

**Letter of Amendment # 1 to:**

**HPTN 078: Enhancing Recruitment, Linkage to Care and Treatment for HIV-Infected Men Who Have Sex with Men (MSM) in the United States**  
**Version 1.0, dated 8 October 2015**  
**DAIDS Document ID: 11995**

**Final Version of LoA # 1: 15 January 2016**

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The following information impacts the HPTN 078 study and must be forwarded to all responsible Institutional Review Boards (IRBs) as soon as possible for their information and review. This Letter of Amendment (LoA) must be approved by all responsible IRBs before implementation.

The information contained in this LoA does NOT impact the sample informed consent forms.

Upon receiving final IRB approval for this LoA, sites should implement the LoA immediately. Sites are still required to submit a LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). Sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. A LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with the LoA and any IRB correspondence should be retained in the site's regulatory files.

If the HPTN 078 protocol is amended in the future, this LoA will be incorporated into the next version. Deletions to the protocol text are indicated by ~~strikethrough~~; additions are indicated in **bold**.

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**Summary of Revisions and Rationale**

1. The number of care visits used to assess retention in care in one of the secondary objectives was increased from two to four. During protocol development, the duration of follow-up was changed from 12 months to 24 months, but the number of care visits was not adjusted accordingly. This revision brings the secondary objective into alignment with the study's follow-up period of 24 months.
2. The inclusion/exclusion criteria were revised to more clearly indicate which criteria apply to screening and which to enrollment. In addition, verbiage was removed to allow sites to seek a waiver of parental consent from their IRBs for DC-RDS activities alone or for both DC-RDS and CM activities. Information about obtaining a waiver of parental consent was added to Section 8.2 (Informed Consent). These clarifications were made to address questions raised by site IRBs, as all sites are seeking a waiver of parental consent for DC-RDS activities. Finally, one of the inclusion criteria was revised to clarify that

potential participants must be able to receive HIV care at a pre-determined clinic (as chosen by each site) to be eligible for enrollment.

3. The time periods between the S1 and S2 visits and the S2 and Enrollment Visits were revised so that the S2 visit can coincide with DC-RDS activities when appropriate, while ensuring that there will be no study-related delay in linking HIV-infected participants to HIV care.

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## Implementation

### Revision 1

#### Schema (Secondary Objective)

Assess linkage to care and retention in care in the two study arms by comparing the 1) proportion of men with at least one care visit within 30 days of enrollment, 2) time to the first care visit, and 3) proportion of men with at least ~~two~~ **four** care visits (one in each six month interval, with at least 60 days between these visits) over the 24 months after enrollment.

#### 2.2 Secondary Objectives

Assess linkage to care and retention in care in the two study arms by comparing the 1) proportion of men with at least one care visit within 30 days of enrollment, 2) time to the first care visit, and 3) proportion of men with at least ~~two~~ **four** care visits (one in each six month interval, with at least 60 days between these visits) over the 24 months after enrollment.

#### 7.6.2 Secondary Analysis

We will also compare the proportion of MSM who are retained in care (defined as at least ~~two~~ **four** care visits [one in each six month interval, with at least 60 days between these visits] over the 24 months after enrollment) between the CM intervention and SOC control arm. Any randomized participant who drops out of the study without at least two care visits as defined above will be counted as “not retained” for the purpose of this analysis. The absolute difference in the probability of retention between the CM intervention and SOC control arms and a 95% CI will be reported. A chi-squared test with a two-sided alpha level of 0.05 will be used for hypothesis testing. The analysis will follow the intent to treat principle.

### Revision 2

#### 3.1 Inclusion Criteria

Individuals who meet all of the following criteria are eligible for ~~inclusion in the study screening (screening, CM intervention arm and SOC control arm):~~ **inclusion in the study screening**:

- Biological male (currently and at birth)
- Self-report of history of anal intercourse with another man within the last 6 months
- 16 years or older (~~At sites with IRB approval, MSM age 16-17 years old can be recruited and enrolled if they are willing and able to provide written assent, and if a parent or legal guardian is willing and able to provide written informed consent.~~)

~~In addition to the criteria above,~~ Individuals who **are eligible for screening and who** meet all of the following criteria are eligible for enrollment into the CM intervention and SOC control arms:

- HIV-infected, as defined in the HPTN 078 Study-Specific Procedures (SSP) Manual
- Not virally suppressed (defined as HIV VL > 1000 copies/ml, note that this VL cut-off is being used as an indicator of adherence or resistance issues for study inclusion only)
- Can receive **HIV** care at one of the **pre-determined participating clinics (as chosen by each site)** (~~listed in the HPTN 078 SSP Manual~~)
- No current plan to relocate in the 24 months following enrollment

### 3.2 Exclusion Criteria

Individuals who meet any of the following criteria will be excluded from ~~the study screening (screening, CM intervention arm and SOC control arm):~~ **the study screening** (screening, CM intervention arm and SOC control arm):

- Unable or unwilling to provide consent/**assent** (~~or assent for a minor with parent or legal guardian consent~~) for study participation
- Transgender women
- Active or previous participation in an HIV vaccine trial, unless evidence can be provided documenting randomization to the placebo arm.
- Any condition that, in the opinion of the Investigator of Record (IoR), would make participation in the study unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives.

~~In addition to the criteria above,~~ Individuals **who are eligible for screening, but who** meet ~~any of~~ the following criteria are excluded from enrollment into the CM intervention and SOC control arms:

- Current participation in a linkage or ART adherence study

### 3.7 Study Sites

Participants may be followed at **pre-determined participating** HIV clinics in each of the four cities. All **pre-determined participating** clinics must be able to provide the current SOC for HIV-infected MSM and be willing to provide participant information to the study team for analysis. In addition, a survey documenting standard-of-care practices will be completed for each clinic that cares for HIV-infected MSM enrolled in the study.

### 8.2 Informed Consent

Written informed consent will be obtained from each study participant prior to conducting study-related procedures. Each study site is responsible for developing a study informed consent form for local use, based on the templates in Appendix IV, which describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation, in accordance with all applicable regulations. **Based on local IRB approval and state law, sites may seek a waiver of parental consent for either the DC-RDS activities alone or both the DC-RDS and CM activities. However, only sites that are granted a waiver of parental consent for the DC-RDS activities will be allowed to screen minors (16 and 17 year olds).**

## Revision 3

### 5.1.2 Second Screening Visit (S2)

All participants will be asked to return for a second Screening Visit (S2) (~~a maximum of 14 days after S1~~) to receive the results of their HIV, syphilis and HCV tests. Post-test HIV counseling and HIV and sexually transmitted infection (STI) risk reduction counseling will be provided, as appropriate. If an individual is found to be HIV-infected or has discordant or inconclusive HIV test results, blood will be drawn for CD4 and viral load (HIV RNA) testing and additional plasma storage. They will also undergo a social impact assessment. Additional blood will be collected for HIV testing and plasma storage at the second Screening Visit if the HIV test results from the first Screening Visit were not conclusive. A post-recruitment questionnaire will be administered to anyone distributing coupons. Blood will not be collected from individuals who tested negative for HIV infection at the first screening visit (i.e., those who did not have reactive or positive HIV test result from the S1 visit).

### 5.2 Enrollment Visit (MO)

**The Enrollment Visit will take place as soon as participants are determined to be eligible.** During this visit (~~a maximum of 14 days after S2~~), participants will be consented for enrollment and randomized to either the CM intervention or SOC control arm. Participants will be asked to sign a release of medical information, locator information will be confirmed and they will be asked to complete a questionnaire (see Appendix II).

All participants will be offered HIV testing for their partners. Depending on the results of the partners' HIV test results, partners will be referred to appropriate HIV care services or other HIV-related studies. [Note: partner testing will be done outside of the study and results will not be recorded.] In addition, the intervention will begin at this visit for those randomized to the CM intervention arm, and, if appropriate, ART may be initiated at this visit. (Note that ART is not provided by the study, nor prescribed by the CM.)