

Letter of Amendment # 3 to:

HPTN 061: Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men, Version 2.0, dated 02 April 2009, DAIDS Document ID# 10666

Letter of Amendment Date: 01 April 2010

The following information impacts the HPTN 061 study and must be forwarded to all responsible Institutional Review Boards (IRBs)/Ethics Committees (ECs) as soon as possible for their information and review. This Letter of Amendment must be approved by all responsible IRBs/ECs before implementation.

The following information may also impact the Sample Informed Consent. Your IRB/EC will be responsible for determining the process of informing subjects of the contents of this Letter of Amendment.

This Letter of Amendment and any IRB/EC correspondence must be filed in the site regulatory file and in other pertinent files. Submission of these documents to the DAIDS/RCC Protocol Registration Office is not required unless the changes result in a change to the informed consent form for your site.

Section 1: Summary of Revisions and Rationale

1. A change was made to expand the subset of participants who will be considered “index” participants, to now include participants who test negative at enrollment and are eligible for follow up visits. This group includes the first 200 community-recruited participants who test HIV negative and those HIV negative men referred as sexual partners of index participants. It is expected that this change will partially offset the lower-than-expected rate of accrual of referred participants in the study to date.

Index participants are a subset of the community-recruited and referred participants who are able to refer up to five of their Black male sexual partners for enrollment into the study. It was originally thought that with “index” defined only as: 1) men who were known HIV infected but not in care, 2) those newly diagnosed as HIV infected at enrollment, and 3) a small percentage of those who tested HIV negative, that 17% of study participants would be index-referred participants. However, currently only 9% of participants are index-referred, which, if uncorrected, could lead to 145 fewer participants enrolled in the study than originally expected.

Based upon the trends in the data so far, opening up the index criteria to include participants who test negative at enrollment and are eligible for follow up visits can be expected to result in about 85 additional referred participants joining the study. This increase in referrals will not only help the study get closer to its recruitment target overall, but may provide some preliminary data on whether the referred partners from HIV negative Black MSM are more or less likely than partners of HIV positive men to be known positive and not in care, or undiagnosed positive.

The initial per-site sample size calculations included in Table 2 of the protocol have not been altered as part of this Letter of Amendment. The calculations in Table 2 were an estimate of enrollment generated before study implementation based upon numerous pre-study assumptions and projections. As such, the protocol team feels they should not be updated in response to on-study outcome data, or to account for changes in study procedures made after study activation.

Section 2: Implementation of the Protocol Modifications

The modifications detailed below will be formally incorporated into the body of the protocol with the next full amendment. Deletions to the protocol text are indicated by strikethrough; additions are indicated in bold.

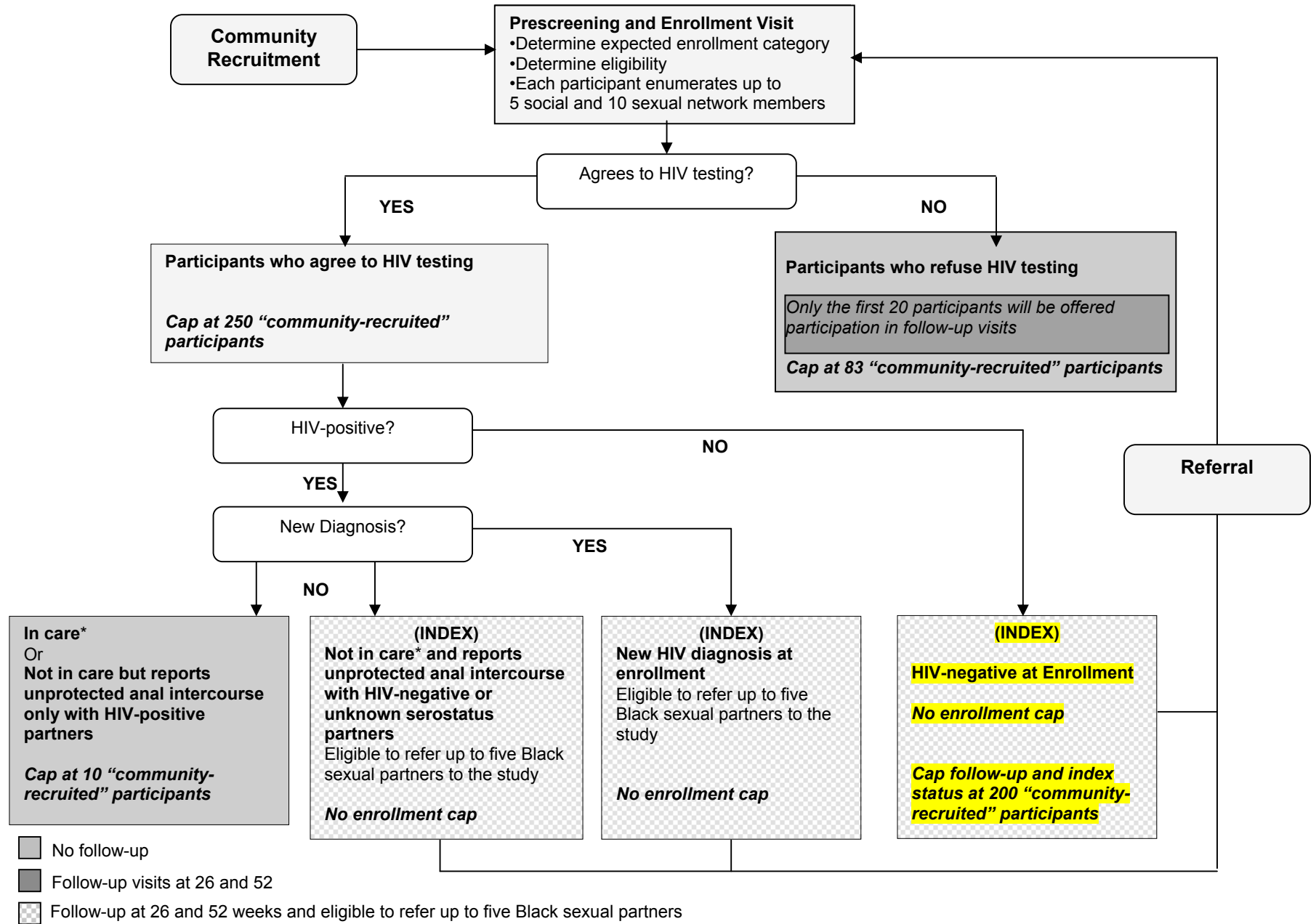
Revision 1 Modifications were made to the schema, Figure 4, Section 2.3, Section 4.1, and Section 7.3 that in addition to the current inclusion criteria for index participants, participants who test negative at enrollment and are eligible for follow up visits will also be considered index and able to refer up to five Black male sexual network partners.

Schema

Study Size

- A subset of community-recruited and referred participants will be considered “index” participants. Index participants are those who are newly identified with HIV infection, those with previously diagnosed HIV infection who are not receiving HIV care, and **participants who test negative at enrollment and are eligible for follow up visits** ~~a random sample of~~. This ~~last category~~ **includes the first 200 community-recruited, HIV negative participants, and HIV negative participants referred as sexual partners of index participants.** Index participants will be asked to refer **up to five** sexual partners.

Figure 4- Study Design of the Main (Quantitative) Component of HPTN 061 (Recruitment at One Site)



* "In care" = has engaged with health care provider for HIV care within the last six months

2.3 Study Design: Main (Quantitative) Component

Index participants meet one of the following criteria in addition to the study inclusion criteria listed in Section 3.1:

- Newly diagnosed with HIV infection at HPTN 061 the enrollment visit (no cap).
- Diagnosed with HIV prior to enrollment in HPTN 061, but are not in care (for this study, “not in care” means not having engaged with a health care provider for HIV-related care in the last six months) and have had unprotected anal sex with HIV uninfected partners or partners of unknown status in the last six months (no cap).
- ~~HIV negative participant randomly selected as eligible to refer partners (cap at 20 HIV negative participants designated as index~~ **Among the first 200 community-recruited, HIV negative participants or those who enroll as an HIV negative referral from an index participant.**

Those participants newly diagnosed with HIV, or chronically infected but not in care (the first two bullets above), are expected to pose a high risk for transmission of HIV to their partners because they either do not know they are infected, or, if infected, have a viral load unsuppressed by ART. The partners of these high-risk men, therefore, are expected to be at especially high risk for having, or acquiring, HIV, and recruiting them into the study will allow the intervention to be targeted at the sub-population where it may be most effective. Therefore there will be no cap for enrollment of these participants into the study.

~~Up to 20 HIV negative participants will be designated as index participants at each site during the study (third bullet above). This will be accomplished using a selection method that randomly identifies a fraction of the 20 men during each month in which negative participants are enrolled.~~ **The first 200 community-recruited, HIV negative participants will be designated as index, as will those who enroll as an HIV negative referrals from an index participant (third bullet above).** HIV-negative participants are being included as index participants so that: **1) a participant’s HIV status will not be automatically disclosed if he is referring participants to the study, 2) adequate numbers of index-referred participants are enrolled into the study, and 3) preliminary data can be obtained about differences in the HIV risk profile of referred partners of HIV negative men versus men with either newly diagnosed HIV infection or known infection who are not in care.**

All index participants, whether HIV-positive or HIV-negative, are encouraged to refer up to five of their Black male sexual network members for enrollment.

4.1- Network Recruitment

Participants who meet the criteria to be index participants will be asked to refer up to five Black MSM sexual network members from their list of sexual network partners. This process will be continued through multiple waves. To minimize risk that a referring participant in HPTN 061 will have his HIV status disclosed, ~~up to 20 randomly selected~~ **the first 200 community-recruited, HIV negative participants, and HIV negative participants referred as sexual partners of index participants,** ~~per site will also be selected at random and~~ asked to refer their partners. Index participants will be provided with individual cards marked with a unique identification number to facilitate the recruitment of their network members. There will be no information on the cards to indicate that a participant is in an HIV study. The prospective index participants will be asked to give the cards to their sexual network members and to encourage their network members to bring the card with them when they report to the study site for study screening.

7.3 Accrual, Follow-Up, and Sample Size

Participants who are newly diagnosed with HIV or who were previously diagnosed but not in care, ~~and 20 randomly selected~~ **the first 200 community-recruited, HIV negative participants, and HIV negative participants referred as sexual partners of index participants** will be classified as index participants and will be asked to refer their Black MSM sexual network members. Successful screening of these sexual network members (referred participants) will result in recruitment of additional participants in each of the above categories in the next wave of recruitment. This process will be repeated until the recruitment waves self-extinguish, expected to be approximately two to three waves.

Table 2 (following page) shows the expected number of men enrolled in each category at the city level, using the following assumptions:

- Each city will enroll 250 participants who agree to HIV testing through community recruitment. An expected 75% HIV testing consent rate would yield an additional 83 Enrolled Not Tested participants, and a total of 333 community-recruited participants.
- Twenty-five percent of participants who agree to test will be HIV-infected.
- Fifty percent of those who tested positive will be unaware of their HIV status.
- Fifty percent of those who tested positive will be previously diagnosed. Among them, 10% will be either in care or not in care but will report UAI with HIV-positive partners only.
- The following groups of participants will be asked to refer their Black MSM sexual network members: 1) newly diagnosed with HIV, 2) previously diagnosed but not in care and who report UAI with HIV-negative or unknown serostatus partners, and 3) a randomly selected sample of 20 HIV-uninfected participants at each site.
- Seventy-five percent of participants asked to refer will have at least one of their Black MSM sexual network members enroll in the study.
- The following groups of participants will be followed at 26 and 52 weeks: 1) newly diagnosed with HIV, 2) previously diagnosed but not in care and who report UAI with HIV-negative or unknown serostatus partners, 3) the first 160 HIV-uninfected participants, and 4) the first 20 Enrolled Not Tested participants at each site.

Note: With the implementation of Letter of Amendment 3 to this protocol, the number of HIV negative participants who will be identified as “index” will increase beyond the assumptions reflected in Table 2. However, since Table 2 represents an estimate of sample size estimate based upon pre-study assumptions, these estimates have not been altered to reflect on-study outcome data, or adjustments to study implementation made after study activation.