans were living with HIV, and 46,000 were newly infected.[37] Women were more likely to be HIV-positive (5.2%) compared to men, and women in the reproductive ages were particularly vulnerable.[38] Southwestern Kenya is disproportiantelly affected by HIV. Kisumu County, Homa Bay County, and Migori County in this part of Kenya, are among the top five counties in Kenya with the highest HIV prevalence[41] and report over half of the country's new infant HIV infections.[42]

In 2013, Kenya rolled out Option B+[48, 96], a policy to implement universal, lifelong antiretroviral therapy (ART) for all pregnant and breastfeeding women living with HIV (WLWH), recommended by The World Health Organization (WHO) in settings with generalized HIV epidemics.[4, 13] By 2017, the mother-to-child transmission (MTCT) rate at 18 months after birth in Kenya decreased from 14% in 2013 to 11.5%. New HIV pediatric infections (children 0-14 years) also decreased by 38% between 2011-2017.[38]

Lifelong ART (Option B+) holds promise for improving maternal and child health, but critical challenges remain in achieving long-term ART adherence and retention in HIV care at individual and healthcare system levels.[26] To address these challenges and a lack of trained healthcare personnel, WHO and The Joint United Nations Programme on HIV/AIDS (UNAIDS) recommend taskshifting, community

involvement, and engagement of WLWH in service provision as a critical means of achieving the prevention of mother-to-child transmission (PMTCT). [53-55, 57, 119] Research also shows that services provided by properly trained lay community health workers focusing on WLWH can promote adherence to healthy behavior through shared culture, language, and community.[69] A recent review by Schmitz, et..al.[70], demonstrates the positive impact of lay community health workers on WLWH-infant pairs in terms of increased MTCT awareness, retention, adherence to care, and infant testing.

A specific approach shown to increase uptake of PMTCT services in several settings in sub-Saharan Africa (SSA) is The Mother2mothers (m2m) program, established in South Africa in 2001 and implemented across SSA, including Kenya.[60, 107, 120-126] Mentor mothers (MMs) are HIV-infected women who have been through PMTCT in the past six months to two years and are adhering well to treatment, have disclosed their status; and who are tasked with providing one-on-one peer education to pregnant/postpartum women living with HIV on PMTCT and health-related topics, as well as psychosocial support[11, 60-63] and encouragement for enrollment, adherence, and retention in HIV care. [62, 64] Additionally, MM programs have been an innovative and cost-effective means to increase community employment and the availability of health services in underserved communities.[68]

Mentor mothers have generally been based at health facilities in Kenya providing services to women when women come in to the clinic, as opposed to being implemented at the community level. In our NICHD-funded implementation science study in Kenya (The Mother Infant Visit Adherence and Treatment Engagement

(MOTIVATE) Study, R01HD080477, PIs: Turan and Abuogi)[100], community-based mentor mothers (cMMs) were recruited and trained to conduct community outreach and home visits for HIV-positive women and male partners in order to assist with safe disclosure, support safe infant feeding, promote safer sex and family planning, encourage early infant testing and follow up, and encourage adherence ART and return for HIV care visits.[127] cMMs were trained and utilized a detailed protocol of home visits during pregnancy and postpartum, with a total of 4 monthly visits stipulated during pregnancy, 4 after the birth up to six weeks (1 day, 3-4 days, 1 week, and 6 weeks after the birth), and 5 from six weeks up to 12 months postpartum (10 and 14 weeks; 6, 9, 12 months after the birth). Standardized requirements and expectations of mentors mothers include standardized PMTCT-specific curriculum, monitoring and supervision standards, and evaluations. Incorporating such a structure assists in integrating mentor mothers into existing health systems and establish peer and patient respect for the vital role they play in the community.[128]

The goal of this study was to explore the experiences, perceptions, and mechanisms through which cMMs provide support for HIV-positive pregnant women in the context of Option B+ in the context of the MOTIVATE! Study in southwestern Kenya. The results of this study will help us to understand ways to strengthen adherence and retention in ART care for pregnant and postpartum HIV-positive women in Kenya and potentially elsewhere in SSA.

Based on our formative work in the parent MOTIVATE! Study [127], we hypothesized that the cMM strategy will be perceived as an acceptable intervention in this setting. Furthermore, we hypothesized that higher numbers of cMM visits will be

associated with better early postpartum PMTCT behaviors; including facility delivery, increased adherence to ART at six weeks postpartum, undetectable viral load at six weeks postpartum, and timely infant HIV testing at six weeks. We further hypothesized that HIV status disclosure to the male partner would mediate the relationship between the number of cMM visits and our outcomes.

Methods

The current study includes primary analysis of qualitative interviews and secondary analysis of longitudinal data conducted in the context of a larger randomized control trial, the Mother Infant Visit Adherence and Treatment Engagement (MOTIVATE!) study (R01HD0808477; MPIs: Abuogi and Turan). The MOTIVATE! study utilized a 2x2 cluster-randomized factorial research design. The individual and combined effects of two interventions, community mother mentors (cMMs) and text messaging, on ART adherence and retention in care were examined compared to standard care. MOTIVATE! Study participants were pregnant, HIV-positive women 18 years and older accessing care at one of the 24 government antenatal clinics that had been randomized into one of the four study arms in three high HIV prevalence counties of southwestern Kenya: Homa Bay, Migori, and Kisumu. Study participants were enrolled during pregnancy from December 2015-August 2017 and followed until at least 12 months postpartum. More details on the parent study are published elsewhere.[100]

In this sub-study, we conducted a prospective, mixed-methods study to better understand how cMMs influence HIV-positive pregnant women's health behaviors

and outcomes in the context of Option B+ in Kenya, utilizing a convergent parallel mixed-methods study design (see Figure 1).[129] A convergent parallel research design includes the concurrent collection and analysis of qualitative and quantitative data, each method addressing related aspects of the same research question in a complementary way. Merged results produce a comprehensive understanding of the research problem.[129] Specifically, in the qualitative phase of this study, we explored experiences and perceptions of cMMs themselves on their role in supporting HIV-positive pregnant and postpartum women, while in a quantitative phase, we aimed to understand how cMMs' support impacts the health behaviors and outcomes of HIV-positive pregnant women.

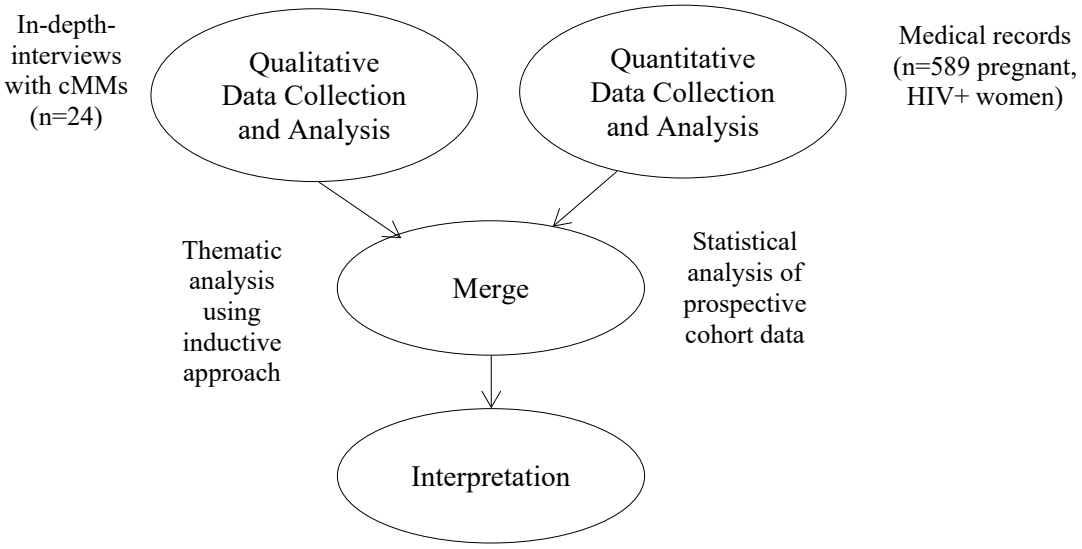

Figure 1. Process flow diagram of the procedures. Convergent parallel mixed-methods research design.

Setting

Kisumu County (16.3%), Homa Bay County (20.7%), and Migori County (13.3%) are among the top five highest HIV-burden counties in Kenya.[41] This region represents about half of Kenya's new infant HIV infections (54%) and 45% of its need for PMTCT services.[42] The ART coverage in these counties ranges from 79-90% in adults and 87-90% in children.[38] High pregnancy rates (5.3%-9.0%), total fertility rates (3.6-5.3), and suboptimal access to and utilization of healthcare services (Kenya DHS 2014)[43] result in increased infections, MTCT, and delayed initiation into treatment for both women and infants.[44]

Qualitative Phase

Data Collection Methods

To explore the perceptions of cMMs on their role in supporting HIV-positive pregnant and postpartum women, we conducted a total of 24 individual in-depth interviews with cMMs from ten of the study communities in Kisumu, Migori, and Homa Bay Counties (formerly Nyanza Province), Kenya between April-May 2016, when the cMMs had been providing services in the communities for about 6 months. To participate in this sub-study, cMMs had to be providing support to pregnant and postpartum women utilizing MCH services at healthcare facilities included in the MOTIVATE! Trial of interventions to support adherence and retention in the context of Option B+ (Clinicaltrials.gov # 14-0331). Eligibility and interest in participating were determined during a short private session. Clear explanations were given to the participants that the study was separate from their employment and regular medical

care and that they had the option of refusing to participate in any part of the research. Participant characteristics were collected, including demographics, pregnancy, and HIV-related information. Individual interviews were conducted in private settings in English or Dhuluo language, depending on the preferences of the participant by one of the two gender-matched interviewers (AH, an American graduate student and GO, a masters level Kenya research assistant). Interviewers underwent additional training in qualitative research methods and the study topics prior to the initiation of the study. A qualitative in-depth interview guide (Appendix A) was developed based on a review of the literature, prior studies on pregnancy and HIV in this setting, [79, 80], and preliminary results from the formative phase of the parent MOTIVATE! Study. The main topics explored in the interviews with community mentor mothers included: 1) experience working as a cMM (responsibilities, benefits/challenges, comparison to facility-based mentor mothers, based in community vs. facility, impact of their work, characteristics of "ideal" cMM), 2) acceptability of cMMs in community and at health care facilities, 3) personal experiences with being a cMM, 4) Option B+ compared to PMTCT prophylaxis regimens, and 5) suggestions for improving the cMM program.

Data Management and Analysis

Interviews were digitally recorded, translated to English if applicable, and transcribed verbatim by a professional transcriptionist, excluding any identifying information. All files were password-protected and stored in a secure location. Subsequently, transcripts were coded by two researchers (AH and SK) using the

Dedoose qualitative software program. Coding and analysis followed a thematic analysis approach. [81, 82] The coding framework was based on the literature, topics from interview guides, and emerging themes from transcripts. Transcripts were initially broad-coded based on topics covered in the interview guide as well as emerging themes, and were fine-coded using an inductive approach by two researchers (AH and SK). Major themes were refined and sub-themes identified.

Quantitative Phase

Data Collection Methods

In the quantitative phase, we performed a secondary analysis of prospective data from the MOTIVATE! Study with the aim of understanding the effects of cMM visits and possible mechanisms for the impact of cMM support on health behaviors and outcomes of HIV-positive postpartum women.The cohort for this sub-study consisted of 589 HIV-infected pregnant women aged 18 years or older attending an ANC clinic at one of the MOTIVATE! Study sites who were randomized into one of the cMM intervention arms of the study.

Data on study indicators and sociodemographic characteristics were abstracted from medical records by study data clerks, with confirmation and supplementation from the national viral load database. Data were abstracted for the period from study enrollment (in pregnancy) up to 6 weeks after the birth. The six weeks postpartum was selected as one of the most critical steps in the PMTCT cascade.[21]

Data Management and Analysis

Outcomes:
In the quantitative part of this manuscript, we explored predictors of two primary outcomes and one composite outcome:

(1) The woman's self-reported ART adherence at 6 weeks postpartum from medical records (binary variable 1=yes, 0=no, coded 'yes' if a woman self-reported during the clinic visit adhering to ART treatment as prescribed >95% of the time);

(2) The woman's viral load at 6 weeks postpartum (coded as 1=detectable, and 0 = undetectable);

(3) A composite outcome of optimal PMTCT behaviors, consisting of mother's >95% ART adherence at 6 weeks postpartum, mother's undetectable viral load at 6 weeks postpartum, health facility delivery, and infant HIV testing at 6 weeks after birth (binary for all four outcomes 'yes', 0=no). Women who had a 'yes' for all four of these behaviors were classified as having optimal PMTCT behaviors (1) and those who had 'no' for one or more behaviors were classified as not having optimal behaviors (0). Exclusive breastfeeding was excluded from the composite variable due very high reported rates with almost no variability.

Predictors: The main predictor was the total number of cMM visits that the women received during pregnancy and up to six weeks postpartum. We controlled for the number of weeks of pregnancy at the time of study enrollment. The number of cMM visits were treated as a binary variables, specifically for the antenatal and postnatal

period treated separately categorized into ≥2 cMM visits and <2 cMM visits, and for the total period categorized into ≥4 cMM visits and <4 cMM visits up to 6 weeks postpartum. The cut off for each of these variables represented half of visits recommended for the time period. Other independent variables included in these analyses as potential predictors included the baseline sociodemographic and patient characteristics (abstracted from medical records): age (categorized into <25 & ≥25 years), marital status (married vs. not), gravida (primigravid vs. 2 or more pregnancies), gestational age at the first antenatal visit during this pregnancy (≤28 weeks vs. >28 weeks), study arm (cMM & cMM+text messages), timing of HIV diagnosis vis-à-vis the current pregnancy (women newly diagnosed with HIV at their first antenatal visit of this pregnancy vs. known HIV-positive prior to the current pregnancy), male partner's baseline HIV status (positive vs. negative or unknown status), and male partner HIV testing at baseline (yes=1, no=0).

We hypothesized that more cMM visits would result in better PMTCT behaviors up to 6 weeks postpartum. Based on the current evidence in the literature on the positive effects of disclosure to a male partner on PMTCT behaviors[130-132], we also hypothesized that disclosure to a male partner would mediate the relationship between a number of cMM visits and the outcomes. Disclosure to a male partner by the time of the birth was treated as a binary variable (yes=1, no=0).

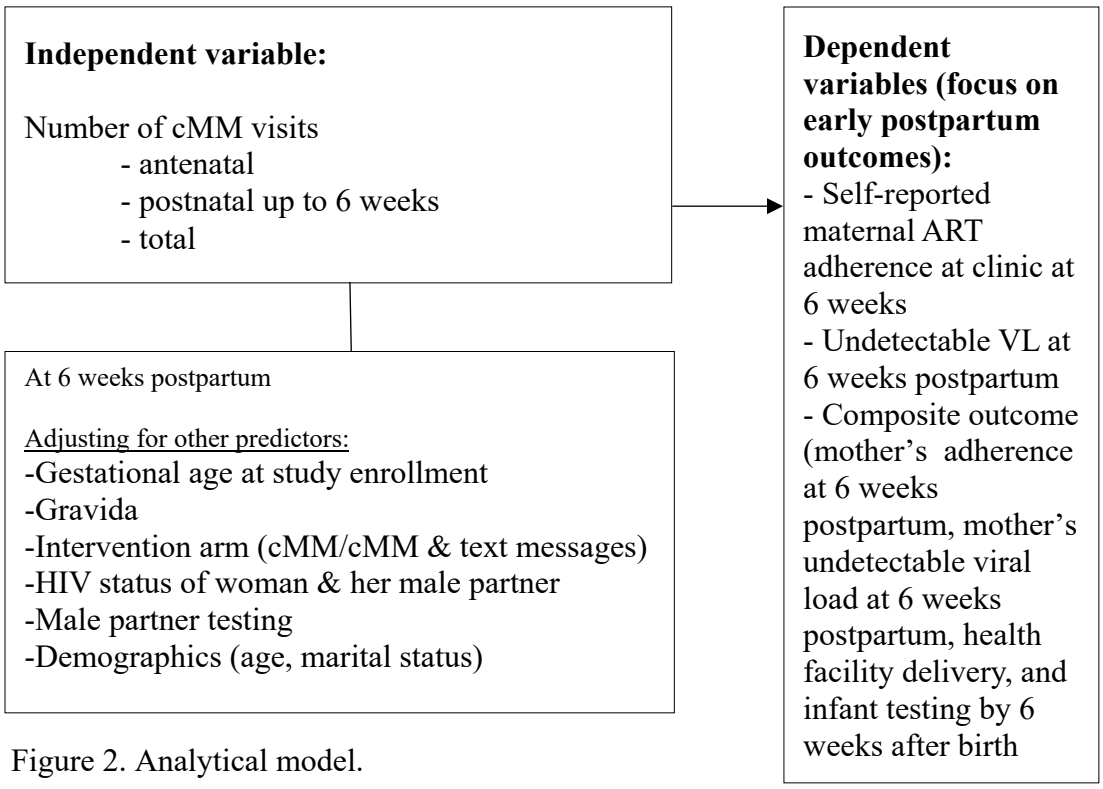

Figure 2. Analytical model.

The data were de-identified using a unique, database-specific identifier for the confidentiality of individual-level data. All statistical analyses were conducted using Stata SE 16 (StataCorp, College Station, Texas, USA), and p levels <0.05 were considered statistically significant.

Quantitative data analyses:

Main analyses: Distributions of all variables were examined with descriptive statistics; counts (percentages) and means (± standard deviations [44]). Outliers were inspected and truncated when necessary. Variables were tested for multicollinearity, and strongly correlated variables ($r \geq 0.60$) were excluded from the model. Covariates with a p-value of <0.2 in bivariate analyses were considered for inclusion in multivariable models. Both bivariate and multivariable models are presented. Given

the clustered study design of the MOTIVATE! Study (24 study sites), Generalized Estimating Equation (GEE) models were used to test for differences of interest in bivariate and multivariable models, adjusted for relevant covariates, and accounting for clustering by site. Results were summarized as relative risks for models based on binary responses. Relative risk estimates were selected instead of the odds ratios as a more accurate measure for prospective data, and given the high prevalence of the outcome measures. Statistical significance, set at a two-sided p-value <0.05, was also reported based on the robust variance estimates from the GEE models. The outcomes were adjusted for weeks of pregnancy at the start of the study, given that this variable influenced the duration of time that women had available to receive the stipulated number of cMM visits. In addition, we intended to test 'disclosure to male partner' as a mediator. However, there was almost no variability in this variable and the relationship did not meet the criteria for a mediating effect, i.e., we have not found significant associations between the main predictor (cMM visits) and presumed mediator, and between presumed mediator and outcome variables.

Integration of quantitative and qualitative findings

Results from both qualitative and quantitative data were integrated into the final phase of the study following the convergent parallel mixed methods research design. Matrices were created, which placed findings from the qualitative and quantitative data collection on major themes side-by-side. Merged results from in-depth interviews in the qualitative phase and prospective cohort study produce a

triangulated understanding of how cMMs' support impacts HIV-positive pregnant and postpartum women in terms of early postpartum PMTCT behaviors.

Results

Mechanisms of cMM influence on PMTCT behaviors

Utilizing an adapted conceptual framework for the role of community health workers in facilitating patients' adoption of health behaviors developed by Katigbak, et al., [69], Figure 3 below summarizes the most crucial components of cMM's role in facilitating healthy PMTCT behaviors of HIV-positive pregnant/postpartum women based on analyses of the qualitative data from the cMMs' perspective. CMMs provided social support, leveraged cultural congruence, shared PMTCT and ART experience, and had good interpersonal communication with HIV-positive women which led to building a trusting relationship and rapport to assist HIV-positive pregnant/postpartum women with adopting healthy PMTCT behaviors. CMMs believed that the most important pathway to good PMTCT behaviors was through the women's disclosure of their HIV status, particularly to a male partner. Good PMTCT behaviors were believed to, in turn, result in an increased engagement in care, improved VL monitoring, and a reduction of adverse health and PMTCT outcomes. The cMMs also described how the cMM program increased community capacity and had positive effects on cMMs themselves.

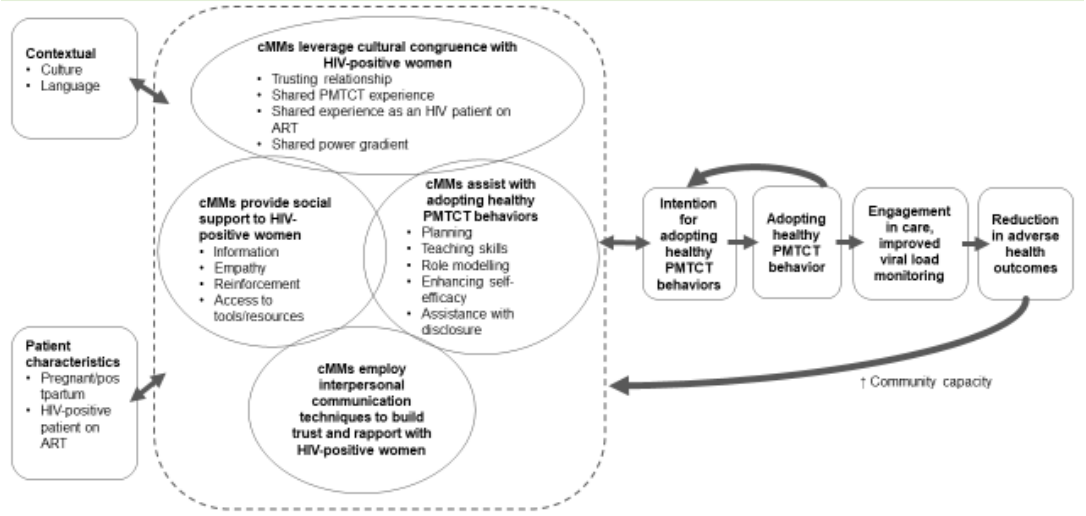

Figure 3. Adapted conceptual framework of community mentor mothers (cMMs) and HIV-positive pregnant/postpartum women served

Qualitative Findings

Twenty-four cMMs (mean age 34.2 years , SD = ±6.7) participated in the individual interviews. The majority of cMMs were married (62.5%), living in an HIV-concordant relationship (58.3%), and had, on average, 2.9 living children. All cMMs had completed at least primary education, and 62.5% had completed secondary education or higher. Sociodemographic and HIV-related characteristics of participants are presented in Table 1.

Five major themes were identified through the thematic analysis that shows how cMM perceive their role in supporting HIV-positive pregnant and postpartum women, including (1) high acceptability of the cMM intervention in the community and at health facilities, (2) cMM job responsibilities/type of services provided, (3) positive impact of cMM work on the women served, (4) challenges of cMM work, and (5) personal story and the impact of being a cMM on self.

Theme 1: High acceptability of the cMM intervention in the community and at health facilities.

Most of cMMs believed that the cMM intervention is well accepted by women and their male partners. Several cMMs expressed that cMMs are preferred over the facility-based mentor mothers due to services that have privacy, convenience, and dedicated attention. It was their perception that they are also highly accepted by healthcare workers due to their assistance with clinic patients and other tasks.

"As the people doing the visits, they know us, they take us as sisters (nurses) who they can share their problems with. Whenever they come here [healthcare facility] they don't open up but the moment you go to them in their houses, there they are so free and confide in you whenever they face problems." (31 years, HIV discordant relationship)

Despite the fears of the inadvertent disclosure of their HIV status to study participants, cMMs preferred working in their own community due to the familiarity with community culture and beliefs, and close geographical proximity to the women they served, particularly during births and emergency situations.

"It is good because in the community where you live you will know the behavior of people. You will also know the kind of problems women have. You know when you are close to her she will come and tell you her problems in a better way compared to those from far. You know sometimes those who are far have problems but they cannot reach you quickly." (28 years, HIV concordant relationship)

Theme 2: cMM job responsibilities/type of services provided

cMMs take pride in being "on-call" around the clock and going beyond their formal duties. They feel they are serving as role models and confidants to HIV-positive pregnant/postpartum women. They are helping with acceptance of HIV-positive status, providing encouragement about the potential of having an HIV-negative child, and assisting with partner disclosure/communication.

"I wanted them to know that you can give birth and raise a HIV negative baby. […] it was something I had experienced, and did as I was taught and I was successful. You know when you are teaching someone something that you have experienced, it becomes very easy and the person also understands quickly." (41 years, HIV concordant relationship)

cMMs described how they link and refer women to HIV care, PMTCT services, and maternal and child health services. They also described providing tangible support, including the development of birth plans, picking up medications, and even help with planning household finances. At health facilities, cMMs were helping with MCH/HIV services, including paperwork and scheduling.

"What makes me happy is that they listen to what I teach them, I tell them to take a motorbike to the hospital whenever they are in labour, I advise them to save some money. For instance, if the husband is a fisherman and brings home a thousand Bob, I tell them to save 500 shillings and budget with the remaining 500, so when she is in labour, she can use the 500 to get to the hospital and that's what they've been doing

and that makes me happy, the fact that they listen to what I teach them makes me glad. Most of the clients delivered here at the hospital, not even a single baby died and that made me happy." (42 years, HIV discordant relationship)

Theme 3: Positive impact of cMM work on pregnant/postpartum women and families

All interviewed cMMs expressed the pride in their work and believed in the value of their work, particularly by having an impact on women's improved adherence and retention in HIV care, decision to deliver at a health facility, increased infant's HIV testing and adherence to ARV, infant's immunization, and safe infant feeding.

"The hospital deliveries has increased, that one I know because when we sit down with them we go through the pros and cons of home delivery, we compare the two. That one I know has improved, again when we go there we keep on reminding them about drug adherence. You find a mother who is stressed up, she want to do this, she want to do this, she is advised to give nevirapine and nevirapine is given once a day, she has forgotten everything, you find that she gives the child nevirapine in the morning and in the afternoons when you enquire she says "I give her twice," I said, "no you give her once." So by going there at least some adherence is maintained. Yes because we are human beings we are bound to forget. The more we work there the more we realize she is giving it the wrong way then we correct the gaps." (51 years, HIV concordant relationship)

Many cMMs mentioned increased rates of HIV-status disclosure, and improved couple communication and male involvement as the most critical impacts of their work.

"When you go to these people's homes you get time for disclosure, you sit down with couples and talk to them but here at the facility most people are afraid to come. At the homes you find that they are so happy with what you teach, in fact, when you come back next visit you find that the man of the house is now willing to sit and listen to you." (31 years, HIV discordant relationship)

Theme 4: Challenges of cMM work

In interviews, cMMs expressed challenges faced when visiting homes of HIV-positive pregnant/postpartum women. Initial nondisclosure of HIV status, especially to a male partner but also to other members of the household and community, was mentioned as a number one challenge, particularly in the first few days after the birth. The cMMs explained that nondisclosure led to lack of male partner involvement in the pregnancy and lack of support of the positive PMTCT behaviors. The cMMs also explained that disclosure to a male partner was avoided by women due to their fear of being blamed for bringing HIV into a house, beaten, and possibly chased away. The context of disclosure becomes even more complex when a woman lived in a polygamous marriage, a common relationship type in this area. The presence of other people during the cMM visit, particularly if they are not aware of a woman's HIV-positive status, was also cited as an obstacle in the provision of the CMM intervention. CMMs emphasized that even women who have not disclosed their status

want to participate in cMM's visits; however, a cMM must be agile enough to know that disclosure has not been done and to handle the situation in a manner that does not disclose the woman's HIV status.

"You see these people who have not disclosed can accept that you go and visit them at home then the husband catches you abruptly. The husband must ask what you are doing there and that may bring a quarrel. They know that people from the facility normally follow those on ARVs so they must quarrel. Again another issue with those who have not disclosed is that when you are caught you have to change the topic then you give her another appointment but you will not know what will happen after you have left."(41 years, HIV concordant relationship)

Additionally, cMMs voiced concern about the ability to deliver three home visits during the first week after baby's birth to the full extent, particularly if a woman has not disclosed her HIV status.

"When she delivers […] I have to go day one, day three, day seven, this is within one week, this man sees you in this family for three days and he doesn't understand what you are doing. It becomes a challenge and now you will also find some other women who have come, to see the newborn, at times its very challenging." (25 years, HIV concordant relationship)

In addition, cMMs described facing logistical challenges when delivering the cMM intervention, some due to the natural causes (rainy season, floods, mud), but also limited financial resources, e.g., insufficient cell phone minutes, lack of finances to utilize other transportation modes when walking was not feasible. However, they ultimately felt the necessity to visit their "clients" no matter what the circumstances.

"Currently it's a rainy season, it rains heavily to an extent this place gets flooded, so sometimes you are so tired but then you have to go and the place is muddy, that's the challenge we go through. Also we travel long distances and this place is hilly and you have to go because we have to go to this people you can't abandon them." (31 years, HIV discordant relationship)

Theme 5: Personal story and the impact of being a cMM on self

Many cMMs expressed that being a cMM resulted in a self-empowerment and motivation to adhere to their own ART treatment and retention in care. It also increased their self-worth and belief in their value.

"It has really changed me […] because you feel so nice when a baby comes out negative. And it also feels good when you talk to a client, you tell her your experience then she sees you as a friend." (24 years, HIV discordant relationship)

Many cMMs expressed that after this experience, they would like to further their skills and training, possibly by becoming a nurse. cMM also discussed that HIV-positive people are often stigmatized in the job market. They often expressed that

being a cMM was a unique opportunity for HIV-positive women, requiring an HIV-positive status. Lastly, employment increased their income and provided them with much-needed resources for them and their families.

"Being a community mentor mother has helped me in so many ways, the people who looked down upon me now view me as a person of value, one that can impart some knowledge on them. My children are now able to go to school but before they wouldn't go for two weeks without being sent back home for fees [...]. Also right now am able to dress neatly, am more knowledgeable about things. "(28 years, HIV concordant relationship)

Quantitative Phase

In the quantitative phase of this sub-study, data were included for 589 HIV-positive women who received cMM intervention (mean age 28.9 ±5.6 years), most of whom were married (92.7%), and had two or more children (92.7%). The majority of women were enrolled in the MOTIVATE! Study prior to reaching 28 weeks of gestation (mean 23.6 ±7.6 weeks) and initiated the ART prior to the index pregnancy (82.8%). According to medical records, most women didn't know their male partner's HIV status at enrollment (77.5%), and 18.6% lived in an HIV-positive concordant relationship. Interestingly, 85.0% of men underwent HIV testing based on reports in the women's medical records. Health facilities attended by the women were randomly assigned to one of the intervention arms, with 50.5% of participants in the cMM only study arm and 49.5% in the cMM + text messaging study arm. Sociodemographic and HIV-related characteristics of participants are presented in Table 1.

The distribution of cMM visits and outcomes is presented in Table 1. Around 43.0% of women received the intended full 'dose' of cMM visits (4 visits) during pregnancy, while 4.7% didn't receive any cMM visit, and an additional 15.2% only had one cMM visit. In the period between birth and 6 weeks postpartum, nearly two-thirds of women (72.6%) had four cMM visits, and 10.7% of women had 1 or no cMM visits. In total, the mean number of CMM visits up to 6 weeks postpartum was 6.2 ±1.9. About one-third of participants received the full dose of all eight cMM visits (33.0%), and 5.3% received a low 'dose' of this intervention defined as two or fewer cMM visits during this period.

The majority of women had disclosed their HIV status to their male partners by the time of delivery (96.3%). Most women (97.1%) self-reported good adherence (>95% of the time) at 6 weeks postpartum clinical visit. About 72.3% of women achieved undetectable viral load at 6 weeks postpartum (VL=0), an additional 21.6% achieved viral suppression (VL >0 to 1,000 copies/ml), and 6.1% were not virally suppressed (VL>1,000 copies/ml). Most women delivered their baby at a health care facility (91.5%), and 97.9% of the infants were tested for HIV at 6 weeks. The majority (99.8%) of women self-reported exclusive breastfeeding to clinicians at the 6 weeks postpartum visit. Overall, nearly 70.0% of women (69.8%) achieved all optimal PMTCT behaviors, consisting of infant testing at 6 weeks, facility delivery, good ART adherence, and undetectable viral load at 6 weeks postpartum.

Table 1
Sociodemographic and HIV-related characteristics of study participants

Characteristics /N (%)/mean (SD)	**Community Mentor Mothers (n=24)**	**Pregnant Women Living with HIV (n=589)**
Age (mean, SD)	**34.2 (±6.70)**	**28.88±5.57**
≤ 25		169 (28.74%)
25 – 28 years		130 (22.11%)
29-32		144 (24.49%)
≥ 33 years		145 (24.66%)
Education		
Did not complete secondary	9 (37.50%)	not available
Completed secondary educ.	15 (62.50%)	
Number of living children (cMMs)/Number of pregnancies (pregnant women)	**2.9 (±1.30)**	**3.49 (±1.70)**
1		43 (7.31%)
≥ 2		545 (92.69%)
Weeks of pregnancy when started study	N.A.	**23.64 (±7.64)**
≤ 28 weeks gestational age		439 (74.66%)
> 28 weeks gestational age		149 (25.34%)
Marital status		
Married	15 (62.50%)	545 (92.69%)
Not married	9 (37.50%)	43 (7.31%)
HIV at 1st ANC visit		
Newly positive	N.A.	101 (17.18%)
Known positive		487 (82.82%)
Partner's HIV status		
Positive	14 (58.30%)	108 (18.56%)
Negative	8 (33.30%)	23 (3.95%)
Unknown	2 (8.30%)	451 (77.49%)
Male partner tested	N.A.	
Yes		494 (85.03%)
No		87 (14.97%)
Intervention arm	N.A.	
cMM		297 (50.51%)
cMM + text messaging		291 (49.49%)
# of cMM antenatal visits	N.A.	**2.82 (±1.26)**
0		27 (4.65%)
1		88 (15.15%)
2		101 (17.38%)
3		114 (19.62%)
4		251 (43.20%)

# of cMM postnatal visits	N.A.	**3.39 (±1.12)**
0		18 (3.10%)
1		44 (7.57%)
2		54 (9.29%)
3		43 (7.40%)
4		422 (72.63%)
Total # cMM total visits	N.A.	**6.19 (±1.87)**
0		7 (1.20%)
1		11 (1.89%)
2		13 (2.23%)
3		24 (4.12%)
4		39 (6.70%)
5		80 (13.75%)
6		108 (18.56%)
7		108 (18.56%)
8		192 (32.99%)
Disclosure to male partner at the time of birth	N.A.	
Yes		546 (96.30%)
No		21 (3.70%)
Mother's ART adherence at 6 weeks postpartum	N.A.	
Good (>95%)		564 (97.07%)
Less than good (≤95%)		17 (2.93%)
Mother's VL at 6 weeks postpartum	N.A.	N=408
Undetectable (0 copies/ml)		295 (72.30%)
Viral suppression (>0, <1000 copies/ml)		88 (21.57%)
Not virally suppressed (1000 copies/ml)		25 (6.13%)
Health facility delivery	N.A.	
Yes		538 (91.50%)
No		50 (8.50%)
Infant exclusive breastfeeding at 6 weeks after birth	N.A.	N=493
Yes		492 (99.80%)
No		1 (0.20%)
Infant testing at 6 weeks after birth	N.A.	
Yes		570 (97.94%)
No		12 (2.06%)
Composite outcome for PMTCT behaviors (infant testing at 6 weeks, facility delivery, good adherence, undetectable VL at 6wks postpartum)	N.A.	N=374
Yes		261 (69.79%)
No		80 (30.21%)

In bivariate analyses, HIV-positive women participants who received more than four cMM visits during the period of pregnancy and up to 6 weeks postpartum

were more likely to achieve an optimal PMTCT behaviors outcome, consisting of infant testing at 6 weeks, facility delivery, good adherence, and undetectable viral load at 6 weeks postpartum (RR=1.089, p value= 0.034). This relationship also held in the multivariate analysis when adjusted for gestational age and selected sociodemographic and HIV-related characteristics (ARR=1.414, p value= 0.045). The results of bivariate and multivariate analyses are presented in Tables 2 and 3, respectively. We had planned to examine disclosure of HIV status to male partner at the time of delivery for potential mediation; however, there was limited variability in the disclosure variable and we didn't find statistical evidence for this mediation between the cMM visits and the three outcomes.

Table 2
Bivariate analyses

Factor	**Mother's ART adherence at 6 weeks postpartum**		**Mother's undetectable VL at 6 weeks postpartum**		**Composite outcome for PMTCT behaviors** (infant testing at 6 weeks, facility delivery, good adherence, undetectable VL at 6 weeks postpartum)	
	RR*	**p-value**	**RR**	**p-value**	**RR**	**p-value**
# of cMM ANC visit						
≤2	Ref.		Ref.		Ref.	
>2	1.015	0.268	1.082	0.425	1.089	0.425
# of cMM PNC visit						
≤2	Ref.		Ref.		Ref.	
>2	1.017	0.357	1.099	0.390	1.153	0.237
# of total cMM visits						
≤4	Ref.		Ref.		Ref.	
>4	1.022	0.200	1.345	0.091	1.456	**0.034**
Age at baseline						
<25 years	Ref.		Ref.		Ref.	
≥25 years	1.019	0.298	1.177	0.081	0.150	0.111
Gravida						
Primigravid	Ref.		Ref.		Ref.	
≥ 2	--	--	0.969	0.793	0.940	0.607
Weeks of pregnancy when started study						
≤ 28 weeks	Ref		Ref		Ref	
> 28 weeks	1.006	0.670	0.934	0.470	0.937	0.495
Marital status						
Not Married	Ref.		Ref.		Ref.	
Married	1.010	0.700	0.999	0.994	0.961	0.615
HIV at 1st ANC visit						
Newly positive	0.969	0.068	0.966	0.776	0.975	0.844
Known positive	Ref.		Ref.		Ref.	
Partner's HIV status						
Positive	Ref.	0.919	Ref.	0.616	Ref.	0.658
Negative/ Unknown	1.002		1.043		1.037	
Intervention arm						
cMM	Ref.		Ref.		Ref.	
cMM + text messaging	1.011	0.658	0.962	0.757	0.985	0.912

Disclosure to male partner						
Yes	1.033	0.581	1.226	0.485	1.258	0.510
No	Ref.		Ref.		Ref.	
Male partner tested						
Yes	1.002		0.868		0.857	
No	Ref.	0.900	Ref.	0.066	Ref.	0.070

*The relative risk (RR) or risk ratio is the ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group. Relative risk estimates were selected instead of the odds ratios as a more accurate measure for prospective data, and given the high prevalence of the outcome measures.

Table 3
Multivariate analyses

Factor	**Mother's ART adherence at 6 weeks postpartum**		**Mother's undetectable VL at 6 weeks postpartum**		**Composite outcome for PMTCT behaviors (**infant testing at 6 weeks, facility delivery, good adherence, undetectable VL at 6 weeks postpartum)	
	ARR*	**p-value**	**ARR**	**p-value**	**ARR**	**p-value**
# of total cMM visits						
≤4	Ref.	0.177	Ref.	0.121	Ref.	**0.045**
>4	1.025		1.299		1.414	
Age at baseline						
<25 years	Ref.		Ref.		Ref.	
≥25 years	1.024	0.245	1.182	0.063	1.150	0.100
Weeks of pregnancy when started study						
≤ 28 wks	Ref.	0.103	Ref.	0.454	Ref.	0.550
> 28 wks	1.015		0.937		0.951	
Partner's HIV status						
Positive	Ref.		Ref.		Ref.	
Negative/Unknown	1.004	0.810	1.104	0.309	1.091	0.365
Male partner tested						
Yes	0.998	0.807	0.894	0.213	0.885	0.200
No	Ref.		Ref.		Ref.	

*The relative risk (RR) or risk ratio is the ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group. Relative risk estimates were selected instead of the odds ratios as a more accurate measure for prospective data, and given the high prevalence of the outcome measures. Adjusted RR (ARR): the outcomes were adjusted for weeks of pregnancy at the start of the study, given that this variable influenced the duration of time that women had available to receive the stipulated number of cMM visits.

Integration of Qualitative and Quantitative Results

Based on converged data, we identified the following key points related to the impact of cMMs in supporting HIV-positive pregnant/postpartum women: (1) the cMM intervention was utilized and was highly acceptable by women; (2) cMM visits and their activities improved PMTCT behaviors of pregnant/postpartum women, consisting of infant testing at 6 weeks, facility delivery, good adherence, and undetectable viral load at 6 weeks postpartum; and (3) disclosure of HIV status to a male partner might be a promising pathway to improved PMTCT behavior, but this has not been established in this study. Integrated results are presented in Table 4.

Table 4
Side-by-side comparison of qualitative and quantitative results

	Themes	**In-Depth Interviews with cMMs (N=24)**	**Main quantitative dataset (N=589)**
1.	**Acceptability of the cMM intervention**	cMMs felt they were highly acceptable for the following reasons: • Serve as role models & confidantes • Preferred over the facility-based mentor mothers due to privacy, convenience, and dedicated attention	The overall number of cMM visits achieved may indicate high acceptability of the cMM visits. • Participants had, on average, 6.2 cMM visits during pregnancy and up to 6 weeks postpartum. Nearly a third of women completed the intended full dose of 8 visits up to 6 weeks postpartum, 43% had the intended 4 visits during pregnancy, and 73% had the 4 intended postpartum visits.
2.	**CMM activities**	• Supporting acceptance of HIV status & providing encouragement about the potential of having an HIV-negative child • Assisting with partner disclosure/communication • Linking and referring women to HIV care, PMTCT & maternal and child health services	• 96.30% of women reported having disclosed their HIV status to their male partner by the time of the delivery. • 88.7% of women were retained in in the study and HIV care up to 6 weeks postpartum.

		• Providing tangible support (development of birth plans, picking up medications, help with household finances)	
3.	**Effects on PMTCT behaviors**	<u>CMMs reported their clients achieved:</u> • Improved adherence & retention in care • Delivery at a health facility • Infant's HIV testing, adherence to ARV, immunization, safe infant feeding	• Having four or more cMM visits in pregnancy and up to 6 weeks postpartum was associated with achieving a composite outcome for optimal PMTCT behaviors, including infant testing at 6 weeks, facility delivery, good adherence, and undetectable VL at 6 weeks postpartum (ARR=1.414, p=0.045)
4.	**Main mechanisms for the impact of cMM visits on outcomes**	cMMs felt that these were the most important ways that their visits positively impacted outcomes: • Assistance with partner disclosure • Linkage to health services • Provision of health education, • Tangible assistance • Helping women to accept their HIV status	• Disclosure of HIV status to a male partner by the time of the birth was not significantly associated with optimal PMTCT behaviors (RR=1.258, p=0.510), mother's adherence at 6 weeks postpartum (RR=1.033, p=0.581), or maternal undetectable viral load at 6 weeks postpartum (RR=1.226, p=0.485).

Discussion

In this mixed-methods analysis, we explored the experiences, perceptions, and mechanisms through which cMMs provide support for HIV-positive pregnant women in southwestern rural Kenya.

We found that the cMM strategy was perceived as an acceptable and effective intervention in this setting. In our study, cMMs believed that their support to pregnant/postpartum women during the home visits improved maternal and infant outcomes, and perhaps had a bigger impact than facility-based mentor mothers, due to the rapport they build with their clients. In our quantitative analysis, four or more

cMM home visits improved PMTCT behaviors, including infant testing at 6 weeks, facility delivery, strengthened adherence, and undetectable maternal viral load at 6 weeks postpartum.

These results are consistent with current research and practice indicating that the involvement of HIV-infected peer mentors providing PMTCT services in communities and through home visits has multiple positive benefits for pregnant women livng with HIV and their infants, including initiation of pregnant women on ART[133, 134] uptake of PMTCT services and improved retention in care for pregnant WLHW and infants[61, 123, 135-137], as well as other PMTCT behaviors.[55, 127, 138, 139] Services provided by lay health workers have been also linked to increased facility deliveries[140], timely infant diagnosis[107, 121, 123, 133, 135, 141, 142], and exclusive breastfeeding.[141, 143, 144]

However, the literature is inconclusive on the impact of lay community workers on specifically on ART adherence and viral load suppression. While some studies using lay health worker strategies showed improved ART adherence[122, 145], some showed no impact on adherence[123, 145] or retention to care.[134, 146, 147] It is, therefore, not surprising that PLWH community peer support strategies have had mixed results when it comes to viral suppression of pregnant/postpartum women[122, 148], and the MTCT rates.[149] This is consistent with our findings in the qualitative and quantitative phases of the current study. CMMs in their interviews often voiced concern about the early postpartum period, and their ability to deliver the intervention and home visits to the full extent. In the quantitative phase, we were not able to establish a direct impact of cMM visits on ART adherence or viral suppression

at 6 weeks when they were treated as standalone outcome variables, but only when they were included in the composite variable.

Despite many benefits of taskshifting to PLWH lay health workers delivering services in the communities[70], many have raised concerns about intervention attrition rates[61, 146, 148], particularly in the postpartum period[150], as well as a lack of trust in community workers, and lack of fidelity of the intervention.[107, 121, 151, 152] Other studies warn that the low remuneration of community health workers[153] and heavy workload[154] might undermine the delivery of the intervention. The cMMs interviewed in the study also perceived limited funding for their communication and transportation needs, the intensity of the intervention, unpredictable work outside of the normal schedule, and cultural barriers/myths as major challenges to the success of this intervention.

On the other hand, this study also shows how committed and personally invested in the delivery of this intervention the cMMs become, and that the delivery of the intervention also has a positive impact on their own ART adherence and retention in care, as well as self-empowerment. Other studies show how WLWH are motivated during their pregnancy and postpartum and perceive reduced stigma related to their HIV status based on the openness and acceptance of HIV status by their peer mentors.[135] In some cases, community health workers become so involved with the WLWH they support that they continue delivering the intervention despite the fact that the study ends.[153] Many have also brought attention to potential negative impacts on those delivering services, particularly inadvertent disclosure of their own status and stigma, and by extension inadvertent disclosure of clients. Concerns over

confidentiality and status disclosure to a male partner and community while delivering community intervention have been well-documented.[128] As in the MOTIVATE! Trial, numerous programs do not have community workers wear a uniform indicated that they are from the HIV clinic, in order to protect their community workers and clients served.[134, 153] It appears that the mixed findings of the impact of PLWH peer community-based mentors might be greatly affected by the degree of fidelity with which the intervention is ultimately delivered, due to these challenges.

In this study, we did not detect a direct effect of the HIV status disclosure to a male partner on good PMTCT behaviors despite the existing evidence that disclosure positively affects uptake and retention in care for HIV-positive pregnant/postpartum women.[130-132] Building on our own work[155], several other reports from Kenyan and other Southern African sites, we speculate that the HIV status disclosure to a male partner is complex and might have bidirectional effects. While for some women and their infants, this disclosure results in a positive outcome, social support, adherence, reduced stigma, and decreased MTCT[156, 157], for some, it might result in conflict, blame, intimate partner violence, or being chased away, particularly in complex relationships, e.g., polygamous marriage, a common relationship type in this area.[155, 158, 159] Additionally, our data were based on the self-reported disclosure to a male partner at clinic visits and showed an unexpectedly high level of disclosure compared to other surveys and studies conducted in this area.[135, 160-162] It is possible that true disclosure levels are lower those reported at the antenatal clinics, due to social desirability bias. It is also possible that even low doses of the cMM

intervention (<4 visits) were enough to support very high levels of male partner disclosure by the time that the women gave birth. Since virtually all the women in the current analysis received some dose of the cMM intervention, we were unable to compare disclosure levels with those for women who did not receive any cMM visits.

The robustness and potential applicability of these results to similar settings across SSA were strengthened by mixed-methods study design, nesting the study within a the 2x2 randomized clinical trial, a relatively large sample size consisting of both women on ART prior to the index pregnancy and newly diagnosed HIV-positive women, recruitment from 24 clinics in three counties in southwestern Kenya, and longitudinally observed cohort throughout the pregnancy and up to 6 weeks postpartum. However, the study results should be considered within the context of some limitations and possible biases. The study recruited pregnant women visiting antenatal clinics who meet additional eligibility criteria (≥18 years, have access to a mobile phone and have disclosed their HIV status to any person sharing the phone, and are willing to have home visits). Thus, women enrolled in the study might be inherently different from women who do not utilize antenatal care or did not meet the other eligibility criteria. Quantitative data were abstracted from medical records that lack detailed sociodemographics, social and psychosocial variables that are know to play an important role in PMTCT outcomes, and adherence to care (e.g., poverty, mental health issues, intimate partner violence, other medical conditions). Some information in the medical records, such as disclosure to the male partner or self-reported adherence are subject to recall and social desirability bias. Additionally, the study was conducted in the context of frequent changes to policies and standard care

provision, as well as service disruptions due to adverse weather conditions and health worker strikes.

Conclusions

Kenya, similar to other countries, is in need of innovative approaches to overcome challenges associated with the scale-up of lifelong ART services for pregnant and postpartum women. This study suggests that a cMM strategy may play an important role in enhancing PMTCT as well as maternal and child health in Kenya, and may also have positive effects on the cMMs themselves.

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Ethical Approvals

Ethical approval was obtained from the Kenya Medical Research Institute (KEMRI) Scientific and Ethical Review Unit (SERU), the University of Colorado, Denver Institutional Review Board, and the University of Alabama at Birmingham

Institutional Review Board. All participants provided their written informed consent and were reimbursed for travel or other expenses related to study participation.

CONCLUSIONS AND FUTURE DIRECTIONS

Under the current Kenyan guidelines[48] and WHO recommendations[4, 118], pregnant and postpartum women who test HIV-positive, are immediately put on the lifelong ART therapy (Option B+) and are initiated into the PMTCT protocol. ART initiation [118] immediately upon diagnosis and as early in pregnancy as possible increases a chance of viral suppression by the time of delivery and thus decreases the likelihood of passing HIV to an infant. However, gaps at each step of the PMTCT continuum (uptake of HIV testing for women and infants, linkage to ART treatment, initiation, adherence, and retention) undermine the positive impact of lifelong ART.[21] Challenges at the individual, interpersonal, community, and health facility levels contribute to these gaps.

The most important biomedical indicator of ART adherence is viral load testing. Under the current national guidelines in Kenya, pregnant WLWH should receive viral load monitoring at confirmation of pregnancy (if already on ART) or 6 months after ART initiation, and then every 6 months thereafter until the complete cessation of breastfeeding.[48] Non-suppressed viral load results obtained in time prior to the delivery could introduce changes to the ART regimen in time for an intervention for women's well-being and reduces the chance of MTCT.[35] Viral load suppression can also as an indicator for the clinician and the patient that the ART regimen is in fact "working" and effective.

In addition to biomedical treatment, behavioral interventions supporting adherence to ART and retention in care, are being tested and implemented across

sub-Saharan Africa. One such intervention is the community-based mentor mother (cMM) program, designed and tested under a MOTIVATE! randomized clinical trial.[100] The cMM program embodies many attributes recommended by WHO, namely taskshifting support of pregnant/postpartum WLWH to lay community workers and utilization of peer mentors living with HIV.[53-55, 57, 119]

Taken together, the three manuscripts comprising this dissertation were based on research that used qualitative and quantitative methods with the aims of 1) understanding challenges to implementation of the lifelong ART (Option B+) for pregnant and postpartum WLWH in southwestern rural Kenya at the health care facility level; 2) evaluating the implementation and potential challenges related to the important PMTCT service of viral load testing during pregnancy and postpartum; and 3) examining the potential effectiveness at the cMM program in addressing challenges related to adherence and retention in care. The first aim used qualitative data from individual in-depth interviews with Kenyan pregnant and postpartum WLWH women (N=20) and male partners (N=20), as well as from four focus groups with health care providers (N=30). The second aim was completed using analysis of longitudinal data extracted from medical records for a cohort of PWLWH participants in the MOTIVATE! Study (N=1,165) during pregnancy and up to 12 months postpartum. The third aim used a convergent parallel mixed-method design and utilized an adapted conceptual framework for the role of community health workers in facilitating patients' adoption of health behaviors[69], integrating qualitative data from in-depth interviews with cMMs (N=24) who delivered the cMM intervention to a cohort of pregnant and postpartum WLWH, and longitudinal medical data of

pregnant and postpartum WLWH randomized into a cMM intervention study arm of the MOTIVATE! Study (N=589) and their infants.

The main challenges that were identified during the in-depth interviews with pregnant and postpartum women, male partners, and skilled and lay health care providers providing Option B+ services and summarized in paper #1 included: Option B+ specific challenges (same-day initiation on a lifelong ART, health care providers doubting the benefits of Option B+, insufficient training); facility resource constraints (staff/drug shortages, long queues, space limitations); and lack of client-friendly services (scolding of patients, inconvenient operating hours, lack of integration of services, administrative requirements).[71]

Barriers related to the implementation of viral load testing guidelines in the cohort of pregnant and postpartum women in paper #2 further emphasized barriers in the provision and monitoring of lifelong ART. Although the results of paper #2 indicated that fidelity to national testing guidelines was associated with sustained undetectable viral load during pregnancy and up to 12 months postpartum, the literature and our research show show that many WLWH are not tested according to the national guidelines and importantly are not getting viral load testing at crucial times during pregnancy and breastfeeding.[48] Furthermore, as we have shown in paper #2, only about 3 out of 4 women in our cohort achieved sustained viral suppression, and only just over half of WLWH achieved undetectable sustained viral load over the observation period. Yet, viral suppression and undetectable viral loads are crucial to prevent MTCT.[35]

In the environment of 'Treat All' approach to PLWH and the increasing demands on the healthcare and laboratory systems[32, 34], it is pertinent to ensure that VL testing for pregnant, postpartum, and breastfeeding women are prioritized as a critical population. These women have limited time for response to an elevated viral load during pregnancy/postpartum in time to reduce the risk of MTCT.[35, 36] It is therefore crucial to identify the opportunities and gaps at all levels, including persisting systematic barriers and gaps in the viral load testing protocols and practices at the health system level for this vulnerable group, as well as develop approaches to address suboptimal adherence and barriers at the individual level. Furthermore, it is pertinent to identify the sub-groups of PWLWH that are particularly vulnerable when it comes to the lack of retention in HIV care, sub-optimal adherence to ART, and an increased risk of viremia, and develop effective approaches of support for these sub-groups.

Our findings in all three papers suggest that the most vulnerable sub-groups of pregnant and postpartum women might include younger women, women who have not disclosed their HIV status to their male partners, and women newly tested with HIV during pregnancy. Among women with a known HIV-positive status prior to the pregnancy, the more vulnerable women were those with history of viremia, less engagement in HIV care, and who are on a second-line ART regimen. In our paper #2 focusing on viral load testing, significantly fewer newly diagnosed women had a viral load test performed during the pregnancy, compared to women diagnosed prior to this. Also, women who tested in the first trimester of the index pregnancy were more

likely to achieve sustainable undetectable viral load during the observation period (pregnancy and up to 12 months postpartum). However, according to the current guidelines, given that newly diagnosed women during pregnancy do not have their first viral load measurement until 6 months after their diagnosis, many newly initiated women give birth prior to their first viral load test. Pregnant WLWH, who were not virally suppressed during pregnancy, had a significantly lower chance of achieving undetectable VL at 12 months postpartum.

Multi-level strategies to overcome some of these challenges and address those most at risk of MTCT have been suggested by our participants in qualitative in-depth interviews and focus groups (pregnant/postpartum WLWH, male partners, and health care providers) at various levels according to the socioecological model, as well as implied in our quantitative findings. At the individual client level, suggested strategies for engagement in care and PMTCT continuum included continuous adherence counseling, assisted disclosure, incentive programs, couple testing, treatment buddies, and support groups. Community strategies included reduction of stigma, use of community health care workers, health education, and increased awareness. Suggested approaches at the health care facility level were centered around the concept of reduction of stigmatizing attitudes of providers, and increasing confidentiality, privacy, and convenience for clients, as well as integrating ART with other services, privacy for individual and couple counseling, convenient clinic hours, ensuring shorter waiting times, appropriate staffing and health care personnel training, elimination of administrative barriers, consistent drug supply, and promotion of positive patient-provider relationships.[71]

We hypothesized that the cMM intervention is an acceptable and effective strategy that may increase linkage, retention, and adherence to life-long ART treatment for pregnant HIV-positive women in Kenya. This strategy may be successful at addressing barriers related to women's uptake of PMTCT services and Option B+, linking women with healthcare services, and addressing women's challenges related to uptake of HIV care and viral load testing in this population identified in all three papers.

Integrated results of paper #3 based on the qualitative and quantitative results revealed that the cMM services are acceptable to WLWH and their male partners, as well as the health care providers. In relation to the barriers identified in papers 1 and 2, at the individual level cMMs provide continuous individual and couple support, assist with the acceptance of HIV diagnosis, help with partner disclosure, strengthen the hope that it's possible to prevent transmission of HIV to your infant if you adhere to treatment, provide continuous adherence counseling, and emphasize the need for viral suppression and engagement in care. They also inspire women to come to terms with and become 'free' with their HIV status and challenge stigma. Additionally, cMMs help WLWH to navigate facility resource constraints, skip long waiting lines, help with referrals, and administrative paperwork, and sometimes deliver ARVs to WLWH.

cMMs seemed to be preferred over the facility-based mentor mothers by WLWH due to their assurance of privacy, convenience, and dedicated attention. At the healthcare facility level, cMMs help reduce the impact of staff shortages, helping with tasks around the clinic. cMMs also relate to their clients not only as a

knowledgeable health provider but also as a peer with a shared experience. As such, cMMs may provide an alternative to what is often perceived as a lack of friendly services at clinics. CMMs pride themselves on being 'on-call' 24 hours/7 days a week, always just a phone call/text away. They schedule the home visits with WLWHs when it's convenient for pregnant and postpartum women.

In paper #3, we utilized an adapted conceptual framework for the role of community health workers in facilitating patients' adoption of health behaviors[69]. The quantitative analysis revealed that having at least half of the eight recommended cMM home visits during pregnancy and up to 6 weeks postpartum was associated with improved composite outcome for PMTCT behaviors, consisting of facility delivery, infant testing, good adherence, and undetectable viral load at six weeks postpartum. The model presented in paper #3 summarizes the most crucial components of cMM's role in facilitating healthy PMTCT behaviors of PWLWH and suggests possible pathways for this impact. In our study, cMMs described providing social support, leveraging cultural congruence, sharing PMTCT/ART experience, and having good interpersonal communication with WLWH, which led to building a trusting relationship and rapport to assist PWLWH with adopting healthy PMTCT behaviors. Good PMTCT behaviors were believed to, in turn, result in a reduction of adverse health and PMTCT outcomes, increased community capacity, and to have positive effects on cMMs themselves.

cMMs believed that one of the most important pathways to good PMTCT behaviors was through the women's disclosure of their HIV status to a male partner.

Even though the quantitative analyses did not reveal a significant association between disclosure by the time of the birth and good PMTCT behaviors, we speculate that the HIV status disclosure to a male partner is complex and might have bidirectional effects, resulting in a positive outcome, social support, adherence, reduced stigma, and decreased MTCT for some[156, 157], but resulting in conflict, blame, intimate partner violence, or being chased away for others.[155, 158, 159] Additionally, our data were based on the self-reported disclosure to a male partner at clinic visits and might, therefore, be over-reported.[135, 160-162] It is also possible that even low doses of the cMM intervention were sufficient to support very high levels of male partner disclosure by the time of delivery.

Another crucial point is the fidelity of the cMM intervention. Our analysis in paper #3 revealed that only about a third of women completed the intended full dose of eight visits up to 6 weeks postpartum, only 43% had the intended four visits during pregnancy, and only 73% had the intended four cMM visits between delivery and six weeks postpartum. It is possible that if all women had received the full dose of visits the impact on healthy PMTCT behaviors would have been higher. Additionally, the extent to which the delivery of the cMM intervention content was complete, standardized, and consistent is unclear.

The robustness and extrapolation of the study results to a similar setting across SSA were strengthened by triangulation of results utilizing qualitative and quantitative methods, in which we integrated 1) perspectives of health care providers, pregnant and postpartum women, and their male partners on the healthcare facility

level challenges in the provision of Option B+, as well as perspectives of cMMs on the support of pregnant and postpartum WLWH in the context of a lifelong ART therapy; and 2) longitudinal medical record data from a large sample of women on ART prior to the index pregnancy and newly diagnosed HIV-positive women, and their infants, who were recruited from 24 clinics in three counties in southwestern Kenya, and followed during pregnancy and up to 12 months postpartum.

However, the study results should be considered within the context of some limitations and possible biases. Views on acceptability of same-day initiation of ART among patients based on individual interviews in the formative part of the MOTIVATE! Study (paper #1) might have been influenced by the characteristics of the sample. Female client participants in this study had agreed to HIV testing and disclosure of HIV status to their partner. Thus, their perception might be different from women who were not tested, women who have not disclosed their status, women who have not utilized antenatal/postnatal care or are categorized as non-starters. In the randomized part of The MOTIVATE! Study in which we tested the effectiveness of the interventions, we utilized data from pregnant WLWH visiting antenatal clinics who met study eligibility criteria (≥18 years, have access to a mobile phone and have disclosed their HIV status to any person sharing the phone, and are willing to have home visits). Thus, women enrolled in the study might be inherently different from women who do not utilize antenatal care or did not meet the other eligibility criteria. Quantitative data were abstracted from medical records that lack detailed sociodemographics, social and psychosocial variables that are known to play an important role in PMTCT outcomes, and adherence to care (e.g., poverty, mental

health issues, intimate partner violence, other medical conditions). Some information in the medical records, such as disclosure to the male partner or self-reported adherence are subject to recall and social desirability bias. Additionally, health facilities were not always able to achieve sufficient VL monitoring for many women at key time points (around 12 months postpartum), resulting in missing data on viral loads. This study represents three counties in predominantly rural southwestern Kenya, and results might not be generalizable to other communities in Kenya or other parts of sub-Saharan Africa. Additionally, this project was conducted in the context of frequent changes to policies and standard care provision, as well as service disruptions due to adverse weather conditions and health worker strikes.

This dissertation revealed important challenges related to the provision of a lifelong ART (Option B+) for pregnant and postpartum women in southwestern Kenya at the health care facility, community, and individual levels. Significant gaps also exist in viral load testing, the biomedical measure of ART adherence, and the effectiveness of treatment. Large proportions of women are not getting viral load measurements at crucial times during pregnancy and breastfeeding, and do not have viral load testing according to current Kenyan guidelines. Improved follow up of WLWH, but particularly sub-groups of these women most at risk; i.e., younger women, women newly diagnosed with HIV and immediately initiated on a lifelong ART, those who have not disclosed their status to their male partner, and women with a history of viremia, less engagement in HIV care, and those on a second-line ART regimen; is urgently needed. A comprehensive approach, biomedical and behavioral,

is crucial to reach the ultimate goal, reduced and potentially eliminated MTCT and improvements in maternal health. This study suggests that a cMM strategy may play an important role in enhancing PMTCT behaviors in the crucial early postpartum period, and may also address barriers related to provision of the Option B+ and viral load testing uptake. Addressing these specific challenges may increase linkage, retention, and adherence to life-long ART treatment for pregnant HIV-positive women in Kenya, contribute towards the elimination of mother-to-child HIV transmission, and improve maternal and child outcomes.

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APPENDIX A
INSTITUTIONAL REVIEW BOARD APPROVAL

OMB No. 0990-0263
Approved for use through 3/31/2015

Protection of Human Subjects
Assurance Identification/IRB Certification/Declaration of Exemption
(Common Rule)

Policy: Research activities involving human subjects may not be conducted or supported by the Departments and Agencies adopting the Common Rule (56FR28003, June 18, 1991) unless the activities are exempt from or approved in accordance with the Common Rule. See section 101(b) of the Common Rule for exemptions. Institutions submitting applications or proposals for support must submit certification of appropriate Institutional Review Board (IRB) review and approval to the Department or Agency in accordance with the Common Rule.

Institutions must have an assurance of compliance that applies to the research to be conducted and should submit certification of IRB review and approval with each application or proposal unless otherwise advised by the Department or Agency.

1. Request Type	2. Type of Mechanism	3. Name of Federal Department or Agency and, if known, Application or Proposal Identification No.
[X] ORIGINAL [ ] CONTINUATION [ ] EXEMPTION	[X] GRANT [ ] CONTRACT [ ] FELLOWSHIP [ ] COOPERATIVE AGREEMENT [ ] OTHER:_____	
4. Title of Application or Activity Maximizing Adherence and Retention in Women and Infants in the Context of Option B+ in Kenya		5. Name of Principal Investigator, Program Director, Fellow, or Other TURAN, JANET M

6. Assurance Status of this Project *(Respond to one of the following)*

[X] This Assurance, on file with Department of Health and Human Services, covers this activity:
Assurance Identification No. FWA00005960 , the expiration date 01/24/2017 IRB Registration No. IRB00000726

[ ] This Assurance, on file with *(agency/dept)*_____, covers this activity.
Assurance No._____, the expiration date_____ IRB Registration/Identification No._____*(if applicable)*

[ ] No assurance has been filed for this institution. This institution declares that it will provide an Assurance and Certification of IRB review and approval upon request.

[ ] Exemption Status: Human subjects are involved, but this activity qualifies for exemption under Section 101(b), paragraph_____.

7. Certification of IRB Review (Respond to one of the following IF you have an Assurance on file)

[X] This activity has been reviewed and approved by the IRB in accordance with the Common Rule and any other governing regulations.
by: [ ] Full IRB Review on (date of IRB meeting) _____ or [X] Expedited Review on (date) 8-13-14
[ ] If less than one year approval, provide expiration date _____

[ ] This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by the Common Rule will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

8. Comments	Title X140408002
Protocol subject to Annual continuing review.	Maximizing Adherence and Retention in Women and Infants in the Context of Option B+ in Kenya

IRB Approval Issued: 8-13-14 IRB Approval No Longer Valid On: 8-13-15

9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided.	10. Name and Address of Institution University of Alabama at Birmingham 701 20th Street South Birmingham, AL 35294
11. Phone No. *(with area code)* (205) 934-3789 12. Fax No. *(with area code)* (205) 934-1301 13. Email: irb@uab.edu	
14. Name of Official Marilyn Doss, M.A.	15. Title Vice Chair, IRB
16. Signature Marilyn Doss	17. Date 8-13-14

Authorized for local Reproduction — Sponsored by HHS

According to the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0990-0263. The time required to complete this information collection is estimated to average 30 minutes per response. If you have comments concerning the accuracy of the time estimate(s) or suggestions for improving this form, please write to: U.S. Department of Health & Human Services, OS/OCIO/PRA, 200 Independence Ave., S.W., Suite 336-E, Washington D.C. 20201. Attention: PRA Reports Clearance Officer.

Project Revision/Amendment Form

Form version: June 26, 2012

In MS Word, click in the white boxes and type your text; double-click checkboxes to check/uncheck.

- **Federal regulations require IRB approval before implementing proposed changes. See Section 14 of the IRB Guidebook for Investigators for additional information.**
- **Change means any change, in content or form, to the protocol, consent form, or any supportive materials (such as the Investigator's Brochure, questionnaires, surveys, advertisements, etc.). See Item 4 for more examples.**

1. Today's Date	10/14/2014	7446

2. Principal Investigator (PI)

Name (with degree)	Janet M. Turan	**Blazer ID**	jmturan
Department	Health Care Organization and Policy	**Division (if applicable)**	
Office Address	1665 University Boulevard, Birmingham, AL 35294	**Office Phone**	(205) 934-6780
E-mail	jmturan@uab.edu	**Fax Number**	(205) 934-3347

Contact person who should receive copies of IRB correspondence (Optional)

Name	Paula Garman	**E-Mail**	garman@uab.edu
Phone	(205) 934-6780	**Fax Number**	(205) 934-3347
Office Address (if different from PI)	**Same as PI**		

3. UAB IRB Protocol Identification

3.a. Protocol Number	X140408002
3.b. Protocol Title	Maximizing Adherence and Retention in Women and Infants in the Context of Option B+ in Kenya

3.c. Current Status of Protocol—Check ONE box at left; provide numbers and dates where applicable

- ☐ **Study has not yet begun** — **No participants, data, or specimens have been entered.**
- ☒ **In progress, open to accrual** — **Number of participants, data, or specimens entered:** 29
- ☐ **Enrollment temporarily suspended by sponsor**
- ☐ **Closed to accrual, but procedures continue as defined in the protocol (therapy, intervention, follow-up visits, etc.)**
  - **Date closed:**
  - **Number of participants receiving interventions:**
  - **Number of participants in long-term follow-up only:**
- ☐ **Closed to accrual, and only data analysis continues**
  - **Date closed:**
  - **Total number of participants entered:**

4. Types of Change

Check all types of change that apply, and describe the changes in Item 5.c. or 5.d. as applicable. To help avoid delay in IRB review, please ensure that you provide the required materials and/or information for each type of change checked.

- ☐ **Protocol revision (change in the IRB-approved protocol)**
  In Item 5.c., if applicable, provide sponsor's protocol version number, amendment number, update number, etc.
- ☐ **Protocol amendment (addition to the IRB-approved protocol)**
  In Item 5.c., if applicable, provide funding application document from sponsor, as well as sponsor's protocol version number, amendment number, update number, etc.
- ☒ **Add or remove personnel**
  In Item 5.c., include name, title/degree, department/division, institutional affiliation, and role(s) in research, and address whether new personnel have any conflict of interest. See "Change in Principal Investigator" in the IRB Guidebook if the principal investigator is being changed.
  - ☐ **Add graduate student(s) or postdoctoral fellow(s) working toward thesis, dissertation, or publication**
    In Item 5.c., (a) identify these individuals by name; (b) provide the working title of the thesis, dissertation, or publication; and (c) indicate whether or not the student's analysis differs in any way from the purpose of the research described in the IRB-approved HSP (e.g., a secondary analysis of data obtained under this HSP).
- ☐ **Change in source of funding; change or add funding**
  In Item 5.c., describe the change or addition in detail, include the applicable OSP proposal number(s), and provide a copy of the application as funded (or as submitted to the sponsor if pending). Note that some changes in funding may require a new IRB application.

☐ **Add or remove performance sites**
In Item 5.c., identify the site and location, and describe the research-related procedures performed there. If adding site(s), attach notification of permission or IRB approval to perform research there. Also include copy of subcontract, if applicable. If this protocol includes acting as the Coordinating Center for a study, attach IRB approval from any non-UAB site added.

☐ **Add or change a genetic component or storage of samples and/or data component—this could include data submissions for Genome-Wide Association Studies (GWAS)**
To assist you in revising or preparing your submission, please see the IRB Guidebook for Investigators or call the IRB office at 934-3789.

☐ **Suspend, re-open, or permanently close protocol to accrual of individuals, data, or samples (IRB approval to remain active)**
In Item 5.c., indicate the action, provide applicable dates and reasons for action; attach supporting documentation.

☐ **Report being forwarded to IRB (e.g., DSMB, sponsor or other monitor)**
In Item 5.c., include date and source of report, summarize findings, and indicate any recommendations.

☐ **Revise or amend consent, assent form(s)**
Complete Item 5.d.

☐ **Addendum (new) consent form**
Complete Item 5.d.

☐ **Add or revise recruitment materials**
Complete Item 5.d.

☐ **Other (e.g., investigator brochure)**
Indicate the type of change in the space below, and provide details in Item 5.c. or 5.d. as applicable.
Include a copy of all affected documents, with revisions highlighted as applicable.

▶

5. Description and Rationale

In Item 5.a. and 5.b, check Yes **or** No **and see instructions for** Yes **responses.**
In Item 5.c. and 5.d, describe—and explain the reason for—the change(s) noted in Item 4.

☐Yes ☐No **5.a. Are any of the participants enrolled as normal, healthy controls?**
If yes, describe in detail in Item 5.c. how this change will affect those participants.

☐Yes ☐No **5.b. Does the change affect subject participation, such as procedures, risks, costs, location of services, etc.?**
If yes, FAP-designated units complete a FAP submission and send to fap@uab.edu. Identify the FAP-designated unit in Item 5.c.
For more details on the UAB FAP, see www.uab.edu/cto.

5.c. Protocol Changes: In the space below, briefly describe—and explain the reason for—all change(s) to the protocol.

Addition of Personnel:
Full Name: Anna Helova ✓ Added in SIRB. ckw
Degree(s)/Job Title: DrPH Candidate
Primary UAB Dept: Department of Health Care Organization and Policy, School of Public Health
Institution Affiliation: University of Alabama at Birmingham
Role in Research: Research Assistant to Dr. Turan
Additional Qualifications Pertinent to the Study: Mrs. Helova is a research assistant to Dr. Turan. She is a DrPH student at the University of Alabama at Birmingham. During coursework for her master's degree and relevant work experience in health care organization and policy and public health in general, she developed a research and managerial foundation in all aspects of conduct of clinical trials including 20 clinical trials under the four NIH/DAIDS funded HIV/AIDS networks: Microbicides Trials Network, Prevention Trials Network, International Maternal Pediatric Adolescent AIDS Clinical Trials Group and AIDS Clinical Trials Group; management of service projects under the CDC sponsored Prevention of Mother-To-Child Transmission (PMTCT) project, and other projects including but not limited to PMTCT Cost Effectiveness Analysis and Antiretroviral Therapy Cost Effectiveness Analysis, projects under the general umbrella of President's Emergency Plan for AIDS Relief; and management of Fogarty sponsored HIV/AIDS related training programs.

Conflict of Interest:
Name: **Anna Helova – None of the below apply**
Do you or your immediate family have any of the following? (check all that apply)
☐ An ownership interest, stock options, or other equity interest related to the investigator's responsibilities of any value.

☐ Compensation related to the research unless it meets two tests:
- Less than $5,000 in the past year when aggregated for the immediate family.
- Amount will not be affected by the outcome of the research.

☐ Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright, or licensing agreement.

☐ Board of executive relationship related to the research, regardless of compensation.

5.d. Consent and Recruitment Changes: In the space below,
(a) describe all changes to IRB-approved forms or recruitment materials and the reasons for them;
(b) describe the reasons for the addition of any materials (e.g., addendum consent, recruitment); and
(c) indicate either how and when you will reconsent enrolled participants or why reconsenting is not necessary (not applicable for recruitment materials).

Also, indicate the number of forms changed or added. For new forms, provide 1 copy. For revised documents, provide 3 copies:
- **a copy of the currently approved document (showing the IRB approval stamp, if applicable)**
- **a revised copy highlighting all proposed changes with "tracked" changes**
- **a revised copy for the IRB approval stamp.**

▶

Signature of Principal Investigator Janet M. Turan Date 10/14/2014

FOR IRB USE ONLY

☐ Received & Noted ☑ Approved Expedited* ☐ To Convened IRB

Signature (Chair, Vice-Chair, Designee) Date 10/16/14

DOLA 8-13-14

Change to Expedited Category **Y / N / NA**

*No change to IRB's previous determination of approval criteria at 45 CFR 46.111 or 21 CFR 56.111

APPENDIX B
IN-DEPTH INTERVIEW GUIDE, COMMUNITY MENTOR MOTHERS

I. INTRODUCTION

My name is _____. I am working with the Kenya Medical Research Institute, the University of Colorado, Denver, and the University of Alabama at Birmingham in the United States on a project aiming to improve HIV services in Kenyan communities. We would like to talk to you about your perceptions of prevention of mother-to-child transmission of HIV, HIV treatment for mothers, and your experiences as a community Mentor Mother (cMM). Everything you share during this interview will be kept confidential and we will not share your name or other information that will identify you if results of the study are discussed with anyone outside the research team afterwards or published. The information that you provide will be used to inform efforts to strengthen and improve health services in Kenya.

Remember, you don't have to talk about anything you don't want to and you may end the interview at any time. This interview will take around one and a half hours. If you have questions you want to ask on other topics, I can assist you to find answers after the interview is over.

(***Go through the informed consent form for in-depth interview participants out loud*** and give the participant a copy. If she agrees to participate, ask her to sign the informed consent form. Complete the participant characteristics form. Ask permission to tape record the discussion, and if she agrees, start the tape recorder AFTER the completion of the participant characteristics form and the introductions part of the discussion. This guide includes the topics to be covered and questions that may be helpful in facilitating the interview. You do NOT have to ask all the questions or follow the order given in the guide.)

II. DISCUSSION TOPICS

A. Experiences working as a mentor mother and acceptability of mentor mothers

1. Can you tell me about what you do in your job as a cMM? Can you tell me the story of a typical day on your job? (Or tell me what you did on your most recent day of work?)
2. What different types of services do you provide as a cMM? How does this differ from what Mentor Mothers based at health facilities do?
3. What do you think about mentor mothers being based directly in the community instead of at the health facility where they are usually based? What are advantages? What are the disadvantages?
4. What do you think about mentor mothers being based directly in their own community instead of a different community? What are advantages? What are the disadvantages?
5. Can you tell me about impact you think you have on your clients (pregnant and postpartum women living with HIV)? What changes do they experience (if any) as a result of your services?

6. Can you tell me a story about a positive experience you had or a positive outcome you experienced in your job as a community mentor mother?
7. Can you tell me a story about a negative or challenging experience or a negative outcome you experienced in your job as a community mentor mother?
8. What are the challenges you face in your work as a cMM?
9. Are you experiencing any transportation and time challenges in your job as a cMM? How far and how do you travel to the clients' homes?
10. What are the challenges you face in your work as a cMM from the community? (Also probe for apparel challenges, language related challenges.)
11. What are the challenges you face in your work a cMM from pregnant women? From male partners or other family members?
12. Have women you are visiting generally disclosed their HIV status to their male partner and other family members? How do you handle non-disclosure situation? Are you participating in disclosure process? Do you perceive this to be a barrier in your work?
13. What are the challenges you face in your work a cMM from health workers and community health workers? From other sources?
14. Are there any aspects of your job that are unclear, or times that you are not sure exactly what you are supposed to be doing or handling certain situations?
15. What type of characteristics or skills do you think community mentor mothers need in order to be successful at their job?
16. What do community mentor mothers need to be careful about when working in the community?

B. Personal experiences with being a community mentor mother

1. Tell me about yourself. What did you do before you started working as a community mentor mother?
2. How did you come to apply for this job? Why were you interested?
3. If you feel comfortable, can you share with me your experience of being diagnosed with and living with HIV?
    i. What were your experiences regarding pregnancy and HIV and PMTCT?
    ii. How are you managing with your ART adherence and HIV clinic visits currently?
4. How has working as a cMM affected you personally? (Suggested probes: positively, negatively; financially, community relationships, family, empowerment, status, etc.)
5. Do you live in the community where you work as a cMM? How does where you live affect your work as a cMM?
6. How do people in the community where you are working receive you personally when conducting your job as a community mentor mother?
    i. When you are doing a home visit?
    ii. When you are doing other tasks in the community?

iii. Can you tell me about any negative reactions you have had? (Probe for stigma, unwanted disclosure, avoidance/shunning, and other potential negative reactions.)
iv. Can you tell me about any positive reactions you have had?

7. How is your communication with the pregnant/postpartum women? Are they able to open up and share with you? How much do you generally share from your own life/experiences?
8. How many women are you currently working with?
9. Of those how many do you visit at home and how many at a location other than home? For women who don't want you to visit their homes, what are the reasons?
10. Please tell me about your relationships and experience with health care workers at the health facility. What about experiences with other community workers (such as CHWs, CHeWs, etc.)?
11. How is it going using the mobile phones to enter information about your clients and the home visits? Are there any challenges?
12. Is there any further training or knowledge you wish you had to work more effectively as a community mentor mother? Are there any questions that women/men ask that you are unable to answer? What do you do in those situations? Are there any resources provided to you that have been particularly helpful in your work? (PMTCT flip charts, adherence materials.)

C. Option B+ compared to PMTCT prophylaxis regimens

1. What do you think about Option B Plus in which HIV-infected pregnant women begin HIV medications (ART) for their own health during pregnancy and continue taking them for life?
2. How have you observed the uptake and implementation of Option B Plus among the women you serve as a cMM?
3. What are the advantages of Option B+? What about the disadvantages?
4. What do you think about the same day initiation into treatment after testing HIV positive at the prenatal visit?
5. Do you think it is difficult to continue the ARV medications after you stop breastfeeding? Why or Why not?
6. Why do you think the pregnant women in the community where you work might find it challenging to continue the medications after they stop breastfeeding? What are the reasons?
7. What do you think husbands/male partners think about women continuing ARV medications lifelong? Reasons? Other family members?
8. Overall, what do you think about taking ART medications for the rest of your life, even if you are not feeling sick? What do the pregnant women you serve in the community think about this?

D. Suggestions for improving the cMM Program

1. What are your suggestions for improving the cMM program?

2. Suggestions for making the work easier or more achievable for cMMs?
3. Suggestions for increasing the benefits for pregnant women and infants? Ways to better support their longterm ART adherence and retention in care?

III. CLOSING

Thank you very much for your time. Your responses will be very helpful for improving the health of Kenyan families.

(Correct any important misconceptions and provide referrals to services or support, if appropriate.)

In-depth interview participant characteristics form

OPTION B+ STUDY QUALITATIVE IN-DEPTH INTERVIEWS PARTICIPANT CHARACTERISTICS FORM

PARTICIPANT CHARACTERISTICS FORM FOR IN-DEPTH INTERVIEWS

Study ID#	
Name of community / health facility where recruited	
Age	
Birth place	
Educational level (Circle one)	1. Less than primary 2. Completed primary 3. Some secondary 4. Completed secondary 5. More than secondary
Marital status (Circle one)	1. Single, never married 2. Married 3. Widowed/divorced/separated
Currently living with a spouse/partner? (Y/N)	
Type of relationship (Circle one)	1) Monogamous 2) Polygamous
Type of partnership with spouse/partner (Circle one)	1) Concordant 2) Discordant
Religion	
Number of living children	
Other notes	