# STATISTICAL ANALYSIS PLAN

**VERSION: 1.0**

**DATE OF PLAN:**

08 October 2021

**BASED ON:**

Version 3.1, 17 March 2019

**STUDY TITLE:**

**HIV SELF-TESTING AND PREP TO INCREASE TESTING AND PREVENTION UPTAKE AMONG MALE PARTNERS AND IMPROVE POSTPARTUM ART USE IN PMTCT B+ PROGRAMS IN UGANDA**

**SPONSOR:**

*ICRC*

**Funding:**

*United States National Institute of Mental Health*

*(R01 MH113434)*

This study is being conducted in compliance with good clinical practice, including the archiving of essential documents.

# SIGNATURE PAGE

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# PROTOCOL SUMMARY

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| **Title Of Study:**<br>HIV self-testing and PrEP to increase testing and prevention uptake among male partners and improve postpartum ART use in PMTCT B+ programs in Uganda | |
| **Investigators**:<br>Study Center(s): Infectious Diseases Institute (IDI) Kasangati and collaborating antenatal care (ANC) clinics in Kampala, Uganda | |
| **Studied period (years):**<br>**2 years** | **Phase of development: Randomized implementation study** |
| **Objectives:**<br>Aim 1: Determine whether an enhanced PMTCT program with HIV self-testing for male partners and provision of PrEP to HIV-negative male partners increases the proportion of male partners who test for HIV, and HIV-negative men who initiate PrEP or HIV-positive men who start ART.<br>Aim 2: Evaluate whether HIV testing combined with PrEP and ART use among male partners increases effective post-partum ART use among HIV-infected Ugandan women in PMTCT B+.<br>Aim 3: Assess the acceptability of HIV self-testing and PrEP to pregnant women taking part in PMTCT B+ and to their male partners, using qualitative and quantitative methods**.** | |
| **Methodology:**<br>Pregnant women ≥18 years accessing ANC and PMTCT B+ programs in Kampala, who have a male partner of unknown HIV status will be randomized to the intervention (HIVST) or the control arm. Women will be instructed in the use and interpretation of HIVST and be provided two HIVST kits to give to or use with their male partners. We will recommend that HIV-negative partners in couples (either HIV negative male partners of HIV-positive pregnant women) or HIV-negative pregnant women with an HIV positive male partner) use PrEP until their partner has been on ART for at least 6 months and achieved viral suppression, and that HIV-positive partners take ART. | |
| **Number of Subjects (planned and analyzed):**<br>500 women and enrolled male partners | |
| **Inclusion criteria:**<br>For all participants<br>- Able and willing to provide written informed consent<br>- Able and willing to provide adequate locator information for study retention purposes<br><br>For women<br>- Age ≥18<br>- Currently pregnant<br>- Not currently enrolled in an HIV treatment study<br>- Male partner not known to be HIV-positive or has not tested in the past 3 months<br><br>For men<br>In partnership with a pregnant woman | |

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| **Intervention:**<br>Women are provided HIVST kits to use with their male partners. Pregnant women will be provided a brief demonstration of how to use the self-test, and will be given two oral fluid based HIV self-tests (Oraquick rapid HIV-1/2 test kit with developer fluid vial and stand) to take home with written and pictorial instructions translated into Luganda (the local language) about HIVST to share with their partner. |
| **Duration of intervention:**<br>Kits/Letters are provided at enrollment; male partners can be enrolled in the study up to 12 month post partum. |
| **Standard of Care:**<br>Women in the control arm will be provided invitation letters, the standard of care, to deliver to their partner to come for HIV testing to their ANC clinic for fast-track testing |
| **Criteria for evaluation:**<br>*Efficacy*: *Aim 1:The primary outcome is viral suppression at 12 months in the women* |
| **Hypotheses:**<br>Hypothesis Aim 1a: Providing pregnant HIV-positive women with HIVST will result in an increase in the proportion of partners who know their HIV status<br>Hypothesis: Aim 1b: Providing pregnant HIV-positive women with HIVST kits will facilitate partner testing, and increase uptake of PrEP by HIV-negative men and ART by HIV-positive men.<br>Hypothesis Aim 1c: Providing pregnant HIV-positive women with HIVST will result in an increase in the proportion of HIV-negative men who initiate PrEP<br>Hypothesis: Aim 2: A higher proportion of HIV positive women in PMTCT B+ will continue ART post-partum with high adherence if their partner is tested and uses PrEP or ART, compared to women in PMTCT B+ whose partner is not tested and not using PrEP or ART |

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# 1. INTRODUCTION

The purpose of this document is to provide details on study populations and on how the variables will be derived, how missing data will be handled as well as details on statistical methods to be used to analyze the study data

This SAP addresses the statistical analyses of Aims 1 and 2, and selected secondary objectives.

# 2. STUDY OBJECTIVES AND ENDPOINTS

## 2.1. Study Objectives

### 2.1.1. Primary Objectives

- Assess whether an enhanced PMTCT program with HIV self-testing for male partners increases the proportion of male partners who test for HIV compared to standard of care information letter about HIV testing for male partners.
- Assess whether the HIV self-testing strategy for male partners affects the proportion male partners who initiate HIV/ART, and the proportion of HIV-negative men who begin PrEP.

### 2.1.2. Secondary Objectives

- Evaluate whether HIV testing combined with offer of PrEP for HIV-negative male partners and ART uptake for HIV-infected male partners increases effective post-partum ART use among HIV-infected Ugandan women in PMTCT B+.
- As a women's HIV disclosure to her partner is hypothesized to be the mechanism for increasing her effective ART use, we will evaluate associations between first visit a women reported disclosure of their HIV-infected status to their male partner and the trial endpoints: enrollment of the male partner, uptake of PrEP/ART; viral suppression. We will also assess whether male partner testing, HIV status and disclosure, impact trial endpoints.

## 2.2. Study Endpoints

### 2.2.1. Primary Endpoints

Aim 1a

- Time to HIV testing and enrollment of the male partner (male partners come to the site to receive HIV testing during enrollment). Male partners who do not enroll are assumed

to not know their HIV status. HIV-infected partners who are on ART at enrollment are omitted from the analysis (not at risk for ART initiation)

Aim 1b

- Time to initiation of PrEP/ART for male partners:
    - Amongst all women
        - Time to enrolled male partner with known HIV status initiating PrEP/ARV (Male uptake of PrEP/ART). If the male partner is not enrolled he is defined as unknown HIV status (to his partner), and assumed not on PrEP/ART.
        - Time to enrolled male partner who started ART /PrEP or has female partner who is VS (Couple use of ART/PrEP). VS of the woman is defined as VS at both the prior and subsequent visit
    - Amongst women with enrolled partners,
        - PrEP initiation in enrolled HIV-negative male partners or ART initiation in enrolled HIV-positive partners
        - PrEP initiation OR undetectable VL of female partners in enrolled HIV negative male partners
        - Couple use of ART/PrEP (ART use in enrolled HIV-positive male and female partner or PrEP initiation in HIV-uninfected partners. An alternative (stricter) definition of ART use may also consider the biomarker viral suppression )

Aim 1c

- Time to initiation of PrEP for male HIV-uninfected partners:
    - Amongst women with enrolled partners
        - Time to enrolled male partner with known HIV-negative status initiating PrEP.
        - Time to enrolled HIV-uninfected male partner who started PrEP or has female partner who is VS (Couple use of ART/PrEP). VS of the woman is defined as VS at both the prior and subsequent visit

Aim 2a

- Viral load suppression (Defined as VL < 400 copies) at 12 months post-partum amongst enrolled women.

### 2.2.2. Secondary Endpoints

- Viral load suppression at 6 and 12 months
- Disclosure of HIV-infected status to male partner

- Male partner disclosure to his partner

# 3. STUDY DESIGN

## 3.1. Summary of Study Design

This is an open label randomized trial of HIV-positive pregnant women and their partners. The overall goal is to evaluate the impact of innovative strategies on male partner HIV testing, and engagement in HIV care and prevention among men, on post-partum ART continuation and adherence among HIV-positive women. We will recruit HIV-positive women in PMTCT B+ programs in Kampala to be randomized 2:1 to:

1) the intervention arm in which they receive HIVST kits for their partners with self-instruction materials about HIVST, encouragement to seek confirmatory testing and counseling along with a voucher and referral, and brief educational materials about PrEP and ART, or
2) the control arm in which they receive invitation letters to deliver to their partners that invite men to fast-track HIV testing at the clinic, along with brief educational materials about PrEP and ART.

## 3.2. Sample Size Considerations

### 3.2.1. Sample Size Justifications

The sample size was selected to ensure high power for detecting increases in male partner testing comparing HIV self-testing to SOC information letter. Table 1. shows a range of assumptions for the proportion of women who enroll HIV partners. We assess as a time-to-event outcome, with a range from 20-30% at one year after enrollment in the standard of care arm, and an increase to 55-65% in the intervention arm. Women are enrolled at various times during their pregnancy, and followed for 1 year past partun, Thus we assume follow-up varies from 1-1.5 years (i.e. accrual occurs over ~ 6 months), and enrollment of the male partner can occur anytime during the women's follow-up.

Table 1: Sample size justification

| | | | Total number of males enrolled | |
|---|---|---|---|---|
| Proportion males tested at 1 year in SOC arm | Proportion males tested at 1 year in intervention arm | Hazard Ratio | 90% power | Expected under alternate hypothesis with 200 per arm |
| 20% | 50% | 2.32 | 43 | 175 |
| 20% | 45% | 2.01 | 59 | 162 |
| 20% | 40% | 1.76 | 88 | 150 |
| 30% | 50% | 1.74 | 105 | 200 |
| 30% | 45% | 1.51 | 180 | 188 |
| 30% | 40% | 1.31 | 390 | 175 |

We assume that uptake of testing will be independent of HIV status and uptake of ART in the HIV-positive men will be 100%. To assess overall PrEP uptake for men who are HIV-uninfected (60-70%) by arm and the test uptake in the standard of care arm (20-30%, as observed in and Enhanced testing arms (55-66%).

| Table 2. Sample size calculations for comparison of proportion of men on PrEP/ARV | | | | | | |
|---|---|---|---|---|---|---|
| Proportion of HIV-negative men | HIV test uptake | | Uptake of PrEP | | Sample size to achieve | |
| | SOC | Enhanced | SOC | Enhanced | 80% power | 90% power |
| 60% | 20% | 55% | 18% | 48% | 210 | 280 |
| 60% | 20% | 65% | 18% | 57% | 132 | 176 |
| 60% | 30% | 55% | 26% | 48% | 820 | 1,096 |
| 60% | 30% | 65% | 26% | 57% | 352 | 470 |
| 70% | 20% | 55% | 17% | 47% | 206 | 274 |
| 70% | 20% | 65% | 17% | 56% | 130 | 172 |
| 70% | 30% | 55% | 26% | 47% | 1,028 | 1,376 |
| 70% | 30% | 65% | 26% | 56% | 406 | 542 |
| Randomization is 2:1 for Enhanced: SOC. Assumes 95% retention, 80% PrEP uptake, 100% ARV uptake in HIV-infected men | | | | | | |

Assuming PrEP uptake in HIV-negative men is 80% and 60% of the men are HIV-uninfected, with a sample size of 500 we would have almost 90% power to detect an increase in PrEP use resulting from a change from 30% to 55% in test uptake.

## 3.3. Randomization

HIV-positive pregnant women are randomized in a 2:1 ratio to provision of HIVST kits to use with their male partners or to take an invitation letter to their male partner to be tested at their ANC clinic, or if the male prefers. Randomization was open label, with variable size blocks, without stratification.

## 3.4. Assessments

### 3.4.1. Male visit schedule:

Every three months after enrollment up to 12 month post-partum. Men will undergo informed consent for HIV testing and referral for HIV care and ART if they test HIV-positive, or offered PrEP if they test HIV-negative.

### 3.4.2. Pregnant women schedule:

Antenatal visit schedule to align with the PMTCT schedule. One visit expected every trimester. Study visits occur every three months after birth (post partum). Viral load (VL) monitoring will include plasma HIV RNA levels at enrollment, 6 and 12 months post-partum.

# 4. PLANNED ANALYSES

## 4.1. Interim Analyses

The study has an independent monitoring committee. Interim reviews will occur approximately every 6 months

## 4.2. Final Analyses

Final analyses will occur when all women are 12 months post-partum.

# 5. GENERAL CONSIDERATIONS FOR DATA ANALYSES AND HANDLING

## 5.1. Analysis Populations

### 5.1.1. ITT Population

The ITT women population is all women enrolled and randomized into the study. Women are pregnant and HIV-infected and do not know their male partner's status.

The ITT male partner population includes male partners of all women enrolled and randomized into the study. Male follow-up begins at the time of their enrollment and ends when their partner reaches 12 months post-partum,

### 5.1.2. Women with enrolled partners Population

Women who have male partners who are tested for HIV and enroll in the study; HIV-uninfected will be assessed for PrEP initiation; HIV-positive men for ART initiation.

### 5.1.3. Enrolled male partners

Male partners of women who enroll in the study.

## 5.2. Categorization of variables

### 5.2.1. Baseline demographics of female participants

- Age
- Marital status
- Prior knowledge of HIV status
- ART use at enrollment
- VL at enrollment
- Pregnancy History
- Male HIV status (self-reported by woman)

### 5.2.2. Use in analysis

Key predictors

1) Study arm: HIVST (Intervention arm) versus Letter (standard of care arm). Assigned at randomization of the women.

2) Partner enrolled (time varying): whether male partner was enrolled prior to the current visit.
3) Uptake of PrEP/ART of partner (time varying):
    a. A woman has a partner with PrEP/ART uptake at her visit if her partner knows his HIV status and is either on ART (if HIV-positive) or initiated PrEP (if HIV-negative) prior to that visit. Both male partners who do not enroll and male partners who do not initiate ART or PrEP are defined as no uptake of PrEP/ART. In analyses that use time to PrEP/ART, time of first report of PrEP/ARV will be used.
    b. An alternative definition will also define any HIV-negative men with partners who are virally suppressed as on PrEP/ART. A female partner is defined as being VS if she is virally suppressed at assessments both before and after the visit.
4) Disclosure of HIV-infected status to male partner self-reported at baseline

Effect modifiers:

1) Viral suppression of woman (time varying, measured at baseline, 6 and 12 mo)
2) Trimester of pregnancy at enrollment
3) Partner ever tested for HIV (time varying: reported by female partner)
4) Mutual disclosure status of HIV (time varying, as reported by each partner). If no enrolled male partner, mutual disclosure is assumed to not occur.
5) Male HIV status. If a male partner does not receive HIV testing from the study site, it is assumed their HIV status is unknown to both members of the coupleStudy Population

### 5.3. Missing data

Every effort will be made to minimize missing data through high retention and monitoring of completeness of assessments. Assessments from adjacent visits are carried forward particularly where primary biologic assessments are missing but available at a another time, provided it is within approximately 3 months.

Complete case analysis is planned for self-reported data.

## 6. TABULATIONS

### 6.1. Participant Disposition

A study consort table or diagram will account for the following trial participants disposition, by arm where applicable

- Number of women screened
- Number of women enrolled (optionally by trimester)
- Visit completion (retention) by women for each post-partum visit

- Primary analysis cohort (VL assessment at 12 Mo PP)
- Proportion with male partners enrolled
- Visit completion (retention) of male partners, for all expected quarterly visits

## 6.2. Study Termination Status

- Completion status for all women in the study: lost to follow-up, completed follow-up, death, other (reasons for premature study termination)
- Completion status for all enrolled male partners: lost to follow-up, completed follow-up, death, other (reasons for premature study termination)

## 6.3. Demographic and Baseline Characteristics

### 6.3.1. Pregnant women

Demographic and baseline characteristics of women in the ITT population will be summarized by study arm. This will include:

- Age: characterized as
  - 18 – 24
  - 25 – 29
  - 30 – 34
  - ≥35
- Marital Status
- ART history
- Baseline Viral Load
  - Defined as undetectable if < 50 copies/ml.
  - Median viral load amongst those with detectable viral load.
- Pregnancy history
- Trimesters in reporting is defined as:
  - Trimester 1 is weeks 0 – 14 at Enrollment
  - Trimester 2 is weeks 15 – 27 at Enrollment
  - Trimester 3 is ≥28 weeks at Enrollment
- Partner HIV testing history (reported by women)

The same characteristics will be reported by male partner enrolled.

### 6.3.2. Male partner

Demographic and enrollment characteristics of men in the PP population will be summarized by study arm

- Age: dichotomized into 5 categories
  - 18 – 24
  - 25 – 29
  - 30 – 34
  - ≥35
- Age difference between partner, dichotomized into 5 categories using the age reported by the male partner (of himself and his partner)
  - Male > 5 years older than pregnant partner
  - Male 0 – 5 years older than pregnant partner
  - Male 0 – 5 years younger than pregnant partner
  - Male at least 5 years younger than pregnant partner
- Partnership duration (reported by men)
- HIV testing history

# 7. ANALYSES

## 7.1. General Considerations

Inferential statistical tests will be two-sided and will be performed at alpha levels of 0.05 and 0.10 to declare the significance of main effects and interaction effects, respectively.

No adjustment for multiplicity are planned.

## 7.2. Statement of the Null and Alternate Hypotheses

The null and alternative hypotheses are:

$H_o$: Provision of self-test kits to the male partner by his pregnant partner does not have a differential effect on 1) male partner testing, 2) PrEP uptake in HIV-uninfected male partners or 3) viral suppression at 12 months in the women, compared to the standard of care (letter).

$H_A$: Provision of self-test kits to the male partner increases 1) male partner testing, 2) PrEP uptake in HIV-uninfected male partners and 3) viral suppression at 12 months in the women, compared to the standard of care (letter).

**Subgroup Analyses**

Subgroups of interest:

- Women who have disclosed their HIV-infected status prior to/reported at baseline
- Women who were virally suppressed (VL < 50 copies/mL) at baseline
- Women <=24 vs > 24 years old
- Women who were on ARVs prior to their pregnancy

## 7.3. Analysis of the Primary Endpoints

### 7.3.1. Aim 1a Difference in male partner testing between arms

Endpoint: HIV testing at the study site of a woman's male partner. HIV testing at the site is synonymous with male partner enrollment.

Descriptive analyses:

- We will tabulate the proportion of women with male partner enrollment by the end of the study by arm, and the resulting HIV status (by study testing) of the male partners at enrolment.
- We will tabulate the proportion of men who have been HIV tested, and their HIV test result, according to the women's self-report, by arm. Note that as the HIVST arm provides a test for men at home, this comparison has potential for ascertainment bias.

Statistical analysis

We will use Kaplan-Meier curves to depict the time from women's enrollment until her male partner's site HIV test (i.e. enrollment) by study arm.

We will assess the difference between arms using a time to event analysis of time of randomization of the pregnant women until the event of her male partner's HIV test at enrollment. A Log-rank test will be used to assess the statistical significance of difference between arms; Cox proportional hazard regression will be used to estimate the HR and 95% CI. The Kaplan Meier curve will be used to assess the proportion of male partners tested at 6 and 12 months after female partner randomization. Pointwise confidence intervals will be computed assuming the normal approximation, using the standard error of the estimate from the KM curve.

### 7.3.2. Aim 1b Difference in uptake of PrEP/ART for male partner between arms

Endpoint: Enrolled male partner of an enrolled women initiates PrEP, if he is HIV-uninfected, or initiates ART, if he is infected.

Descriptive analysis.

- We will tabulate the proportion of women whose male partner initiates PrEP/ART by the end of the study, and report initiation of PrEP/ART separately by HIV-status of the male partner

- Amongst the enrolled male partners, we will tabulate the proportion of HIV-infected men who initiate ART, and HIV-uninfected men who initiate PrEP, within each arm, by the end of the study.
- HIV+ men who are on ART at time of study enrollment will be omitted from this analysis

Statistical analysis

We will use Kaplan-Meier curves to depict the time from women's enrollment until her male partner has initiated PrEP/ART by study arm.

We will assess the difference between arms using a time to event analysis of from time of randomization of the woman until the event of her male partner initiating PrEP/ART. For women who never have a partner enroll, the male partner remains at risk for the event throughout the woman's follow-up; time will be censored at the woman's last observed visit. Women with partners already on PrEP/ART with the partner enrolled are not at risk and are omitted from the analysis Log-rank test will be used to assess the statistical significance of difference between arms; Cox proportional hazard regression will be used to estimate the HR and 95% CI. The Kaplan Meier curve will be used to assess the proportion of male partners who initiate PrEP/ARV 6 and 12 months after female partner randomization. Pointwise confidence intervals will be computed assuming the normal approximation, using the standard error of the estimate from the KM curve.

### 7.3.3. Aim 1c Difference in PrEP initiation for HIV-negative male partner between arms

Endpoint: For HIV-negative enrolled male partners, initiation of PrEP.

Descriptive analysis

- As described for Aim 1b

Statistical analysis

Since the intervention could affect the enrollment of the male partner differentially by HIV status, we will assess probability of ever initiating PrEP for HIV-uninfected men both unconditional on enrollment and conditional on enrollment.

We will assess the difference in PrEP initiation by end of study between arms conditional on known HIV-negative status using a t-test restricted to all enrolled male partners and assessing difference in probability by arm. Logistic regression will be used if estimates adjusted for baseline characteristics are needed because of imbalance in important characteristics of women or men between arms in this subset.

For the unconditional estimate, we will assess the difference in PrEP initiation between arms amongst the (unobserved) true number of HIV-negative male partners in the enrolled pregnant women using a likelihood ratio test for H0: $pp_{ssss} = pp_{lllllllllll}$ vs Ha $pp_{ssss} \neq pp_{lllllllllll}$. The likelihood is

computed assuming the baseline probability of an HIV-negative partner is the same in the two arms.

The proportion of HIV-uninfected men initiating PrEP at 6 months is not directly observed, since the HIV status of unenrolled male partners is not known. A log-likelihood approach will be used to estimate the unobserved proportion of HIV-negative partners on PrEP in each arm (including unenrolled men) and compare the proportions by arm within each HIV-status.

The log likelihood for estimating the proportion of HIV-uninfected men of PrEP is

$$LL(xx_{ii}, NN_{ii}) = -\sum_{nn=xx_{ii}}^{NN_{ii}} bbbbbb(xx_{ii}, bb, pp)bbbbbbbbbbbbbb(bb, NN_{ii}, bb, bb)$$

Where $xx_{ii}$ is the number of observed HIV-negative partners starting PrEP in arm *i*

$NN_{ii}$ is the number of women enrolled in arm *i*

$bb, bb$ are beta priors for $pp$, the probability of an HIV-negative partner among all enrolled women.

The likelihood ratio test is computed under the null $H_0$: $pp_{ssss} = pp_{uuuuuuuu}$

### 7.3.4. Aim 2a. Assess whether having a male partner who has initiated PrEP/ART affects viral load suppression at 12 months post-partum in his female partner

Endpoint: Viral suppression (VL < 400 copies/mL) at the 12 month post-partum visit.

Descriptive analysis:

- We will tabulate the number of women by the their partners disposition: 1) No partner enrolled 2) Partner enrolled, not initiated PrEP/ART, 3) partners enrolled and have initiated PrEP/ART. Baseline demographic and risk characteristics of women will be compared by group. If Group 2 is less than 10% of the cohort, it may be combined with Group 1.
- We will describe the characteristics of the women's viral load at 12 months within each group: mean, median, IQR, proportion with suppressed viral load.

Statistical analysis:

We will use modified Poisson regression with robust standard errors to compare the proportion of women who are virally suppressed between groups.

The analysis will include men who were on ART at enrollment.

This comparison is not protected by randomization therefore we will adjust for the following potential confounders:

- Age (in categories)
- Viral suppression at baseline
- Trimester of pregnancy at enrollment

- Randomization arm
- Baseline covariates that demonstrate imbalance between the groups ($p < 0.05$ in comparison of characteristics), not thought to be mediators of differences in outcome.
- Assessments occurring prior to April 2020 (prior to COVID 19)

We will assess for effect modification by analysis of interaction between the subgroups of women who are virally suppressed at enrollment.

Handling of missing VL data:

- If 12 month VL is missing, but VL is available from 9 month PP, the 9 mo VL will be used to estimate the 12 mo VL.

#### 7.3.5. Aim 2b. Assess whether having a male partner who has initiated PrEP/ART affects viral load suppression at 6 and/or 12 months post-partum in his female partner

Endpoint: Viral suppression at the 6 and 12 month visit post partum.

Statistical analysis:

Repeated measure analysis will be used for this aim. The viral load at 6 month and 12 months will use a time-dependent covariate for whether her male partner had initiated PrEP/ARV at least 3 months prior to the VL measurement. We will assess whether initiation of PrEP/ARV 3 month prior increases the probability of viral suppression using GEE logistic or modified Poisson regression

Handling of missing VL data:

- If 12 month VL is missing, but VL is available from 9 month PP, the 9 mo VL will be used to estimate the 12 mo VL.
- If 6 month VL is missing, but VL is available from 3 month PP, the 3 mo VL will be used to estimate the 6 mo VL.

### 7.4. Secondary analyses

#### 7.4.1. Aim 3: Evaluate associations between time of a women disclosing their HIV-infected status to their male partner and the trial endpoints: enrollment of the male partner, uptake of PrEP/ART; viral suppression

Descriptive analysis

- Tabulate the visit where the women first reported disclosure of her HIV-infected status to her partner
- For enrolled male partners, tabulate visit of first disclosure of male HIV status to his partner by male HIV status
- For women with enrolled partners, tabulate the joint disclosure of each partner by the end of the study

Statistical analysis

1) Assess whether a woman's disclosure of HIV-infected status to her partner changes the probability of her male partner testing

   Method: Time to event (event = male partner enrollment) Cox PH model with time varying covariate of women's disclosure. Disclosure is assessed as a cumulative time varying covariate, where a woman is considered disclosed if she self-reports disclosure at any time at or before the outcome is reported (i.e. if she reports disclosure at a visit before or at when her partner is enrolled). Women are assumed undisclosed until first visit she reports disclosure. Time is censored at the earliest of male partner testing (i.e. enrollment) or woman's last attended visit.

2) Assess whether male partner testing changes the probability of disclosure

   Method: Time to event (event = woman's first report of disclosure) Cox PH model with time varying covariate of male partner enrolled. Women who self-report disclosure at baseline are excluded. Time is censored at the earliest of first disclosure or woman's last attended visit.

3) Assess whether a woman's disclosure of HIV-infected status to her partner changes the probability of initiation of PrEP/ART in her partner

   Method: Same as 1) above, only with event = male partner initiated ART/PrEP. Analysis may be conducted in the entire v=cohort, and restricted to women with an enrolled partner

4) Assess whether a woman's disclosure of HIV-infected status to her partner changes VS of women

   Method: Repeated measure analysis of outcome viral suppression in women. At each measurement of VL, primary time-varying covariate is whether the women has disclosed to her partner at or prior to the measurement. GEE model for probability of the outcomes will be used, including all visits where outcome is reported. Baseline viral loads are included

In all of the above models, adjustment for the following covariates will be considered (as appropriate):

- Age (in categories)
- Viral suppression at baseline
- Trimester of pregnancy at enrollment
- Randomization arm
- Women's prior knowledge of her HIV status
- Male Partner HIV status Negative, Positive, not known.

Additional variates may be considered if evidence of confounding is found (greater than 10% change in estimated effect).

### 7.4.2. Pregnancy outcomes

Describe pregnancy outcomes by arm, ARV and VS measures during the pregnancy, HIV status of infant.

### 7.4.3. Partner seroconversion

Describe seroconversions by arm, ARV/PrEP status of the partner, ARV and VS measures of the pregnant woman during the study.

## 8. REFERENCES

## 9. REVISIONS TO THE SAP