Engaging Male Partners in Home-based Couple Education and Testing for Syphilis and HIV

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A dissertation
submitted in partial fulfillment of the
requirements for the degree of

Doctor of Philosophy

University of Washington
2019

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Program Authorized to Offer Degree:
Public Health-Epidemiology

University of Washington

Abstract

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For HIV and other sexually transmitted infections (STIs), men seek care at more advanced stages of disease and are less likely to initiate treatment.[1-4] Male partner participation in antenatal care (ANC) has been shown to increase male and female HIV testing,[5,6] identification of HIV-discordant couples,[7,8] female participation in ANC and uptake of PMTCT services[1,9] as well as reduce infant HIV acquisition and mortality.[10] Despite these significant benefits, rates of male attendance to clinic-based antenatal services remain very low.[1,2],[11] in part because efforts to engage men have focused on reducing HIV transmission risks to mothers and children without directly addressing the sexual health needs of men. Advocating for the health of fathers as equally important and reframing men as positive contributors to the health of the family shifts the balance from a maternal and child health approach to a family health approach that addresses HIV and STI control within the larger community.[12]

The advent of rapid and inexpensive point-of-care (POC) tests for syphilis and HIV has greatly expanded test coverage, especially in areas with difficult-to-reach populations or without access to laboratory diagnostics.[13],[14] POC tests also enabled the development of home-based education and testing (HBT), a novel approach utilizing trained counselors to deliver individualized sexual and reproductive education and testing to couples in the privacy of their homes.[15] Engaging men by providing HBT for syphilis and HIV during pregnancy can have synergistic and cost-saving effects on reducing HIV and syphilis transmission and adverse pregnancy outcomes. HBT has been shown to increase HIV test uptake by men and identify more serodiscordant couples who can be targeted for high-yield HIV prevention, [7,8,15,16] but less is known about the effects of HBT on linking individuals to care and treatment.

Within a randomized control trial of pregnant women attending a first antenatal visit in Western Kenya, women and their male partners received either: (1) a home-based couple education and testing (HBT) intervention, or (2) an invitation letter for clinic-based couple HIV testing. We assessed the uptake of home-based POC syphilis and HIV testing during pregnancy and at 6 months postpartum and assessed whether introduction of syphilis testing affected HIV testing.
At 6 months postpartum, we examined whether HBT affected male partner utilization of STI and HIV prevention and care services (i.e. STI consultation, medical male circumcision and HIV care and treatment) and female partner HIV viral suppression.

Syphilis testing was highly acceptable to male partners during early pregnancy (93% of 80 men) and 6 months postpartum (98% of 230 men). Therefore, uptake of paired syphilis and HIV testing uptake was also high (91% during pregnancy and 96% postpartum). Introducing syphilis testing did not adversely affect HIV testing as uptake remained high before (96%) and after (95%) syphilis testing was introduced. After receiving home-based education and testing during their partners' pregnancy, 75 of 80 (94%) men intended to seek clinic-based services for STI consultation

if testing was positive. By 6 months postpartum, among 525 women exiting the study, we reached 487 (93%) of their male partners in the intervention (n=247) and control arms (n=240). Men who received home-based couple education and testing were 59% more likely to have sought STI consultation during the study period than men in the control arm (n=47 of 247 vs. 16 of 240, respectively; RR=1.59; 95% CI: 0.50-0.96).

However, at 6 months postpartum, one-time home-based education and testing did not have an impact on HIV prevention or treatment as medical circumcision among eligible uncircumcised men and linkage to HIV care among newly diagnosed HIV-positive men remained low in both intervention and control arms. Similarly, home-based couple education and testing did not affect HIV viral suppression in HIV-positive pregnant women in the intervention or control arms at 6 months postpartum. Despite women commencing lifelong antiretroviral therapy, 22 (30%) of 73 HIV-positive women who provided dried blood spots were not virally suppressed at 6 months postpartum. Of these women with unsuppressed HIV, 17 (81%) of 22 were breastfeeding and 8 (38%) of 22 had HIV-negative male partners. These findings indicate continued risk of HIV transmission to young infants and male partners and highlight continuing gaps in the HIV care and treatment cascade.

These results show that syphilis testing is as acceptable as HIV testing and that home-based couple education and testing can be effective in increasing male partners seeking STI consultation and treatment. However, one-time home-based education and testing for HIV appeared insufficient to convince men to obtain medical circumcision or to increase linkage to HIV care among newly diagnosed HIV-positive male partners. HBT also did not have an effect on HIV viral suppression of women at 6 months postpartum. The inherent and social differences between STIs such as syphilis (short-term curative treatment, less stigma) and HIV (long-term non-curative treatment, high stigma) necessitate a recurrent and longer-term approach for linkage and continued engagement in

HIV care and treatment. Providing home-based education and POC testing for HIV and other STIs to men and women as equal and contributing members of a family can help make a family health approach to sexual and reproductive health more holistic, accessible and sustainable.

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ACKNOWLEDGEMENTS

I would like to sincerely thank Carey Farquhar (Dissertation Chair), and Alison Roxby (Committee Member) for their guidance and support, and for providing me an opportunity to work directly in the implementation of this research in Kenya. I have learned much on a professional and personal level through my time on the project under their mentorship. I owe a word of appreciation to our Kenyan Principal Investigators John Kinuthia and Alfred Osoti who established the foundational research for the HOPE study and made possible the integration of the syphilis testing that I hoped to employ. I am grateful to my committee members Barbra Richardson, King Homes, and Stephen Goodreau for their willingness to serve, their invaluable time and feedback.

Numerous others supported this work and deserve recognition. This study would not be possible without the participation of Kisumu District Hospital Kenyan antenatal clinic staff and Leadership. Thank you to the participating pregnant women and their male partners for inviting us to their homes. Thank you to the clinical, outreach, and administrative staff for their work in the field, their willingness to allow me to work and learn alongside them in the implementation of this study, and their friendship during my nearly two years away from home (Coordinators: Molly Anne Gone, Felix A. Otieno. Data manager: Victor Asila. Health Advisors: Michael Obuon'g, Allan Juma, Donald Mboya, Sheila Marienga, Caroline Mungala, Sarah Owino, Grace Obinge, Richard Oginga, Maurice Owino; Study Nurses: Lavender June, Susan Atieno Mosori; Management: Samuel Ndungu, Maggy Ndegwa, and George Ochogo).

A word of thanks to Stephen Gloyd, Kenneth Sherr, and Sarah Gimbel-Sherr for providing me an opportunity to support the continuing work in congenital syphilis elimination and gain new skills in the development of implementation science research.

I would also like to acknowledge the funding sources that supported this work. This Home-based Partner Education and Testing Study was made possible by a grant from the National Institutes of Health [R01 HD 075108-01, PI: Carey Farquhar]. I was generously supported by the NIH Fogarty International Center Northern Pacific Global Health Fellows Program [2014 Research Training Grant #R25-TW009345], Boren International Fellowships (2013), and the Foreign Language Education Area Studies Program [2012 and 2013; #P015B100200].

Finally I would like to thank my family, friends, and most importantly my husband, for their unwavering support.

DEDICATION

To my daughter, Liên. I wish for you everything good this world has to offer, and more.
The road to achieving your dreams might not be easy, but half the riches are in enjoying the journey despite the bumps and turns. Believe in yourself, keep persevering, and somehow you'll get there …. perhaps with a few unexpected treasures along the way.
Oh the places you will go….

Chapter 1. INTRODUCTION

1.1 Overview

Men are generally low utilizers of healthcare. For HIV and other sexually transmitted infections (STIs), men seek care at more advanced stages of disease and are less likely to initiate treatment.[1-4] As HIV emerged and spread globally, resources were channeled into HIV care and treatment and prevention of maternal to child transmission (PMTCT) of HIV. Consequently, funding for STI programs decreased and many STI clinics closed, which further reduced access to clinic-based services for men seeking testing and treatment for non-HIV STIs [17] [18] As a result, men often seek care in private and informal sectors with the risk of improper or inadequate treatment.[19,20]

Links between HIV and other STIs are strong as evidenced by the greatly increased risk of HIV acquisition and transmission in the presence of untreated STIs.[21] Because laboratory tests for most STIs are unavailable or unaffordable in developing settings, syndromic management of STIs has been recommended by WHO since 1990. For example, men presenting with urethral discharge are empirically treated for both gonorrhea and chlamydia and men or women with genital ulcer disease (GUD) are treated for syphilis. Syndromic management of vaginal discharge is limited due to low specificity for STIs as endogenous causes are more common.[22]

As women overall bear a greater burden of reproductive mortality and morbidity, reproductive health has traditionally emphasized maternal health and family planning and overlooked men's sexual health needs. The global spread of STIs, including syphilis and HIV, has had devastating effects on pregnant women and children in utero and during infancy. It soon became evident that for many women their leading risk factor for acquiring HIV and other STIs was the activity of their male partners. This reality that it is often easier to identify, diagnose and treat

men with STIs [22] led to a renewed emphasis on including men in reproductive health in order to reduce risks for mothers and children.

Pregnancy is viewed as an optimal time for engaging male partners due to frequent antenatal care (ANC) visits by women, opportunities for testing and mutual disclosure of STI/HIV status and the high risk of STI/HIV transmission during this period that can lead to adverse pregnancy outcomes. Male partner participation in antenatal care has been shown to increase male and female HIV testing,[7] identification of HIV-discordant couples,[7,8] female participation in ANC and uptake of PMTCT services[1,9] as well as reduce infant HIV acquisition and mortality.[10] Despite these significant benefits and efforts to engage male partners, standard clinic-based approaches that invite male partners to come to antenatal clinics have generally resulted in very low male partner attendance.[1,2,11] In Kenya, less than 5% of pregnant women had a male partner tested for HIV in the last 12 months[23] and less than half of male partners of syphilis-positive women presented for recommended treatment after notification.[24] Even when male community health workers in Mozambique were hired and trained to recruit and encourage men to participate in ANC, uptake for men increased but remained modest (from 5% to 34%).[25]

Involving men in sexual and reproductive health has generally focused on reducing transmission risks to pregnant mothers and children without directly addressing the sexual health needs of men. Indeed, regarding testing and treatment for STIs, men are said to have "responsibilities" while women are deemed to have "rights" to choices and access to sexual and reproductive health.[26] To expect men to participate fully as responsible partners in improving and protecting their own and their partners' sexual and reproductive health, the sexual health needs and rights of men also need to be addressed and championed. Proponents of a male-inclusive approach suggest framing male sexual and reproductive health as a right rather than as a responsibility.[26-28] Advocating for the health of fathers as equally important and reframing men as

positive contributors to the health of the family shifts the balance from a maternal and child health approach to a family-centered approach that addresses HIV and STI control within the larger community.[12] A more holistic family health approach is more likely to be able to recruit men to participate and continue to actively engage them throughout pregnancy and beyond. Unfortunately, such comprehensive approaches are rare, particularly in developing settings.

The advent of rapid and inexpensive point-of-care (POC) tests for HIV has greatly expanded test coverage, especially in areas with difficult-to-reach populations or without access to laboratory diagnostics.[13],[14] POC tests also enabled the development of home-based education and testing (HBT), a novel approach utilizing trained counselors to deliver individualized sexual and reproductive education and testing to couples in the privacy of their homes.[15] HBT has been shown to increase HIV test uptake by men and identify more serodiscordant couples who can be targeted for high-yield HIV prevention.[7,8,15,16] Less is known about the effects of HBT on linking individuals to care and treatment.

Rapid POC syphilis tests present a similar opportunity to greatly increase access to syphilis testing and treatment of men and women during and outside of pregnancy. Syphilis testing and treatment of pregnant women and their male partners are among the most cost effective maternal and child health interventions[29,30] as it greatly reduces the effects of congenital syphilis, reduces the risk of syphilis and HIV transmission and supports existing HIV PMTCT program goals.[31,32] Recent research indicates high acceptability of syphilis testing in conjunction with HIV testing,[33],[34] and a tripling or greater of syphilis testing among women in rural settings in Kenya, Uganda, and Zambia.[35-37] A dual strategy including syphilis and HIV testing during pregnancy has increased HIV testing of pregnant women and their male partners and can have synergistic and cost-saving effects on reducing HIV and syphilis vertical transmission.[14,38,39],[37] Offering home-based education and testing for syphilis to pregnant women and their male partners could help reduce the 930,000

maternal infections and 350,000 syphilis-associated perinatal deaths that occur globally each year.[40,41]

1.2 REMAINING CHAPTERS

This dissertation assesses the effects of employing novel testing approaches (home-based POC syphilis and HIV testing) on uptake of male partner testing, health-seeking behaviors for clinic-based STI and HIV prevention, care and treatment, as well as HIV viral suppression among HIV-positive women postpartum. The second chapter presents a study of male partner uptake of syphilis and HIV point-of-care testing within a randomized controlled trial of a home-based education and testing intervention. This chapter was published as a peer-reviewed article in Sexually Transmitted Diseases, August 2017, as an original article. The third chapter examines how home-based education and testing influenced male partner use of clinic-based STI and HIV services, including seeking STI consultation, HIV care and medical circumcision. This manuscript has been submitted and is under review by Sexually Transmitted Diseases. The fourth chapter describes HIV viral load testing results of HIV-positive women at 6 months postpartum.

CHAPTER 2. Uptake of Home-based Syphilis and HIV Testing Among Male Partners of Pregnant Women in Western Kenya

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Publication citation:

Mark J, Kinuthia J, Roxby A, Krakowiak D, Osoti A, Richardson BA, Gone MA, Asila V, Parikh S, Farquhar C. Uptake of Home-based Syphilis and Human Immunodeficiency Virus Testing Among Male Partners of Pregnant Women in Western Kenya. Sexually Transmitted Diseases. September 2017; 44(9):533-538. doi: 10.1097/OLQ.0000000000000649.

PMID: 28809770 / PMCID: PMC5657390

2.0 ABSTRACT

Background: Few men are tested for syphilis or HIV during their partner's pregnancy, a high-risk period for HIV and syphilis transmission. Offering home-based rapid testing of syphilis to couples during pregnancy can support prevention efforts to reduce transmission of sexually transmitted diseases and adverse pregnancy outcomes.

Methods: We assessed men's uptake of paired (separate tests, single blood draw) point-of-care syphilis and HIV tests within a randomized controlled trial of pregnant women who received clinic or home partner HIV testing. We evaluated acceptance of paired HIV-syphilis testing during pregnancy or at 6 months postpartum, and evaluated whether addition of syphilis testing affected the uptake of HIV testing among men.

Results: Out of 601 women, we were unable to meet 101 male partners, and 180 tested before syphilis tests were available. Paired syphilis and HIV testing was offered at home to 80 men during pregnancy and to 230 men postpartum. For syphilis, 93% of men agreed to test during

pregnancy and 98% agreed postpartum. For paired syphilis and HIV testing, 91% of men tested for both during pregnancy and 96% tested postpartum. Before syphilis test introduction, 96% of men accepted HIV testing, compared to 95% of men who accepted HIV testing when paired testing was offered.

Conclusions: Uptake of syphilis and HIV testing was high among male partners offered couple testing at home. Introducing syphilis testing did not adversely affect HIV testing among men. Point-of-care diagnostics outside facilities can increase testing of male partners who rarely accompany women to antenatal clinics.

2.1 INTRODUCTION

Engaging male partners of pregnant women is an important, but often neglected, pillar of maternal and child health program success in sub-Saharan Africa. Despite recent efforts to engage men during their partners' pregnancy, rates of male clinic-based antenatal attendance, including couple HIV testing[1,2] and antenatal syphilis treatment,[34,42,43] are generally low. The effects of male engagement during female pregnancy have mainly been studied in the context of prevention of mother-to-child-transmission of HIV (PMTCT), in which male partner involvement within antenatal care increases male HIV testing[5,6] and identifies more HIV-discordant couples.[7,8] Furthermore, male engagement improves women's uptake of PMTCT services[1,9] and reduces infant HIV acquisition and mortality.[10] Offering male partner syphilis education and testing could lead to similar program improvements and reduce the 930,000 maternal infections and 350,000 syphilis-associated perinatal deaths that occur globally each year.[40,41]

The advent of rapid and inexpensive point-of-care (POC) tests for both HIV and syphilis has expanded test coverage, especially in areas with difficult-to-reach populations or without access to laboratory diagnostics.[14] These novel tools make elimination of congenital syphilis possible, but will likely require high screening coverage and effective partner management strategies.[39] In Kenya, presumptive treatment of male partners of women who tested positive for syphilis during pregnancy led to a reduction of stillbirths and low birth weight babies compared to children of untreated male partners.[24] Syphilis testing can also benefit existing HIV PMTCT efforts as demonstrated in Uganda and Zambia, where addition of syphilis tests led to small but significant increases in HIV testing as well as increased uptake of maternal single-dose nevirapine prophylaxis and combination antiretroviral treatment.[37] Syphilis and HIV testing during pregnancy are highly cost-effective interventions during pregnancy[30,44] and can be scaled up in low- and high-resource settings.[29]

In contrast to low rates of antenatal clinic-based HIV (12-15%)[1,9,45] and syphilis testing of male partners (<2%),[34] home-based STI education and testing has been shown to be highly acceptable (>83% HIV test uptake) and feasible in several settings in Africa.[7,15,16] Additionally, cost-effectiveness models in sub-Saharan Africa suggest that paired HIV and syphilis testing strategies, including single-cartridge duplexed HIV-syphilis tests, are cost saving and result in fewer disability-adjusted life-years lost compared to HIV-only testing programs.[44] We examined whether paired POC syphilis and HIV testing at home were acceptable to male partners of pregnant women as part of a randomized controlled trial. We determined uptake of syphilis and HIV tests during pregnancy and at 6 months postpartum and conducted a comparison of HIV test uptake among male partners before and after the addition of syphilis testing.

2.2 METHODS

This was an observational cohort study; study participants were male partners of women who participated in a randomized controlled trial (RCT) of home-based partner education and testing (HOPE) that enrolled 601 pregnant women presenting to a first antenatal clinic visit at Kisumu County Hospital in Nyanza Province, Kenya from September 2013 to June 2014.[7] Pregnant women were eligible to enroll in the study if they were married or cohabiting, had not experienced intimate partner violence within the preceding month, aged ≥14 years and living within 40 kilometers of the hospital. Consenting women were randomized to receive either: (1) home-based partner education and HIV testing with their male partner (HOPE intervention, n=306); or (2) a male partner invitation letter for clinic-based HIV testing at the maternal and child health clinic (control, n=295). Couples received counseling in the home about family health, including HIV, STI symptoms and clinic-based treatment, syphilis POC tests, exclusive breast feeding, facility delivery and family planning, and were encouraged, but not required, to test together as a couple with mutual disclosure. HIV testing included standard pretest and posttest counseling.

In the larger randomized controlled trial, staff encountered male partners of the intervention arm at the home-based HOPE intervention visit during pregnancy. Outcomes for all participants of the RCT were then assessed at a home-based 6-month postpartum follow-up visit, at which time men of the control arm were first encountered. This exit visit included HIV testing to determine final infection status.[7] As this is an area of high HIV incidence, men were classified as having unknown HIV status if they did not self-identify as HIV positive.

We assessed uptake of a POC treponemal syphilis test (SD Bioline Syphilis 3.0; Standard Diagnostics Inc., South Korea) when conducted concurrently with rapid HIV testing.

First, we examined uptake of first-time offer of syphilis testing within the intervention arm (during pregnancy) and control arm (6 months postpartum) of the RCT. Due to test unavailability at the study start, syphilis tests were offered to intervention participants after some men received HIV-only testing and education during pregnancy. Second, we assessed whether the addition of syphilis testing affected HIV testing, by comparing HIV test uptake during pregnancy before and after syphilis testing was added to the home-based HOPE HIV couple education and testing intervention.

Home-based Couple Education and Paired HIV-syphilis Testing Visit

After syphilis testing became available, men could accept HIV and syphilis POC testing together (paired), HIV testing only, syphilis testing only, or no testing. If both tests were chosen, syphilis and HIV testing and results were conducted at the same time utilizing a single finger-prick blood draw. Study staff referred men who tested positive for syphilis to maternal and child health clinics for cost-free intramuscular penicillin treatment per World Health Organization guidelines. All HIV-infected participants were referred to HIV comprehensive care clinics per Kenyan national protocol.

At the 6-month postpartum visit, all participants were offered an exit interview and paired HIV and syphilis testing. Therefore, men in the control arm received STI education and a first offer of syphilis testing at this time, while men in the intervention arm were offered repeat testing for HIV and syphilis.

Data Collection and Analysis

Study staff surveyed couples via password-protected mobile phone-based questionnaires in Open Data Kit (ODK) software.[46] Among men enrolled in the study, first-time syphilis test uptake data proportions were calculated, and HIV test uptake before and after syphilis test introduction was analyzed using chi-square tests. Data were analyzed using Stata 12 (StataCorp LLC, College Station, TX).

Human Subjects

The study protocol was approved by Kenyatta National Hospital Ethics Review Committee in Nairobi and the Institutional Review Board at the University of Washington. Written informed consent was obtained in Swahili, Luo, or English for all participants prior to enrollment.

2.3 RESULTS

Study Population

Among 601 pregnant women enrolled in the parent randomized controlled trial, 101 male partners (17%) were not located or did not agree to discuss participation: 46 men (15%) in the HOPE arm and 55 men (19%) in the control arm were never able to be contacted, and 32 women and partners in the control arm (11%) were lost before the postpartum testing visit. Of the remaining 500 male partners, 180 men were enrolled and tested for only HIV before the syphilis test was available. After syphilis testing was available, 320 male partners were enrolled in the study. **[Figure 2.1].** Of these men, 80 in the HOPE arm were offered paired syphilis and

HIV testing at home during their partners' pregnancy, and 240 in the control arm were offered paired syphilis-HIV testing at home during a postpartum visit. Test uptake data were missing for 10 men in the control arm.

The median age of participating men was 30 [interquartile range (IQR) 27 to 35] **[Table 2.1].** All were married and 95% were living together with their female partners. Most men had children prior to the study-enrolled pregnancy, as only 20 (25%) and 36 (22%) were first-time parents in the intervention and control arms, respectively. Among experienced parents with at least one previous child, 21% (11 of 52) of men in the intervention arm and 16% (20 of 127) of men in the control arm attended any ANC visit during the last pregnancy that occurred prior to female study enrollment.

HIV POC testing was familiar and acceptable to this population of men, and self-disclosure of female HIV testing to their male partners was reported by men to be high. A total of 93% (74 of 80) of men in the intervention arm and 88% (143 of 172) of men in the control arm reported previous experience with HIV testing prior to the home-based couple visit. A total of 8% (6 of 80) of men in the intervention arm and 11% (18 of 163) of men in the control arm reported known HIV-positive status. Most men reported knowing their female partner's HIV status during pregnancy (81%, 65 of 80) and postpartum (93%, 149 of 230). Of these men, 17% (11 of 65) in the intervention arm and 14% (22 of 158) in the control arm had known HIV-positive female partners.

Male Partner Uptake of Syphilis & HIV Testing and the Effect of Introducing Syphilis Testing

Among male partners who received a first-time offer of paired syphilis and HIV testing during pregnancy or at 6-months postpartum, 93% (74 of 80) of men accepted syphilis testing in

the intervention arm and 98% (226 of 230) of men in the control arm **[Table 2.2]**. Reasons for refusing syphilis testing were not available for the three HIV-positive men who refused syphilis testing during the intervention in pregnancy, but were captured among all study participants completing 6-month postpartum visits (intervention and control arms). Out of 10 men (1 HOPE, 9 control) who refused syphilis testing, 3 men indicated that they "Did not think it is necessary" and 7 men "Did not want to know." Refusal options that were not cited included, "Not understanding the test," "Fearing a test finger prick," or "Female partner unwilling to couple test or share results".

Syphilis test positivity among male partners was low in this population with 1.4% (1 of 74) of intervention arm men and 0.9% (2 of 226) of men in the control arm testing positive **[Table 2.2].** All three syphilis-positive men were in syphilis-discordant couples as their partners tested negative for syphilis. The man who tested positive for syphilis during pregnancy in the intervention arm had also declined HIV testing and did not know his female partner's HIV status. At 6 months postpartum, he reported that he had sought clinic-based STI services for syphilis treatment during pregnancy and accepted couple HIV testing at the 6-month postpartum visit. He was HIV-negative and his female partner was HIV-positive. The two male partners in the control arm who tested positive for syphilis postpartum were both HIV-negative and their female partners were negative for both HIV and syphilis. Among female partners of all male participants, 1.3% (4 of 310) of couples offered paired testing during pregnancy or postpartum had tested positive for syphilis (1 intervention, 3 control). Overall, syphilis testing revealed a total of 2 intervention and 5 control couples affected by syphilis; all 7 couples were syphilis-discordant.

Considering paired syphilis and HIV testing, first-time uptake of paired syphilis and HIV testing was high among men of unknown HIV status who were eligible for paired testing **[Table 2.2].** In the intervention arm, out of 74 male partners of unknown HIV status, 91% (67) accepted

both HIV and syphilis testing, 5.4% (4) accepted syphilis testing only, 4.1% (3) accepted HIV testing only and none refused both tests. In the control arm, out of 211 men with unknown HIV status, 96% (204) accepted both HIV and syphilis testing, 1.4% (3) accepted syphilis testing only, none accepted HIV testing only and 1.9% (4) refused both tests**.** We also assessed the acceptability of syphilis testing among HIV-positive men who were ineligible for HIV testing. Among 25 men who reported known HIV-positive status, 3 of 6 (50%) of men in the HOPE arm and all 19 (100%) of men in the control arm accepted syphilis testing.

Lastly, we examined the effect of adding POC syphilis testing to the home-based HIV test **[Table 2.3].** Among male partners who were eligible for HIV testing, 96% (151 of 158) accepted HIV testing prior to syphilis test introduction compared to 95% (70 of 74) of men who accepted HIV testing when both HIV and syphilis testing were offered (Chi-square, p=0.6).

2.4 DISCUSSION

This study demonstrated high acceptability of both syphilis and HIV testing among male partners of pregnant women when offered together at home in a couple testing environment. Home-based testing visits were accepted by more than 80% of enrolled couples in both pregnancy and postpartum. Of those reached by the intervention, uptake of syphilis testing was nearly as high or higher (93% and 98%) compared to HIV test uptake (95% and 96%) among men with unknown HIV status during early pregnancy and at 6 months postpartum, respectively. Consequently, most men with unknown HIV status accepted both syphilis and HIV testing (91% during pregnancy and 96% postpartum) when offered together at home. We had small numbers

of HIV positive men, who were more likely to decline a syphilis test, which we speculate was due to desire to avoid a blood draw since HIV status was known.

The acceptability of syphilis and HIV testing found in this study is higher than findings in prior studies. In neighboring Uganda, where syphilis prevalence is higher (6.2% among males and 4.0% among females), 81% of male partners who sought clinic-based testing following invitation letters accepted both HIV and syphilis testing, 17% accepted only HIV testing, and 1.7% accepted only syphilis testing.[34] In rural Brazil, home-based POC syphilis and HIV testing of were highly acceptable and feasible, with 85% accepting paired HIV-syphilis testing.[33] The higher uptake in our study may be a result of participants' experience with previous HIV testing, as well as the positive effects of home-based couple testing on male partner HIV test uptake. Home-based couple HIV testing is desired by male partners[16] and has resulted in two-fold greater (87% vs. 39%; RR=2.10) HIV test uptake among men during pregnancy compared to clinic-based invitation of the control group.[7] Our qualitative research also shows that home-based testing enables close rapport between counselors and partners in a comfortable home environment that can be more conducive to POC testing than clinic-based options (Krakowiak, submitted).

In addition to our finding that syphilis testing was acceptable to men of unknown HIV status, it was also acceptable to most HIV-positive men. Among the 25 previously diagnosed HIV-positive male partners, testing acceptance was 50% (3 of 6) among men in the intervention arm and 100% (19 of 19) among men in the control arm. Given the higher prevalence of syphilis among HIV-positive men (6.4%) and women (3.2%) in Kenya,[47] prioritizing syphilis testing among HIV-positive individuals and their partners before and during pregnancy could be a cost-effective approach to preventing antenatal syphilis transmission and adverse pregnancy outcomes and support overall PMTCT program success.[31] Although the prevalence of syphilis in

this study was low, it is notable that all 3 men and 4 women testing positive for syphilis were in a syphilis-discordant couple, indicating a high yield for preventing maternal-to-child transmission of syphilis with successful treatment and repeat testing of both partners. Identification and treatment of male partners throughout pregnancy is critical to successful joint elimination of mother-to-child transmission of syphilis and HIV. This is particularly important among discordant couples with a syphilis positive male partner in order to prevent adverse pregnancy outcomes or neonatal infections, which occur with 52% greater frequency among untreated mothers with syphilis infection compared to women without syphilis infection.[48]

We were unable to determine whether men were more motivated to test for syphilis during pregnancy (to benefit the unborn child) versus in the postpartum period (for their own benefit), as uptake of the test was similar and high during both periods. This suggested that home-based couple counseling, rather than timing, mattered. Men received counseling messages that emphasized both their own general health and the health of their partner and infant as part of counseling encouraging them to test for syphilis and HIV.

Since the syphilis POC test became available halfway through the study, our study design allowed assessment of the effect of introducing syphilis testing to HIV testing. HIV test acceptability among men of unknown HIV status did not change and remained high at 95%, indicating that syphilis test introduction did not negatively affect male partner HIV testing. Similarly, a systematic review found no adverse effects on existing female rapid HIV-testing rates among 6 studies that introduced maternal rapid syphilis testing.[36] In some study sites (Peru, Cambodia, Uganda, and Zambia), maternal HIV testing increased after paired HIV-syphilis testing was introduced.

A strength of this research is the home-based couple testing approach to increasing male partner engagement, which directly recruited male partners of pregnant women.

We previously demonstrated that offering home-based couple HIV testing increases HIV testing and identifies more male-positive HIV discordant couples during pregnancy compared to clinic-based couple HIV testing.[7,15,16] This current study shows that home-based couple syphilis testing is equally acceptable, and this family-centered approach identifies syphilis discordant couples during a high-risk time for adverse pregnancy outcomes. Additional approaches involving male partners, such as combined phone-tracing and home visits in a Malawi study, have been shown to increase clinic-based male participation from 50% to 72% compared to invitation letters alone.[6] A combination of these approaches may provide a cost-effective strategy for scaling up couple-based antenatal services.

Given the success of this strategy and its modest cost, scale-up should be considered in countries seeking to improve HIV and syphilis testing in the antenatal period. Further implementation research would be useful to characterize the minimum factors that may be key to the successful recruitment of male partners, such as financial incentives and use of male counselors.

In summary, home-based POC syphilis testing was as acceptable as HIV testing among male partners of pregnant women in a setting where previous HIV test experience was high and male antenatal attendance was low. New POC diagnostics allow increased access to testing outside of antenatal clinics and may assist men to connect with clinic-based STI treatment. Pairing syphilis and HIV testing is an acceptable and potentially cost-effective approach to traditional syphilis control strategies. Diagnosing and successfully treating syphilis among male partners of pregnant women can improve male partner health and reduce adverse pregnancy outcomes, including neonatal syphilis.

CHAPTER 3. MALE PARTNER LINKAGE TO CLINIC-BASED SERVICES FOR SEXUALLY TRANSMITTED INFECTIONS AND HIV

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Publication information:

Mark J, Kinuthia J, Osoti A, Gone MA, Asila V, Krakowiak D, Sharma M, Parikh S, Ton QT, Richardson BA, Farquhar C, Roxby A. Male Partner Linkage to Clinic-based Services for Sexually Transmitted Infections and HIV. Sexually Transmitted Diseases. (under review)

3.0 ABSTRACT

Background: Home-based HIV testing and education has increased HIV test uptake and access to health services among men. We studied how a home-based intervention influenced male partner use of clinic-based HIV and sexually transmitted infection (STI) services.

Methods: We conducted a randomized controlled trial of pregnant women attending antenatal care in Kenya. Women and their male partners received either a home-based couple intervention or an invitation letter for clinic-based couple HIV testing. Education included identification of STI symptoms, importance of STI and HIV treatment, and circumcision for HIV-negative men. Male self-reported outcomes were compared using relative risks at 6 months postpartum for seeking STI consultation, HIV care, or medical circumcision.

Results: Among 525 women**,** we reached 487 men (93%); 247 men in the intervention and 240 men in the control arm. Men in the intervention were more likely to report an STI consultation [n=47 vs. 16; RR=1.59; 95%CI=1.33-1.89]. Among 61 men with any HIV, linkage to HIV care was reported by 4 of 17 and 3 of 5 men with newly diagnosed HIV in the intervention and control arms [RR=0.69; CI:0.50-0.96]. While our intervention identified 3 times as many men with new

HIV infection, numbers of men were small to find meaningful differences. Few eligible men sought medical circumcision (4 of 72 intervention and 2 of 88 control).

Conclusions: One-time home-based couple education encouraged men to seek clinic STI treatment. However, men identified as HIV positive in home-based testing may require specific outreach for linkage to HIV care and treatment.

3.1 INTRODUCTION

Men are generally low utilizers of healthcare. For HIV and other STIs, men seek care at more advanced stages of disease and are less likely to initiate treatment.[1-4] Given the growing global concern for antibiotic resistance to STIs such as gonorrhea and syphilis, and increased HIV susceptibility due to ulcerative STI infections, an emphasis for men to seek prompt and appropriate clinic-based treatment for STIs is of increasing importance. The World Health Organization estimates 78 million cases of gonorrhea globally, 11.4 million of which are in the Africa region.[49]

The antenatal period may be an optimal time for engaging men due to high health care utilization by female partners and the opportunity for mutual disclosure of HIV status, a predictor of linkage to care.[50] Despite recent efforts to engage men during pregnancy with couple HIV testing and presumptive partner syphilis treatment, rates of male attendance to clinic-based antenatal services remain low.[1,2,11] In Kenya, less than 5% of pregnant women had a male partner tested for HIV in the last 12 months.[23] In addition, less than half of male partners in Nairobi present for recommended syphilis treatment.[24] Syphilis treatment is important because infection with ulcerative STIs is associated with increased risk of HIV acquisition and higher HIV

viral loads, particularly in men.[51] Thus male partners with untreated STIs and HIV pose high risk of transmission or re-infection to female partners, and could result in adverse pregnancy outcomes.[48,52]

In recent years, the movement towards "family health" is a holistic approach engaging men as active contributors to their family's health. It aims to improve male partner health, as well as to bolster existing prevention of mother-to-child HIV transmission (PMTCT) program goals via increased male partner testing and treatment.[12] When men become involved in antenatal care alongside their female partners, inclusive STI services lead to increased male HIV and syphilis test uptake, couple testing with disclosure, and identification of more HIV-discordant couples, in addition to positive PMTCT outcomes.[7,53] Community-based approaches to HIV testing, including home-based testing (HBT) strategies, amplify coverage rates of men compared to clinic-based couple testing.[54] However, while clinic-based couple HIV testing and disclosure with male partners has increased linkage to HIV care in both men and women in Kenya and Malawi,[6,55] studies of linkage to care and treatment following home-based HIV outreach demonstrate promise but have yet to be well defined.

In this study, we assessed the effects of home-based couple education and testing on self-reported male partner return to clinic-based HIV and STI services by 6 months postpartum. Services included seeking additional HIV testing at antenatal clinics, linking to HIV care and treatment programs, seeking voluntary male medical circumcision (VMMC), and presenting for an STI consultation and/or treatment.

3.2 METHODS

Population & Study Design

Study participants were male partners of women who participated in a randomized controlled trial (RCT) of HOme-based Partner Education and testing (HOPE) that enrolled pregnant women at their first antenatal clinic visit at Kisumu County Hospital in Nyanza Province, Kenya from September 2013 to June 2014.[24,56,57] Nyanza province has the highest HIV (15%) and syphilis prevalence (2.3%) in Kenya, as well as the lowest levels of male circumcision (66%) compared to national statistics (HIV 5.6% KAIS 2012, syphilis 1.8% KAIS 2007, circumcision 91% KAIS 2012, published statistics were relevant to the period of this study).[47,58] We randomized eligible and consenting women who were married or cohabiting with a male partner to receive either: (1) home-based partner education and HIV testing with their male partner (HOPE intervention, n=306); or (2) a male partner invitation letter for clinic-based HIV testing at the maternal and child health clinic (control, n=295).[7] In the intervention, couples were encouraged, but not required, to test together for HIV and syphilis with mutual disclosure.

Study staff screened, interviewed and couple tested male partners of the intervention arm at the home-based intervention visit during early pregnancy, within 2 weeks of female partner enrollment. Couples received a 300-shilling (~$3 USD) cash reimbursement for their time at the home visits. Outcomes for all participants were assessed at a home-based 6-month postpartum exit visit, including final HIV and syphilis testing, to assess HIV status at study conclusion. Men's outcomes included seeking the following clinic-based services: an STI consultation, VMMC, and HIV care and treatment. This exit visit included HIV and syphilis testing to determine final infection status.

Home-based Couple Education and Paired Syphilis and HIV Point-of-care Testing

Male-female pairs of community health workers conducted the HBT interventions, which centered on maternal and child health topics[7] as well as point-of-care HIV and syphilis testing for the couple. Testing uptake was 96% for HIV and 93% for syphilis[53]. The intervention also included male-focused STI/HIV topics, including: STI symptom recognition and treatment referral, engagement in HIV care and treatment services and VMMC for HIV prevention among HIV-negative men. Home visits were designed to educate and test partners together. However, if one or both partners objected to couple testing, individual testing was offered.

Study staff referred participants to clinic-based services if participants raised concern for STI symptoms, reported or demonstrated positive HIV or syphilis test results, or demonstrated interest in other healthcare items, including male circumcision following an HIV negative test. STI and HIV care and treatment were free of cost to female participants and their male partners at the maternal and health clinics or the HIV comprehensive care clinics. Male circumcision was offered free of charge through government-sponsored campaigns.

Data Collection and Analysis

Study staff surveyed couples via password-protected mobile phone-based questionnaires in Open Data Kit (ODK) software, an open-source mobile phone platform.[46] Demographic characteristics were assessed using chi-square tests for categorical variables and independent t-tests for continuous variables. All analyses were intent-to-treat. We conducted a relative risk analysis using log linear regression to evaluate whether early pregnancy couple STI education and couple testing affected male partners seeking follow-up consultation by 6 months postpartum. Data were analyzed using Stata 12 (StataCorp LLC, College Station, TX).

Human Subjects

The study was approved by Kenyatta National Hospital Ethics Review Committee in Nairobi and the Institutional Review Board at the University of Washington in Seattle. Written informed consent was obtained in Swahili, Luo, or English.

3.3 RESULTS

Study Population and Male Partner Characteristics

Parent study data have been published. Briefly, we enrolled 601 pregnant women presenting to a first antenatal clinic visit at Kisumu County Hospital in Nyanza Province, Kenya from September 2013 to June 2014.[7] HIV prevalence among pregnant women at enrollment was 19.5% (117/601) with 45.3% (53 of 117) diagnosed for the first time at enrollment. Of 306 women allocated to the intervention arm, we screened 261 married or cohabiting male partners at the home-based intervention during pregnancy, of whom 85% (260 of 306) participated in couple education and testing **[Figure 3.1].**

By 6 months postpartum, 525 women completed the study and received a home-based exit visit in the intervention (86%, 262 of 306) and control groups (89%, 263 of 295).[7] Among these 525 women, 487 (93%) men completed an exit interview in which 94% (247 of 262) of intervention and 91% (240 of 263) control men participated. Most control arm men reported receiving the invitation letter to standard clinic-based HIV testing from their female partner following her study enrollment (220 of 229 responses, 96%).

Male partners had a median age of 30 (IQR: 26-35), all were married and nearly all men were living with their female partner **[Table 3.1].** Intervention men had some primary school education or secondary school education, while control men had more education with greater secondary education experience. Male partners had a median of one living child with the enrolled woman (IQR: 0-2). We characterized previous HIV testing experience and knowledge of partner's HIV status among men of the intervention arm that participated in the home-based intervention during pregnancy. In the intervention arm, most men (84%) had previously tested for HIV before the study and 15% were HIV positive by self-report prior to the home-based intervention visit. In addition, 77% of intervention men knew their female partner's HIV status at baseline, reporting that 19% (32 of 167) of female partners were HIV-positive.

At study exit, 40 of 247 (16%) men of the intervention arm and 21 of 240 (9%) of the control arm reported known HIV-positive status **[Table 3.2].** Of these men, 18 of 40 (45%) in the intervention arm and 5 of 21 (24%) in the control arm were newly diagnosed during the study period, either at the intervention or via self-reported dates post female partner enrollment. Known HIV infections that predated the study were present in 19 of 40 (48%) men in the intervention arm and 13 of 21 (62%) men in the control arm. Timing of HIV diagnosis was unknown for 3 men in each study arm.

Uptake of STI Consultation Following Syphilis Testing and STI Education

Men of the intervention reported high intention to seek STI care following the intervention. As previously described, a subset of 80 of 260 men in the intervention arm were offered home-based syphilis testing after tests became available, of whom 93% (74 of 80) accepted paired HIV and syphilis testing in conjunction with STI and HIV education.[53] While awaiting test results,

94% (75 of 80) reported that they intended to seek STI treatment services if the syphilis testing yielded a positive result. Home-based syphilis testing revealed one male-positive discordant couple (1 of 74, 1.3%) and one female-positive discordant couple (1 of 74, 1.3%). Among the 180 couples in the intervention arm not offered male partner syphilis testing, two women had tested syphilis-positive at the antenatal clinic. By 6 months postpartum, all four men for whom syphilis treatment was indicated reported having sought recommended clinic-based STI services **[Table 3.3].** In the control arm, no women had tested positive for syphilis during standard antenatal testing.

To assess whether HBT influenced men to seek general STI consultation and treatment services, we compared men's self-report of pursuing an STI consultation during the study period **[Table 3.3].** Men in the intervention group were 59% more likely to have sought STI clinic consultations in the intervention arm (47 of 247, 19%) compared to the control arm (16 of 240, 7%) [RR=1.59, 95% CI: 1.33-1.89].

Adult Voluntary Medical Male Circumcision Uptake

Men are recommended for VMMC for HIV prevention if they are uncircumcised and HIV negative. Among male partners at 6 months postpartum, 85 (34%) intervention men and 94 (39%) control men were uncircumcised at study baseline **[Table 3.3].** Of the uncircumcised men, 13 and 6 HIV-positive men of the intervention and control arm, respectively, were excluded from eligibility. The remaining uncircumcised HIV-negative men were eligible for circumcision in the intervention (72 of 85, 85%) and control arm (88 of 94, 93%). By study exit, 3 of 72 (4%) of intervention men and 2 of 88 (2%) of control men reported obtaining circumcision [RR = 1.29; 95% CI: 0.62 –2.70].

HIV-positive Male Partners and Linkage to HIV Care and Engagement in HIV Treatment

We did not study prior history of linkage or engagement in HIV care among men who were known HIV positive before the study period. Among the subset of men with new HIV diagnosis (18 and 5 men, respectively), we assessed the effects of the home-based intervention on linkage to HIV care. Linkage data were missing for 3 of 18 intervention men. As a result, we compared 15 intervention men and 5 control men. Overall, a low proportion of newly diagnosed HIV-positive male participants reported linking to care during the course of the study: 4 of 15 (27%) in the intervention arm and 3 of 5 (60%) in the control arm [RR=0.66, 95% CI: 0.34 - 1.29)].

An additional 4 HIV positive men, 2 in each arm, reported linkage to HIV care; however, whether they were recently diagnosed or HIV positive prior to the study was unknown. Following the exit interview, final HIV testing identified an additional 2 intervention and 2 men. All HIV-positive men after exit testing totaled of 42 and 23 men of the intervention and control arms with HIV who should have ever linked to HIV care and treatment services by the exit interview.

3.4 DISCUSSION

Among male partners of pregnant women in Kisumu, Kenya, men receiving a one-time home-based couple education and HIV and syphilis testing intervention reported high intention (94%) for seeking clinic-based STI treatment services and resulted in nearly 60% greater clinic-

based STI consultations by male partners. By study exit, all four men in the intervention arm who were indicated for syphilis treatment reported attending an STI consultation.

However, despite the intervention previously demonstrating two-fold greater uptake of HIV testing among men (87% vs 39%) and more HIV serodiscordant couples identified,[7] linkage to HIV care among the few newly diagnosed men was uncommon (27% in the intervention arm). Among HIV-negative uncircumcised men, few men (2 and 6%) had been circumcised by study end with no significant difference between intervention and control arms.

These results show that in our population a one-time home-based couple education and testing intervention can be effective in increasing male partners seeking STI consultation and treatment but may be insufficient for linking newly diagnosed HIV-positive male partners to care and treatment or for convincing men to participate in VMMC. The inherent and social differences between STIs (short-term curative treatment, less stigma) and HIV (long-term non-curative treatment, high stigma) necessitate a longer-term approach to link and continue engagement in HIV care and treatment.

In this study, HIV care linkage rates of newly diagnosed men were lower than general rates of linkage in sub-Saharan Africa (range 48% - 66%),[59] but consistent with other studies that showed linkage was lower if HBT was followed by referral alone (<33%) and higher if additional strategies, such as phone calls or point-of-care CD4 count were employed after HBT (>80%).[54,60,61] While one-time home based testing alone may not increase linkage to HIV care at earlier stages of disease, when combined with additional targeted follow-up, HBT can help increase access and linkage to HIV care for difficult-to-reach men. Future design of couple antenatal education and testing might consider a combination of these approaches to provide a cost-effective and community-accepted strategy that could be equivalent to, or better than, facility-based testing with referral alone. One approach is telephone tracing of male

partners to attend clinic-based couple testing, with same day referral to HIV care if HIV-positive. Difficult-to-reach male partners could receive additional home tracing visits with an option of home-based couple testing, and telephone follow-up to facilitate linkage to care if HIV-positive, as was pursued in a Malawi study.[6]

Regarding VMMC, we found that few eligible men sought circumcision after study enrollment, regardless of study arm. The prevalence of circumcised men that we observed at the baseline in this study, as reported by intervention men and control women, are on par with background data in Nyanza Province, which increased from 47% in 2007 to 66% in 2012 following a national policy change in 2008 (national rate of VMMC in Kenya increased from 84% in 2007 to 91%)[62,63] Circumcision funding from the Presidential Emergency Plan for AIDS Relief (PEPFAR) had facilitated widespread scale-up of government supported "catch-up" campaigns in 2008 per high community outreach and services promoting infant and adult male circumcision; Nyanza was the first province of focus for dissemination. For this reason, men who remained uncircumcised after these large national campaigns may have been less likely to adopt VMMC. Exit interviews revealed men's concerns about time healing, days lost from work, and an inability to support their female partner during her own postpartum healing while caring for a new baby.

A strength of this study was that male participation was high at 94%. A handful of men reported that it was important to recognize and treat an STI infection in order to protect the unborn child, stating further that they were unafraid because STI treatment was curative. Supporting research similarly documents pregnancy as motivators for male partners.[53] Studies in Nairobi[24,56,57] and Rwanda[24] further indicate that male partner STI referrals are higher among currently pregnant women than postpartum and non-pregnant women. Lastly, we noted that total number of HIV cases at study exit differed between the intervention (n=40) and the control

arm (n=23), with the intervention arm reporting more cases of HIV diagnosed during pregnancy and similar number of HIV cases diagnosed at the exit visit. Careful efforts were made to ensure comparable study arms and women who were randomized showed no differences with regards to baseline characteristics (18% and 20% HIV at enrollment). Male partners in each arm reported comparable numbers of known HIV prior to the study (n=19, 8% intervention and n=13, 6% control). However, the lower than expected number of cases of HIV detected after exit testing in the control arm may be due to self-selection, as men with probable HIV infection may have opted out of the couple interview and testing at exit.

Important limitations of the study include self-reported outcomes, including previous knowledge of HIV status, circumcision status, and reports of seeking clinic-based services. Second, we did not confirm self-reported HIV status by men through re-testing.

In general, clinic services previously accessible to men are becoming less available as consolidation of sexual and reproductive health services with antenatal care and family planning increases and obviates the need for stand-alone STI clinics. Standard clinic-based approaches, which invite male partners to come to the antenatal clinic, have generally resulted in very low male partner follow-up and are a missed opportunity during a critical time of STI transmission risk.[7] Inclusion of male partners during female partner pregnancy represents a valuable opportunity to improve male access to sexual and reproductive health services, as well as to bolster maternal syphilis and HIV control program success.[1,9,64] This study indicates that a couple education and HBT can increase STI consultations among male partners, but is insufficient to overcome the barriers involved with linkage to HIV care and VMMC. Newly diagnosed men identified in HBT should be targeted for linkage to HIV care, which could result in equivalent or better access than clinic-based services alone.

Chapter 4. Lack of Viral Suppression among Postpartum Women on Antiretroviral Therapy in Western Kenya

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4.0 Abstract

Introduction: Option B+ expedites lifelong antiretroviral treatment for HIV-infected pregnant and breastfeeding women in low-resource settings regardless of clinical stage or CD4+ levels. Concerns remain regarding adherence and sustained HIV suppression in mothers postpartum.

Methods: We conducted a retrospective analysis of HIV-positive postpartum women receiving antiretroviral treatment (ART) under Option B+ within a randomized controlled trial of a home-based HIV couple education and testing intervention. HIV-1 RNA levels were obtained via dried blood spot at 6 months postpartum from June 2014 to June 2015. Correlates of unsuppressed HIV infection (≥550 copies/ml) were assessed using log-linear regression.

Results: Among 91 HIV-positive women followed to 6 months postpartum, 52 (57%) were newly diagnosed with HIV during pregnancy and 74 (82%) continued to breastfeed. Of 73 women who provided a dried blood spot for HIV-1 RNA level, 30% (22 of 73) had unsuppressed HIV infection with median HIV viral load of 6,247/ml (IQR: 1524, 51,286). In the multivariable model adjusted for maternal age, women with unsuppressed HIV were 48% less likely to be living with their male partner (RR=0.52; 95% CI: 0.34 – 0.81), and were 49% less likely to have been prescribed medicine to manage HIV or to protect their child from HIV (RR=0.51; 95% CI: 0.31 – 0.82).

Conclusions: Despite women receiving lifelong antiretroviral therapy starting in pregnancy, nearly one-third of women had unsuppressed HIV infection at 6 months postpartum. Most of these women continued to breastfeed, suggesting ongoing risk of HIV exposure to infants. ART adherence challenges and potential increases in HIV drug resistance may hinder progress towards elimination of mother-to-child HIV transmission despite rapid scale-up of Option B+.

4.1 Introduction

Antiretroviral therapy (ART) for HIV-positive pregnant and postpartum women can significantly reduce perinatal HIV transmission and improve maternal health by suppressing HIV viral replication. The Option B+ strategy expedites treatment for pregnant women by eliminating prequalifying criteria for ART access (clinical status and CD4 count). It directs all pregnant and breastfeeding women to initiate ART immediately and to continue therapy for life. Option B+ has resulted in women initiating ART earlier in pregnancy at earlier clinical stages, and has reduced transmission of HIV to infants.[65] For example, Option B+ in Malawi showed a 7-fold increase in early uptake of ART among pregnant and breastfeeding women,[66] as well as reduced infant HIV transmission to 3.7% overall compared to 19.9% transmission from mothers not taking ART.[65]

However, women prescribed ART during pregnancy or breastfeeding have had lower adherence and retention rates during the postpartum period and afterwards compared to women who initiate ART based on low CD4 count or clinical stage. Qualitative research regarding women's perspectives towards Option B+'s "test and start" approach noted that women struggled with the commitment to lifelong therapy and felt doubtful about their eligibility for treatment, while health care workers cited concerns about poor adherence resulting from women agreeing to initiate treatment under duress.[67,68]

Between 2011 and 2014, more than 20 countries implemented Option B+ with support from the US Presidential Emergency Plan for AIDS Relief (PEPFAR), tripling the number of women receiving ART via PEPFAR.[69] By September 2015, 80% of 144 countries adopted universal lifelong ART for pregnant and breastfeeding women. Monitoring data will be necessary to identify and understand the effects of Option B+ on viral suppression and mother-to-child-transmission (MTCT) of HIV in light of emerging evidence on adherence issues and increasing drug resistance.

In this study, we offered HIV-1 RNA viral load testing via dried blood spot (DBS) collection at 6 months postpartum to HIV-positive women enrolled in a randomized controlled trial (RCT) of HOme-based Partner Education and testing (HOPE) from June 2014 to June 2015. The study took place in Nyanza province in western Kenya, which has the highest HIV prevalence (15%) in the county (KAIS 2012) and which began implementation and scale up of Option B+ in 2014, around the same time as women were participating in this study.

4.2 Methods

Population & Study Design

Study participants were HIV-positive women and their married or cohabiting male partners who participated in the HOme-based Partner Education and testing (HOPE) RCT. The HOPE study enrolled pregnant women at their first antenatal care from September 2013 to June 2014 at Kisumu District Hospital in Nyanza Province. Study methods of the intervention trial are discussed in prior publications. [24,56,57]

Women who were unaccompanied by a male partner attended a first antenatal care clinic visit, which included HIV testing and counseling and referral to PMTCT if HIV-positive. Eligible women were randomized either to a control group, in which their male partners were invited by letter to come to the antenatal clinic for couple HIV testing, or to an intervention group, in which

women and their male partners were offered home-based couple education and testing for HIV. Couples were encouraged but not required to test together. At 6 months postpartum, all women and their male partners in both groups were offered home-based testing for HIV and all HIV-positive women (previously or newly diagnosed) were offered measurement of HIV RNA level via dried blood spot (DBS).

Data collection and analysis

We conducted a retrospective analysis using data from all HIV-positive postpartum female participants and their male partners who participated in the trial. Study staff interviewed couples at 6 months postpartum to collect sociodemographic, clinical, and self-reported health seeking behavior using password-protected mobile phone-based questionnaires in Open Data Kit (ODK) software, an open-source mobile phone platform.[46] Exit HIV and syphilis testing was conducted for participants not known to be positive for either infection. Voluntary dried blood spot collection for HIV-1 viral load testing was offered to all participants known to be HIV-positive (HIV diagnosis prior to study enrollment, during study participation, or at exit testing). Specimens were processed by Abbott m2000 platform (Abbott Laboratories, USA), with a lower limit of detection of 550 copies/ml.

Sociodemographic characteristics were collected at baseline during pregnancy and at 6 months postpartum and were described as proportions for all HIV-positive women. We performed univariate analysis for associations with unsuppressed HIV infection using log-linear regression. Unsuppressed HIV infection was defined as viremia above the lower limit of RNA detection of 550 copies/ml. Variables considered for inclusion in the multivariable model were based on a-priori knowledge for known associations with HIV suppression and those that were considered biologically plausible. A multivariable model for correlates was fitted using backward stepwise

regression and maintained in the model at a significance level of p-value 0.05. Known confounders, such as maternal age, were maintained in the model. All data were analyzed using Stata 12 (StataCorp LLC, College Station, TX).

Human Subjects

The study was approved by Kenyatta National Hospital Ethics Review Committee in Nairobi and the Institutional Review Board at the University of Washington in Seattle. Written informed consent was obtained in Swahili, Luo, or English.

4.3 Results

Study Population and Baseline Characteristics

Primary results for the HOPE study have been published previously.[7] Briefly, we enrolled 601 pregnant women presenting to their first antenatal clinic visit at Kisumu District Hospital in Nyanza Province, Kenya from September 2013 to June 2014. HIV prevalence among pregnant women at enrollment was 19.1% (115 of 601) **[Figure 4.1].** A total of 64 (56%) women were newly diagnosed at enrollment and 51 (44%) had known HIV infection prior to study enrollment. Of these women, 52 (81%) of the newly diagnosed and 39 (76%) of the previously diagnosed were followed to 6 months postpartum. There were 12 previously diagnosed and 12 newly diagnosed (at first ANC visit) HIV-positive women who were lost to follow-up by 6 months postpartum. Reasons for loss-to-follow-up included: miscarriage, stillbirth, neonatal death, participant death, or relocation, as described by Krakowiak, with no differences by study arm.[7] We did not collect baseline CD4 and HIV viral loads at enrollment.

Among 91 HIV-positive women followed to 6 months postpartum, 73 (80%) women accepted viral load testing by DBS collection. Baseline characteristics for women who refused viral load testing did not differ from women who provided a DBS, except women who refused had older male partners (median age: 35 vs. 29 years, p-value= 0.001). Among 73 women who provided DBS for viral load, median age was 27 years (IQR: 23, 30) and median gestation at enrollment was 21 weeks (IQR: 16, 25) **[Table 4.1.A]**. Nearly all women were married (99%), living together with their male partners (93%) and previously pregnant (89%). A total of 49 (67%) male partners had previously tested for HIV prior to pregnancy, of whom 49 (67%) shared results with their partners, including 31 (63%) who were known HIV-positive prior to pregnancy and study enrollment. Among 46 women who had known HIV infection prior to their current pregnancy, 6 had missing data on prescriptions for managing HIV. However, 31 (77%) of 40 women with previously known HIV infection had been prescribed medication in the past to manage HIV or to protect their child from HIV, including 23 (74%) of 31 who were previously prescribed ART, of whom 21 (91%) had been prescribed ART for lifetime.

Six-month Postpartum Viral Load Results

At 6 months postpartum, all children were living. A total of 69 (95%) women were prescribed medicine to manage HIV infection or to protect their child from HIV, of whom 65 (94%) were prescribed ART. All 65 (100%) women on ART reported no missed doses in the past 7days **[Table 4.1.B].** All 69 (100%) women who reported being prescribed medicine for HIV report that their infant was prescribed nevirapine (NVP) prophylaxis, of whom 51 (74%) were currently taking NVP at 6 months postpartum. Infant HIV infection was not assessed in this study.

Of 73 (80%) women who completed viral load testing, 51 (70%) women had undetectable HIV viral loads (suppressed HIV infection) and 22 (30%) women had unsuppressed

HIV infection with a median HIV viral load of 6,247 copies/ml (IQR: 1524, 51,286). There were no significant differences in sociodemographic characteristics between women who declined versus women who agreed to participate in this study. Comparing women with previously known HIV to those with newly diagnosed HIV, there were no significant differences in sociodemographic characteristics or in HIV viral suppression at 6 months postpartum.

Among 22 women who had unsuppressed HIV infection at 6 months postpartum, 21 (95%) women had breastfed their newborns at delivery, of whom 17 (81%) of 21 continued to breastfeed at 6 months, including 3 (18%) women who reported not being prescribed medicine to manage HIV or to protect their child from HIV **[Table 4.2].** Of the remaining 14 women with unsuppressed HIV who were currently breastfeeding and had been prescribed medicine for HIV, 13 (93%) of 14 were currently taking ART and 12 (86%) of 14 of their infants were currently taking nevirapine to prevent HIV prevention without any missed any doses in the last 7 days.

Correlates of Unsuppressed HIV Infection at 6 Months Postpartum

Analysis of correlates of unsuppressed HIV infection was limited to the 73 women who agreed to provide dried blood spot specimens for HIV viral load testing **[Table 4.3]**. Univariate analyses with backward stepwise regression resulted in three significant variables in the final multivariable model, including: 1) maternal age, which was considered a confounder as in other studies; 2) Living together with male partner; and 3) Prescribed medicine to manage HIV or protect child from HIV. Women with unsuppressed HIV were 48% less likely to be living with their male partner (RR=0.52; 95% CI: 0.34 – 0.81), and were 49% less likely to have been prescribed medicine to manage HIV or to protect their child from HIV (RR=0.51; 95% CI: 0.31 – 0.82).

4.5 Discussion

In summary, our study found that after initiating antiretroviral treatment for HIV during pregnancy or breastfeeding, approximately one-third of women had unsuppressed HIV infection at 6 months postpartum, of whom over four-fifths of women were currently breastfeeding. Multivariable analysis for correlates of unsuppressed HIV revealed that women who had unsuppressed HIV infection were less likely to be living with their male partner and less likely to have been prescribed medication to manage HIV and protect their child from HIV.

Despite months of prescribed ART and self-reports of 100% adherence with no missed doses in the past 7 days, 30% of women in this study had unsuppressed HIV infection with median HIV viral load >5000 copies/ml. The high adherence reported in this study is in contrast to other studies that describe a trend of lower and decreasing adherence to ART after pregnancy,[70,71] A meta-analysis on ART adherence during and after pregnancy indicated that only 73.5% of women had adequate (>80%) adherence, including 75.7% during pregnancy and only 53% postpartum.[70] A study in Tanzania reported that postpartum adherence declined steadily over time after pregnancy with adherence of 95%, 85%, 74%, and 65% at 3, 6, 12, and 24 months postpartum, respectively.[71] In this study, counselors and participants often developed a close rapport over antenatal clinic and home visits, so it is possible that self-reported adherence was overestimated if women in the study did not want to disappoint study counselors by reporting less than perfect adherence.

The proportion of unsuppressed HIV infection at 6 months postpartum in this study (30%) is similar to other studies of postpartum women on lifelong ARVs. The above study in Tanzania also showed unsuppressed HIV infection (>400 copies/ml) of 16%, 22%, 61% and 86% at 3, 6, 12, and 24 months postpartum, respectively.[71] Although our study did not test for ARV drug resistance, it is likely that acquired or transmitted drug resistance contributed to the relatively high proportion of

unsuppressed HIV infection. Previously pregnant HIV-positive mothers can acquire drug resistance after nevirapine-based PMTCT treatment and have a higher likelihood of unsuppressed HIV even when subsequently started on ART.[72] In this study, 31 (77%) of 46 women with previously known HIV infection had been prescribed medicine to manage HIV or to protect their child from HIV before their current pregnancy, of whom more than half were prescribed ART (23 of 31; 74%) and 21 (91%) of 23 who were prescribed lifelong HIV medicine. Furthermore, a recent study in Nairobi, Kenya, showed that transmitted drug resistance to ARV among ARV-naïve adults increased from 3.9% in 2006 to 10.9% in 2014 as ART was being scaled up.[73]

Although the main HOPE study showed that one-time home-based education and testing (HBT) for HIV increased HIV test uptake of male partners and identified more serodiscordant couples, HBT did not have an effect on suppression of HIV among women at 6 months postpartum. There was also no significant difference in unsuppressed HIV infection between previously diagnosed and newly diagnosed (at first ANC visit) HIV-positive women in this study.

Initial studies on the effects of Option B+ have shown that women who initiate lifelong therapy soon after diagnosis for pregnancy or breastfeeding are less likely to adhere to treatment over time than women who initiate therapy based on clinical disease or low CD4+ levels.[70] Many women associate ART with treatment during severe illness are reluctant to initiate a lifelong commitment because they doubt their eligibility based on feeling well.[67,68] Additionally, clinical staff describe concerns about women acquiescing to initiate treatment under pressure of the new guidelines, but lacking self-motivation required to continue their regimens. Waning adherence may also be attributable to reduced breastfeeding over time, with women more motivated to adhere to ARVs while breastfeeding in order to reduce risk of infant transmission.[74]

Overall, breastfeeding among HIV-positive women in this study was high (82%), including 81% of women with unsuppressed HIV currently breastfeeding at 6 months postpartum. A notable

proportion (18%) of these women reported that they had not been prescribed medicine to manage HIV or to protect their child from HIV. However, nearly all breastfeeding women with unsuppressed HIV infection who had been prescribed medicine for HIV reported currently taking ART (93%) and most of their infants continued to take nevirapine prophylaxis (86%). Research has shown that for breastfeeding women continuing on ART, MTCT transmission of HIV is reduced to 3.5% at 6 months postpartum[75] compared to 15% at 6 weeks and 32% at 6 months for breastfeeding women not on ART.[76] This study did not perform HIV testing on infants.

Multivariable analysis revealed that women not living with their male partners were twice as likely to have unsuppressed HIV infection after adjusting for age. Of note, as enrollment criteria for this study required the couple to either be living together or to be married, all five women not living together with their male partner were married. Reasons for not living together and level of support from husbands were not specified. Male partner participation in antenatal care has been shown to increase male and female HIV testing,[7] identification of HIV-discordant couples,[7,8] female participation in ANC and uptake of PMTCT services[1,9] as well as reduce infant HIV acquisition and mortality.[10] Conversely, lack of male partner involvement and living arrangement (i.e., not living together with a partner or living alone) during pregnancy and postpartum have not typically been included as risk factors for poor adherence to ART, unsuppressed HIV infection or infant transmission of HIV, but may be important markers for decreased family cohesiveness and social support, which have been shown to decrease adherence to treatment for HIV and other diseases.[77]

In our multivariable model, women with unsuppressed HIV were also 49% less likely to have been prescribed medicine to manage HIV or to protect their child from HIV (RR=0.51; 95% CI: 0.31 – 0.82). As Option B+ was being implemented and scaled-up in this region of Kenya starting in 2014, some women in this study may not have been offered ART or some may have declined ART due to unfamiliarity with new Option B+ guidelines for ART initiation. Our multivariable model also

suggested that younger women were more likely to have unsuppressed HIV, which is consistent with other studies. For example. in Nairobi median age of postpartum women with virologic failure was 3 years younger (24 vs. 27 years).[78] Other studies have shown that, younger age is a risk factor for disenagagment from care, virologic failure and MTCT of HIV. [79-81]

Our study had a number of limitations. A small sample size likely limited our ability to demonstrate significant correlations between unsuppressed HIV infection and possible risk factors. We were also not able to describe details of ARV treatment, including specific antiretroviral drugs used, gestational age when women initiated ARVs during the current pregnancy, or similar details about prior ART use during prior pregnancies. Outside of testing for HIV infection and viral load, this study relied on self-reported data, including ART adherence, which can overestimate actual adherence. As program retention, adherence and drug resistance were not primary foci of the larger HOPE study, detailed questions about current and prior ARV use (i.e. maternal nevirapine for PMTCT) were not included. For women who had known prior HIV infection, we were unable to collect viral load at enrollment during pregnancy to compare with postpartum values. Another limitation is that we did not perform testing for ARV drug resistance in order to understand the potential role of drug resistance in postpartum unsuppressed HIV infection.

A strength of this study is that a majority of newly diagnosed HIV-positive women were, presumably, ARV-naïve, which reduces the likelihood of acquired drug resistance, but not the possibility of transmission of drug-resistant strains of HIV. This study also identified a group of pregnant women (married women not living with their partner) not previously recognized as higher risk but who were found to be twice as likely to have unsuppressed HIV infection. Future studies should not exclude women who are not in stable relationships (including unmarried women not living with a partner) should include questions about mental health, postpartum depression

and family, social and economic supports in order to identify and further explore factors that may place women and their children at higher risk for poor outcomes during and after pregnancy.

In conclusion, our study showed that nearly one-third of women had unsuppressed HIV infection at 6 months postpartum in the setting of recent introduction of Option B+ in western Kenya. Although Option B+ has shown great promise in initiating ART earlier in pregnancy, reducing the risk of transmission of HIV to infants, during pregnancy and postpartum and preserving women's health through uninterrupted ART, there are significant challenges in retaining women in care and ensuring ART adherence among women initiating lifelong ART during pregnancy. These challenges raise concern for increasing acquired drug resistance and for transmitted ARV drug resistance resulting from prior nevirapine-based PMTCT treatment, which are contributing to notably high levels of unsuppressed HIV infection among women receiving lifelong ART in this and other studies. There are clear needs for continuous adherence counseling, interventions to improve adherence and affordable viral load and drug resistance testing to monitor and assess the effectiveness of Option B+ as it scales up further in more countries.

Chapter 5. Conclusion

In this dissertation, we analyzed the effects of a home-based couple education and testing (HBT) intervention on pregnant women and their male partners obtaining HIV and syphilis point-of-care testing and seeking prevention, treatment and care services within a randomized controlled trial in western Kenya. Our first analysis assessed the uptake of paired (separate tests, single blood draw) HIV-syphilis POC testing and whether introduction of syphilis testing affected uptake of HIV testing. Our second analysis assessed the effects of HBT on male partner self-reported outcomes for seeking STI consultation, medical circumcision and linkage to HIV care. Our final analysis described HIV viral non-suppression at 6 months postpartum among HIV-positive women who were previously or newly diagnosed during pregnancy.

Findings from each of these analyses have several important implications. First, in contrast to the very low rates of antenatal clinic-based HIV and syphilis testing of male partners, findings in Chapter 2 showed high acceptability of home-based couple syphilis testing that was equal to home-based HIV testing during pregnancy and at 6 months postpartum. Furthermore, adding syphilis testing midway through the study did not change the high rates of home-based HIV testing among men. We anticipate similarly high acceptability of recently developed single-cartridge, combined HIV-syphilis tests, which should further increase feasibility of dual testing. Although the prevalence of syphilis in this study was low, it is notable that all men and women testing positive for syphilis were in a syphilis-discordant couple. Identification and treatment of both partners of a discordant couple with repeat testing during pregnancy is critical to prevent MTCT of syphilis and adverse pregnancy outcomes, which occur with 52% greater frequency among untreated mothers with syphilis infection.

Chapter 3 reports that male partners had high intention to seek treatment for syphilis in the event of a positive syphilis test result soon after receiving home-based education and testing during pregnancy. At 6 months postpartum, men who received home-based couple STI education that included symptom identification and treatment options for STI syndromes were 59% more likely to report having sought a clinic-based STI consultation. However, at 6 months postpartum one-time HBT did not have an impact on HIV prevention and treatment as medical circumcision among eligible uncircumcised men and linkage to HIV care among newly diagnosed HIV-positive men remained low in both intervention and control arms.

Similarly, Chapter 4 showed that HBT with male partners did not affect HIV viral suppression in HIV-positive pregnant women in the intervention or control arms by 6 months postpartum. Despite women commencing lifelong antiretroviral therapy as part of the Option B+ strategy, nearly one-third of women in the study were not virally suppressed at 6 months postpartum. Over 80% of these women were breastfeeding and over one-third had HIV-negative male partners. These findings indicate continued risk of HIV transmission to young infants and male partners and highlight continuing gaps in the Option B+ care and treatment cascade. The proportion of HIV-positive women who were not virally suppressed in this study is similar to other recent studies of women receiving ART under the Option B+ strategy.

In summary, this dissertation demonstrated that a novel diagnostic (POC syphilis tests) was highly acceptable among an important but insufficiently engaged population (male partners of pregnant women) when employed as part of a novel approach (home-based education and testing). Results showed that a one-time home-based couple education and testing intervention had high uptake of POC syphilis and HIV testing and increased male partners seeking STI consultation and treatment but was insufficient to convince men to obtain medical circumcision or to increase linkage to HIV care among newly diagnosed HIV-positive male partners. HBT also did not have an

effect on HIV viral suppression of women at 6 months postpartum. The inherent and social differences between STIs such as syphilis (short-term curative treatment, less stigma) and HIV (long-term non-curative treatment, high stigma) necessitate a recurrent and long-term approach for linkage and continued engagement in HIV care and treatment. Home-based education and testing is a useful approach that can be implemented at the beginning of the HIV care and treatment cascade and complement subsequent tools (i.e., follow-up phone calls, mobile messaging, subsequent home visits, engagement counselors and directly observed therapy) to help improve linkage and continued engagement in HIV care.

Providing home-based education and POC testing for HIV and STIs such as syphilis can have synergistic benefits without affecting HIV prevention efforts. Given the strong link between STIs and HIV, identifying and treating STIs during pregnancy can not only decrease syphilis transmission and the devastating effects of neonatal syphilis but can also decrease HIV acquisition and transmission risk. As POC testing for other STIs (i.e. gonorrhea, chlamydia, herpes, hepatitis B) are developed and combined STI/HIV tests become more available and less expensive, we expect that they will also be highly acceptable to men and women when offered at clinics or as part of a home-based education and testing approach. Providing home-based education and POC testing for HIV and other STIs to men and women as equal and contributing members of a family can help make a family health approach to sexual and reproductive health more holistic, accessible and sustainable.

Section 6. FIGURES AND TABLES

FIGURES and TABLES: chapter 2

Figure 2.1 Study Flow-chart: Male Partner Follow-up for HIV and Syphilis Testing During Pregnancy or 6-months Postpartum

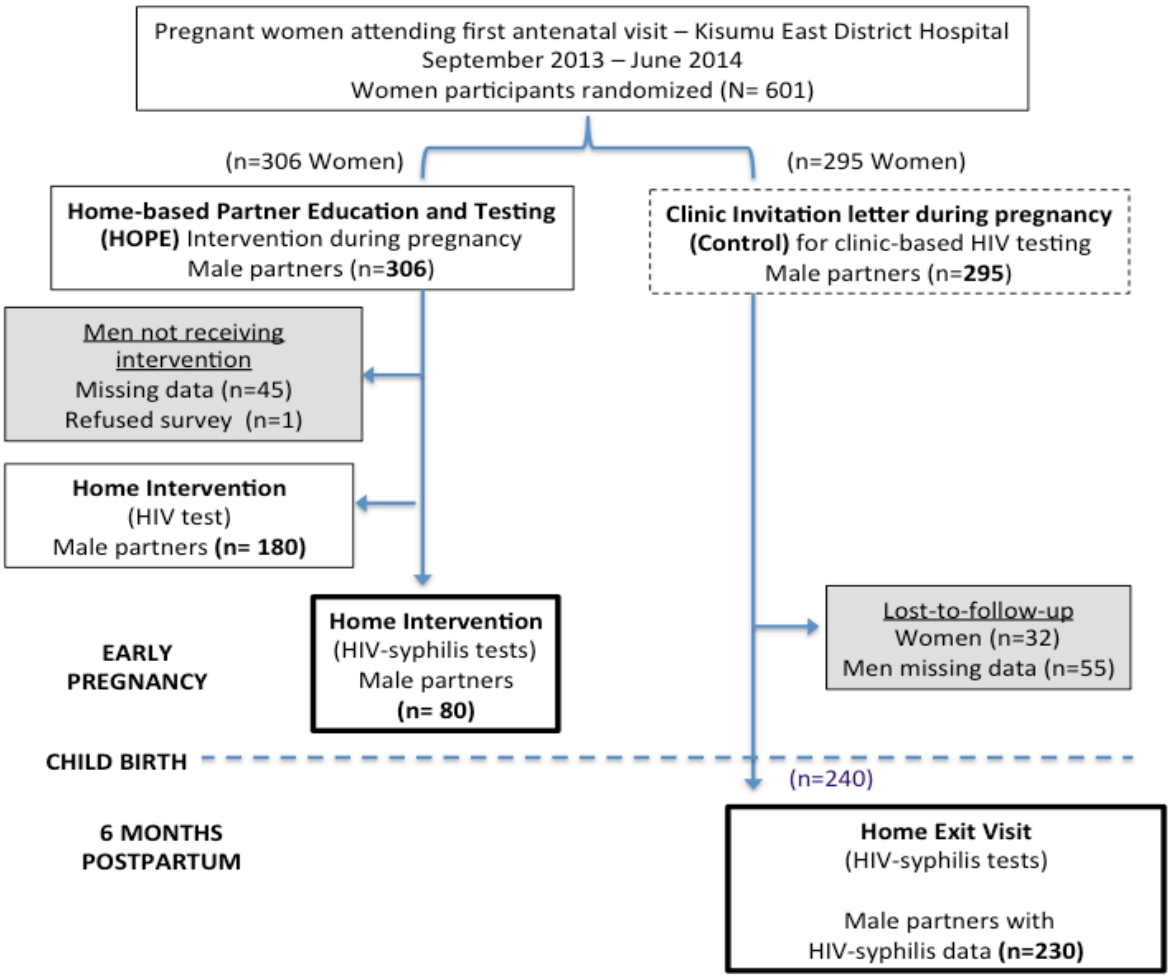

Table 2.1 Characteristics of male partners offered first-time home-based couple education and combined HIV-syphilis testing during pregnancy or postpartum

	Pregnancy Intervention Arm		Postpartum Control Arm	
Baseline characteristics *	(N=80)		(N=163) λ	
	Median	**(IQR)**	**Median**	**(IQR)**
Age (years)	30	(27, 34)	30	(27, 37)
Age of sexual debut (years) †	18	(16, 20)	17	(16, 19)
Age at marriage, if married †	25	(22, 28)	25	(23, 30)
Years married with participant	4	(1, 7)	4.5	(3, 7)
Number of total children †	2	(1, 2)	2	(2,3)
Children with female participant †	1	(0, 2)	1	(0, 2)
	n	**(%)**	**n**	**(%)**
Marital status				
Married, living together	76	(95)	147	(90)
Married, not living together	4	(5)	16	(10)
Parenting experience †				
First-time parent	20	(25)	36	(22)
Any previous children	60	(75)	127	(78)
Attended ANC last pregnancy (n=52, n=127) †	11	(21)	20	(16)
Education				
No formal education	2	(<1)	0	(0)
Some primary school	107	(40)	40	(25)
Some secondary school	108	(40)	94	(58)
> Secondary school	32	(18)	29	(18)
Previous HIV testing experience	74	(92)	143	(88)
Reports being HIV positive †	6	(8)	18	(11)
Knows female partner's HIV status †	65	(81)	149	(93)
Female partner is HIV+ (n=65, n=149)	11	(17)	20	(13)

Eligibility rate total: 100%, Participation rate total: 83%
IQR=interquartile range, ANC= antenatal care
λ: 67 of 230 missing in Control arm
* No significant differences between all arms ($p<0.05$)
† 5 men in Control missing age of sexual debut; 1 in Control missing age at marriage; 2 in Control missing number total children; 3 in Control missing number children with female participant; 8 in Intervention missing attended antenatal care during the previous pregnancy; 1 in Intervention missing HIV status; 3 in Control missing female partner's HIV status.

Table 2.2 Syphilis and HIV test acceptance among male partners offered first-time home-based couple education and paired HIV-syphilis testing

Test Acceptance	**n**	**(%)**	**n**	**(%)**	
Home-based intervention uptake by male partners	**Pregnancy Intervention Arm (N=306)**		**Postpartum Control Arm (N=295)**		
Never able to schedule a home interview	45	(15)	55	(19)	
Met with study, but refused a home interview	1	(<1)	0	(0)	
Mother lost to follow up before home interview	0	(0)	32	(11)	
Total not reached by intervention	46	(15)	87	(30)	
Testing outcomes for male partners	**Pregnancy Intervention Arm (N=80)**		**Postpartum Control Arm (N=230)**		**p-value**
Syphilis test uptake and results					
Accepted syphilis test	74	(93)	226	(98)	0.02
Male syphilis prevalence	1	(1)	2	(<1)	
Female syphilis prevalence	1	(<1)	3	(1)	
Syphilis discordant relationships	2	(2)	5	(2)	
HIV status and test uptake					
Known HIV positive †	6	(7)	19	(8)	0.83
Unknown HIV status	74	(93)	211	(92)	
Accepted HIV test (n=74; n=211)	70	(95)	204	(97)	0.01
Paired testing behavior: HIV status unknown	**Pregnancy Intervention Arm (N=74)**		**Postpartum Control Arm (N=211)**		
Accepted both HIV and syphilis	67	(91)	204	(96)	0.06
Accepted syphilis only	4	(5)	3	(1)	
Accepted HIV only	3	(4)	0	(0)	
Refused both tests	0	(0)	4	(2)	
Syphilis testing behavior: known HIV-seropositive	**Pregnancy Intervention Arm (N=6)**		**Postpartum Control Arm (N=19)**		
Accepted syphilis	3	(50)	19	(100)	0.01

† In addition, 1 man in the Intervention group did not answer regarding HIV status

Table 2.3 Male partner HIV test uptake during pregnancy before and after point-of-care syphilis test addition to a home-based partner education and testing Intervention (HOPE)

HIV test uptake	**Before syphilis test (N=180)**		**After syphilis test (N=80)**		
Reported HIV status	n	(%)	n	(%)	p-value
Known HIV positive status	22	(12)	6	(8)	0.54
Unknown HIV status	158	(88)	74	(92)	
	Before syphilis test (N=158)		**After syphilis test (N=74)**		
HIV test acceptance for those with unknown HIV status	n	(%)	n	(%)	p-value
Accepted HIV	151	(96)	70	(95)	0.60
Refused HIV test	7	(4)	4	(5)	

Figures and Tables: chapter 3

Figure 3.1 Study Flowchart: Male Partner Exit Interview and Testing at 6-months Postpartum

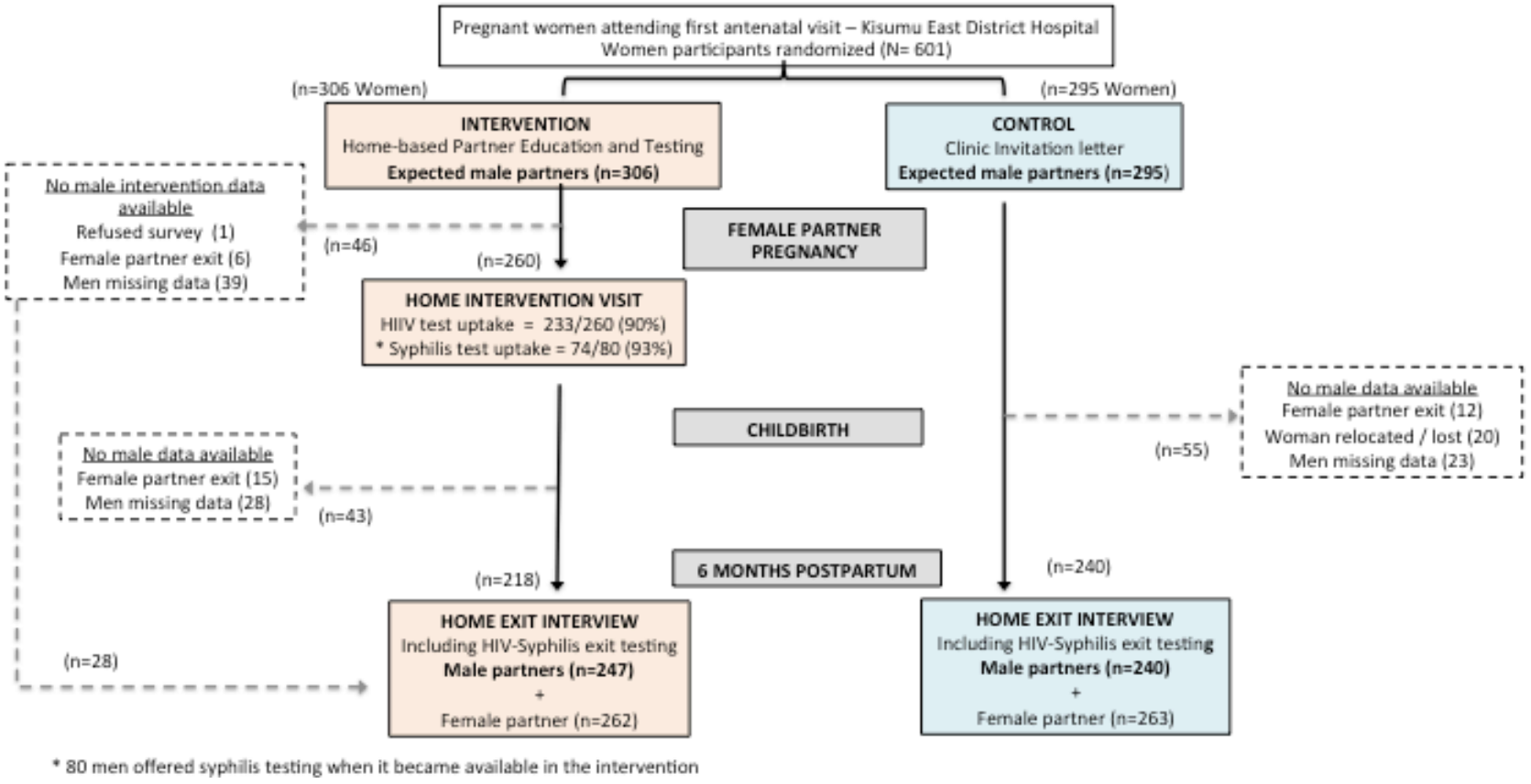

Table 3.1 Characteristics of Male Partners in the Home-based Partner Education and Testing (HOPE) Study

Baseline characteristics [a]	Intervention Arm (N=219) [b]		Control Arm (N=172) [b]	
	Median	**(IQR)**	**Median**	**(IQR)**
Age in years (years)	30	(26, 35)	30	(27, 37)
Age of sexual debut (years) [c]	17	(16, 19)	17	(16, 19)
Number of lifetime sex partners	4	(3, 5)	4	(3, 5)
Age at marriage, if married	25	(22, 29)	25	(23, 30)
Years married with participant	3	(1, 8)	5	(3, 7)
Number of total children [d]	2	(1, 3)	2	(2, 3)
Children with female participant	1	(0, 2)	2	(1, 3)
	n	**(%)**	**n**	**(%)**
Circumcised	162	(66)	146	(61)
Marital Status				
Married	219	(100)	172	(100)
Living together	204	(93)	155	(90)
Attended ANC last pregnancy	32	(20)	23	(13)
Education				
No formal education	1	(<1)	0	(0)
At least some primary school	87	(40)	42	(24)
At least some secondary school	84	(38)	101	(59)
> Secondary school	47	(21)	29	(17)
Previous HIV testing experience	183	(84)	151	(88)
Reports being HIV positive [d]	18 / 183	(10)	16 / 151	(10)
Knows Female partner's HIV status	167	(77)	158	(93)
Partner is HIV positive	32 / 167	(19)	22 / 158	(14)

IQR = interquartile range, ANC = antenatal care

[a] No significant differences between arms (p>0.05) except for "number children with participant" and "partner HIV status known" due to delay in screening control arm until after female partner delivery

[b] No screening data: missing 28 0f 247 in the intervention arm and 67 of 240 in the control arm

[c] Missing data: 9 men in Intervention missing age of sexual debut,

[d] Preferred not to respond: 9 age of sexual debut; 2 in control preferred not to respond regarding number of total children; 1 in control preferred not to respond regarding number of children with female partner enrolled, 1 in intervention preferred not to respond about HIV status

Table 3.2 HIV self-reported status of male partners completing an exit interview with HIV testing at 6 months postpartum

	Intervention (n=247)		Control (n=240)	
	n	**(%)**	**n**	**(%)**
HIV Care and Treatment				
Self-reported HIV positive status before exit HIV testing	40 / 247	(16)	21 / 240	(9)
Newly diagnosed during study period [a]	18 / 40	(45)	5 / 21	(24)
Diagnosed before study	19 / 40	(48)	13 / 21	(62)
HIV positive, other [b]	3 / 40	(7)	3 / 21	(14)
HIV-negative or unknown status before exit HIV testing [c]	207 / 247	(<1)	219 / 240	(<1)
Men newly diagnosed HIV positive at exit testing	2 / 207	(<1)	2 / 219	(<1)
Total HIV positive men by end of study exit interview	42 / 247	(17)	23 / 240	(10)

[a] 10 of 18 men of the intervention were diagnosed at the home-based intervention during pregnancy

[b] Men reported being HIV positive, date of testing not reported

[c] HIV negative (204/207 & 219/219) or never tested before (3/207 & 0/207) in the intervention and control arms

Table 3.3 Male partner self-reported follow-up to clinic-based sexually transmitted infections services by 6 months after birth of child

	Intervention (n=247)		Control (n=240)		Unadjusted RR	95% CI
	n	(%)	n	(%)		
Self-reported Follow-up to Clinic-based services						
STI Services						
Sought any STI clinic services (non-HIV) [a,b]	47	(19)	16	(7)	*** 1.59**	**(1.33 – 1.89)**
Sought clinic if recommended for syphilis treatment	4 / 4	(100)	0 / 0	-	**-**	**-**
Voluntary Male Medical Circumcision						
Uncircumcised at baseline [b,c]	85	(34)	94	(39)	1.02	(0.86 - 1.24)
Recommended for circumcision as HIV prevention	72 / 85	(85)	88 / 94	(94)		
Sought circumcision	3 / 72	(4)	2 / 88	(2)	**1.29**	**(0.62 –2.70)**
Linkage to HIV care and treatment services						
New HIV diagnosis during study period [a]	4 / 15	(27)	3 / 5	(60)	**0.66**	**(0.34 - 1.29)**
HIV positive, other [d]	2 / 3	(66)	2 / 3	(66)	**0.75**	**(0.21 - 2.65)**

RR = Relative Risk; CI = Confidence Interval

[a] Missing data= 1 intervention man missing data on STI clinic-services, 2 men of the intervention missing data on linkage to HIV care and treatment

[b] Prefer not to respond (included as % of respondents): 2 men of the intervention preferred not to respond regarding seeking STI clinic-services, 1 man of the intervention and 2 men of the control arm preferred not to respond to male circumcision status

[c] Does not know (included as % of respondents): 14 men of the intervention and 6 men of the control did not know about their male circumcision status

[d] Men reported being HIV positive , date of testing not reported

Figure and Tables: chapter 4

Figure 4.1 Study Flowchart: Interview and HIV Suppression at 6 months Postpartum (n=91) among HIV Positive Women

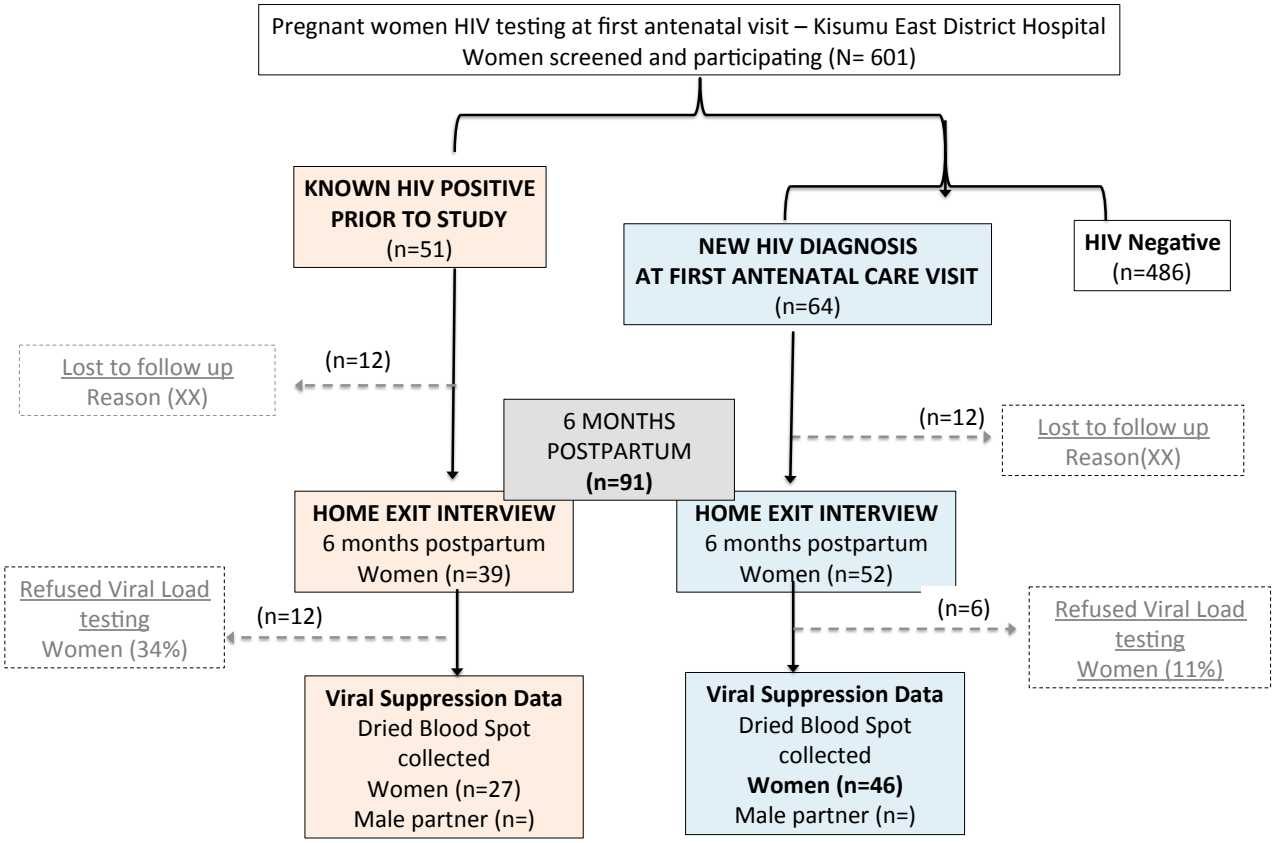

Table 4.1 Characteristics of HIV-positive women who completed the Home-based Partner Education and Testing Study to 6 months postpartum. Western Kenya, 2013-2015 (N=73).

	Median	(IQR)
Age (years)	27	(23, 30)
Gestational age at enrollment (weeks)	21	(16, 25)
Gravidity, including current pregnancy	3	(2, 4)
Number of previous children	2	(1, 2)
Number of lifetime sex partners [a, b]	3	(2, 3)
	N	**(%)**
Married	72	(99)
Living together	63	(93)
Previously pregnant	65	(89)
Education		
Primary school or less	40	(55)
Some secondary	12	(16)
Secondary school completed	18	(25)
> Secondary school	3	(4)
Has separate income	40	(55)
Household income <100 USD(2014) [(c.iii)]	56	(53)
Male partner previously tested for HIV prior to pregnancy [b]	49	(67)
Knows male partner's HIV status [d]	49	(67)
Partner is HIV-positive [d]	31	(63)
HIV tested together with male partner prior to pregnancy	29	(40)
Participated in home-based intervention of RCT	36	(49)
Woman's HIV status at 1st antenatal visit (enrollment)		
New HIV diagnosis during pregnancy	27	(37)
Known HIV infection prior to pregnancy	46	(63)
Woman prescribed medicine to manage HIV or to protect child from HIV before current pregnancy [(c.IV)]	31	(77)
Prescribed triple ART [d]	23	(74)
Prescribed lifelong ART medicine [d]	21	(91)
Self-reported outcomes at 6 months Postpartum	**N = 73**	
Male-partner HIV-negative (discordant couple)	24	(34)
Woman prescribed medicine to manage HIV or protect child from HIV during recent pregnancy [(c.ii)]	69	(95)
Prescribed triple ART [d]	65	(94)
Prescribed lifelong HIV medicine [d]	64	(98)
Currently taking prescribed medicine (n=85)	65	(100)
Did not miss dose of prescribed medicine for HIV last days	62	(95)
Infant prescribed nevirapine [e]	69	(100)
Infant currently taking nevirapine [d]	51	(74)
Infant did not miss dose if neviriaine in last 7 days [d]	51	(100)
Breastfeeding currently [(c.i)]	64	(89)

IQR = interquartile range, ART= antiretroviral therapy, USD= 2014 US dollars

[a] Preferred not to respond: 1 for lifetime sexual partners

[b] Client not sure of response: 1 for lifetime sexual partners, 17 for male partner previously tested for HIV

[c] missing data: (i) 1 missing (ii) 2 missing (iii)7 missing (iv) 6 missing

[d] Denominator is n of the row above (subcategory)

[e] Denominator is *woman prescribed medicine to manage HIV* for *Infant prescribed nevirapine*

Table 4.2.A Baseline correlates of unsuppressed HIV among HIV positive women with a collected dried blood spot (N=73)

	Unsuppressed HIV (N=22)		**Suppressed HIV** (N=51)		
	n	**(%)**	**n**	**(%)**	**P - value**
Maternal age in years					
15 – 19	3	(14)	3	(6)	0.36
20 – 24	6	(27)	12	(24)	
25 – 29	9	(41)	18	(35)	
30 – 34	3	(14)	15	(29)	
>=35	1	(4)	3	(6)	
Multigravida (>=1 pregnancy)	19	(86)	47	(92)	0.39
Number of previous children					
None	2	(10)	8	(16)	0.50
1 child	7	(33)	16	(31)	
>=2 children	12	(57)	27	(53)	
Married	22	(100)	50	(96)	-
Living together	18	(82)	50	(98)	* <0.001
Education					
No formal education	11	(50)	29	(56)	0.33
At least some primary school	3	(14)	9	(17)	
At least some secondary school	6	(27)	13	(25)	
> Secondary school	2	(9)	1	(5)	
Has separate income	12	(55)	28	(54)	0.98
Household income is <100 USD	8	(40)	28	(57)	0.18
Male partner tested for HIV prior to enrollment	14	(64)	35	(68)	0.68
Partner is HIV positive at enrollment [a]	8	(57)	23	(66)	0.57
Prescribed medicine to manage HIV or to protect child from HIV	7 /11	(67)	26/40	(65)	0.85
Prescribed triple ART [a,]	3	(43)	22	(85)	* 0.03
Prescribed lifelong HIV medicine	12	(55)	34	(67)	0.32
Woman HIV newly diagnosed this pregnancy	12	(55)	34	(67)	0.34
Participated in home-based intervention of RCT	9	(41)	27	(53)	0.35

ART= antiretroviral therapy, USD= US dollars, RCT= randomized controlled trial

* p-value is 0.30 or less, for consideration in multi-variate model of correlates of unsuppressed HIV

[a] Denominator is n of the row above (subcategory)

Table 4.2.B. Six-month Postpartum Correlates of unsuppressed HIV among HIV positive women with a collected dried blood spot (N=73)

	Unsuppressed HIV (N=22)		**Suppressed HIV** (N=51)		
	n	**(%)**	**n**	**(%)**	**P - value**
Ever linked to HIV care [a]	17	(81)	50	(98)	* <0.001
Prescribed medicine to manage HIV or to protect child from HIV	18	(86)	51	(100)	* <0.001
Prescribed triple ART [b]	16	(89)	49	(96)	* 0.20
Currently taking prescribed medicine [b]	16	(100)	49	(100)	-
Prescribed lifelong HIV medicine [b]	15	(94)	49	(100)	-
Infant prescribed nevirapine [c]	18	(100)	51	(100)	-
Infant currently taking nevirapine [b]	13	(72)	38	(74)	0.85
Infant did not miss dose of nevirapine last 7 days	13	(100)	38	(100)	-
Breastfed at delivery	21	(95)	51	(100)	-
Currently breastfeeding [b]	17	(81)	47	(92)	* 0.13
Male partner HIV positive- male report	10/	(48)	21/43	(49)	0.93
Male partner linked to HIV care, if HIV+ (n=9 & n=20)	7	(78)	19	(95)	* 0.28
Male partner prescribed ART (n=9 & n=20)	7	(78)	15	(75)	0.78
Male partner still taking ART	7	(100)	15	(100)	-
Male partner link STI consultation (n=21 & n=43)	3	(14)	3	(7)	0.30
Couple is HIV discordant	8	(38)	16	(32)	0.66

ART= antiretroviral therapy

* p-value is 0.30 or less, for consideration in multi-variate model of correlates of unsuppressed HIV

[a] Missing data: 1 unsuppressed & 1 suppressed couple is HIV discordant, 1 unsuppressed linked to HIV care this pregnancy

[b] Denominator is n of the row above (subcategory)

[c] Infant prescribed nevirapine denominator is among women prescribed medicine for HIV management in current pregnancy

Table 4.3 Unadjusted and Adjusted Relative Risks of unsuppressed HIV infection in HIV-positive women at 6 months postpartum

	Unadjusted			Adjusted		
	RR	**(95% CI)**	**p-value**	**RR**	**(95% CI)**	**p-value**
Maternal age	1.18	(0.81-1.71)	0.36	0.91	(0.82 – 1.00)	0.06
Living together with male partner	0.33	(0.18 – 0.60)	<0.001	0.52	(0.34 – 0.81)	<0.01
Prescribed ART prior to study enrollment	0.24	(0.06 – 0.87)	0.03			
Linkage to HIV care and treatment	0.32	(0.17– 0.58)	<0.001			
Prescribed medicine to manage HIV or protect child from HIV	0.32	(0.17– 0.58)	<0.001	0.51	(0.31 – 0.82)	<0.01
Prescribed triple ART by 6 months postpartum	0.49	(0.17 – 1.44)	0.20			
Male partner linked to HIV care	0.28	(0.18 – 1.70)	0.28			
Currently breastfeeding	0.53	(0.24 – 1.20)	0.13			

RR = Relative Risk; CI = Confidence Interval; ART= antiretroviral therapy
All listed variables were considered for the multi-variable model

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