HPTN 061

Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men DAIDS ID: 10666

in preparation for

A Community-Level Randomized Trial to Test the Efficacy of the Intervention in Reducing HIV Incidence Among Black Men Who Have Sex with Men

A Study of the HIV Prevention Trials Network

Sponsored by:

US National Institute of Allergy and Infectious Diseases
US National Institute on Drug Abuse
US National Institute of Mental Health
US National Institutes of Health

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02 April 2009

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I, the Site Principal Investigator, agree to conduct this study in full accordance with the provisions of this protocol. I agree to maintain all study documentation for a minimum of three years from the end of the study, unless directed otherwise by the HIV Prevention Trials Network (HPTN) Coordinating and Operations Center (CORE). Publication of the results of this study will be governed by HPTN and DAIDS policies. Any presentation, abstract, or manuscript will be made available by the investigators to the HPTN Manuscript Review Committee and DAIDS for review prior to submission.

I have read and understand the information in this protocol and will ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about the obligations incurred by their contribution to the study.

_____
Name of Site Principal Investigator

_____ _____
Signature of Site Principal Investigator Date

HPTN 061

Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men

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Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men

LIST OF ABBREVIATIONS AND ACRONYMS

ACASI	audio computer-assisted self interview
AIDS	acquired immunodeficiency syndrome
BED	HIV subtypes B, E and D
BGRG	Black Gay Research Group
CAB	community advisory board
CDC	Centers for Disease Control and Prevention
CCR5	chemokine (C-C motif) receptor 5
CI	confidence interval
CLIA	Clincal Laboratory Improvement Amendments
CORE	(HPTN) Coordinating and Operations Center
CQR	Consensual Qualitative Research Method
CRF	case report form
CRT	community randomized trial
CT	Chlamydia trachomatis
DAIDS	Division of AIDS
EAE	Expedited Adverse Event
EC	ethics committee
FDA	(United States) Food and Drug Administration
GC	gonorrhea
GCP	Good Clinical Practices
GEE	generalized estimating equations
HAART	Highly Active Antiretroviral Therapy
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
HPTN	HIV Prevention Trials Network
HPV	Human Papillomavirus
HRSA	Health Resources and Services Administration
HSN	Health System Navigation
HSV	herpes simplex virus
IATA	International Air Transport Association
ICH E6	International Conference on Harmonization
IQA	Immunology Quality Assurance
IRB	Institutional Review Board
LDMS	Laboratory Data Management System
LL	local laboratory
MAC	Multicultural AIDS Coalition
MSA	metropolitan statistical area

MSM	men who have sex with men
NAAT	nucleic acid amplification test
NHBS	National HIV Behavioral Survey
NIAID	(United States) National Institute of Allergy and Infectious Diseases
NIH	(United States) National Institutes of Health
NL	(HPTN) Network Lab
NYBC	New York Blood Center
OHRP	Office of Human Research Protections
PCRS	partner counseling and referral services
PD	project director
PY	person years
PHI	protected health information
PHN	peer health care system navigators/navigation
QA	quality assurance
QC	quality control
QWG	Qualitative Working Group
RCC	Regulatory Compliance Center
RNA	ribonucleic acid
RR	risk ratios
SAE	serious adverse event
SCHARP	Statistical Center for HIV/AIDS Research and Prevention
SDMC	(HPTN) Statistical and Data Management Center
SES	socioeconomic status
SOP	standard operating procedure
SD	standard deviation
SMC	Study Monitoring Committee
SPNS	Special Projects of National Significance
SSP	study-specific procedures manual
STI	sexually transmitted infection
UAI	unprotected anal intercourse
UCLA	University of California at Los Angeles
US	United States of America
VCT	voluntary counseling and testing
WB	Western blot
YMS	Young Men's Survey

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Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men

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HPTN 061

Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men

SCHEMA

Purpose: To determine the feasibility and acceptability of a multifaceted intervention among Black men who have sex with men (MSM), to prepare for a community-level randomized trial to test the efficacy of the intervention in reducing HIV incidence among Black MSM.

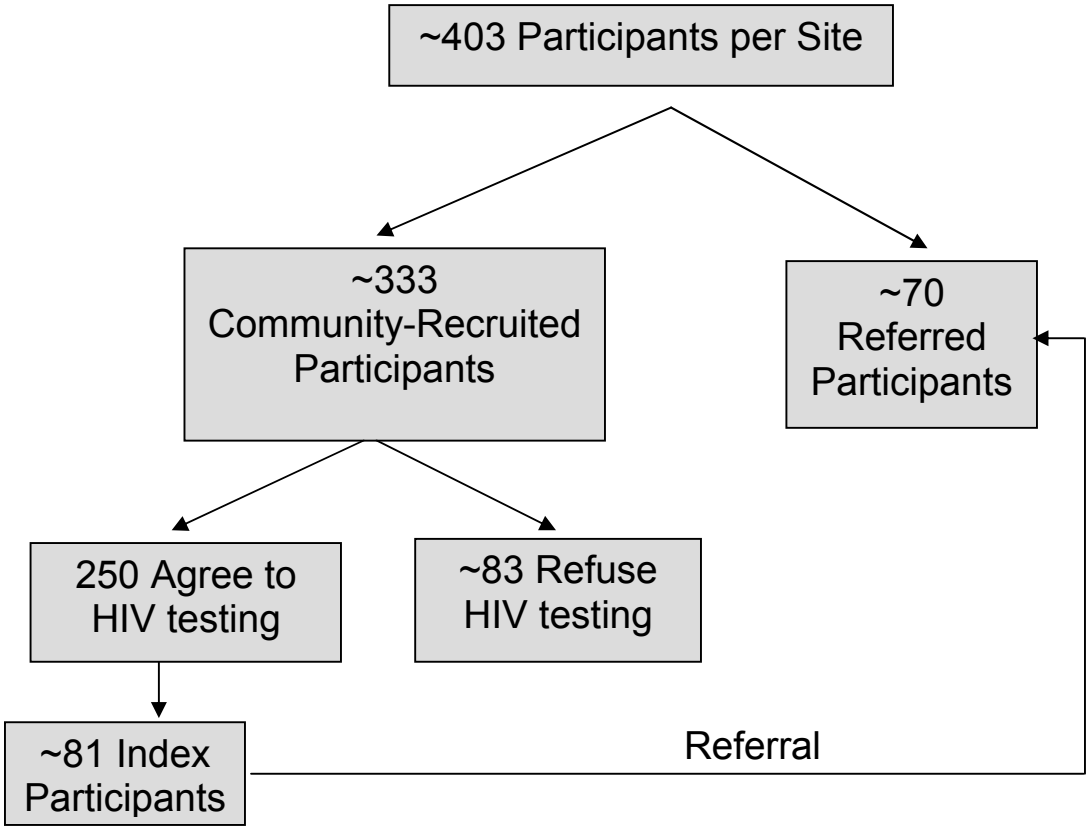
Design: A multi-site, community-level feasibility study, with longitudinal data collected for the majority of participants and only baseline cross-sectional data collected for a minority of participants. A subset of participants will also be recruited for qualitative interviews and focus groups.

Population: Sexually active Black MSM living in select cities in the United States (US).

Study Size: Approximately 2418 participants (403 per site at each of six sites)

- Men enrolling for this study will be recruited in one of two ways—either directly from the community ("community recruited" participants) or as sexual network partners referred by participants ("referred" participants).
- Enrollment of certain sub-categories of community-recruited participants will be limited according to criteria detailed in the protocol. Enrollment of community-recruited participants at a site will cease when 250 community-recruited participants who agree to HIV testing have been enrolled.
- 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 a random sample of HIV-negative participants. Index participants will be asked to refer sexual partners.
- There will be no cap on the number of referred participants enrolled into the study, however enrollment of referred participants will stop two months after closure of enrollment of community-recruited participants.

Figure 1- Participant Categories and Estimated Enrollment by Site



A subset of participants will be recruited from the main study to participate in focus groups (approximately 18-24 participants per site, or 108-134 participants overall) and qualitative interviews (between 10 and 30 participants at each site, or 60-180 participants overall).

Intervention:

The intervention components provided to participants include:

- Referral of up to five sexual partners by index participants for enrollment into the study.
- HIV risk reduction counseling, testing, and referral for care
- STI testing and referral for care.
- Counseling and referral for care offered to participants for issues such as substance use and mental health
- Engagement with peer health care system navigators (PHNs) to facilitate uptake of health care and other services.

Study Duration:

The total duration of the study will be two years. This timeline includes 12 months for participant accrual and up to 12 months of follow-up for each participant.

Primary Objective: To obtain the information needed to design a full, community-wide randomized trial. Specific areas of interest include:

- Recruitment of Black MSM.
- Uptake of the intervention components by Black MSM, including the proportion of enrolled participants who:
    - Agree to HIV testing.
    - Agree to STI testing.
    - Use peer navigation.
- Estimating the following in the course of the study:
    - Proportion of participants who are newly diagnosed with HIV at enrollment.
    - Increase in condom use from enrollment to week 52.
    - Decrease in viral load at week 52 among HIV-infected participants who initiate HAART during their study participation.
    - Decrease in prevalence of STIs from enrollment to week 52.
- Satisfaction of Black MSM with intervention components

Secondary Objectives:

- To collect samples, behavioral data, and HIV test results to improve laboratory measures of HIV incidence in cross-sectional surveys.
- To estimate the HIV incidence rate under intervention conditions.
- To estimate the effect of the intervention on HIV incidence through mathematical modeling.
- To describe the social and sexual networks of Black MSM based on individually self-reported network data.
- To describe risk behaviors of sexual network members of Black MSM, especially of those who are newly diagnosed with HIV infection, or previously diagnosed but not in care.
- To assess attitudes of Black MSM toward other HIV prevention interventions.
- To use qualitative research methods to:
    - Examine individual, interpersonal, cultural, institutional, and geographic-specific processes that influence study participation and uptake of intervention components.
    - Understand how and to what extent stigma and discrimination (and other emergent themes) influence HIV testing and access to care by geographic region.

Study Sites:

- Ponce de Leon Center CRS (site 5802) and Hope Clinic CRS (site 31440) in Atlanta and Decatur, Georgia, respectively
- San Francisco Vaccine and Prevention CRS in San Francisco, California (site 30305)
- New York Blood Center (NYBC)/Union Square CRS (site 30913) and Harlem Hospital Center/Columbia University CRS (site 31471) in New York City, New York
- University of California at Los Angeles (UCLA) Vine Street CRS (site 31607) in Los Angeles, California
- Fenway Community Health CRS (site 31602) in Boston, Massachusetts
- George Washington University CRS (site 31608) in Washington, D.C.

1 INTRODUCTION

1.1 Background

MSM comprise the single largest group of individuals in the US who have become infected with HIV (human immunodeficiency virus) in recent years, with Black MSM affected at dramatically disproportionate rates. Black MSM, who may identify as gay, straight, bisexual, transgendered, or none of these, are estimated to account for one quarter of the new HIV infections in the US annually, yet little prevention research has been directed toward this population. The purpose of this study is to prepare for a randomized trial of a community-level, multi-component intervention to reduce HIV incidence among Black MSM.

Black MSM are not more likely to engage in risky behavior than non-Black MSM, but they are more likely to become infected.[1 2 3 4 5 6] Thus, risk behaviors alone do not account for the disproportionate number of HIV infections in this group, and interventions focused solely on reduction of risk behaviors will not likely stem the high rate of new infections in this population.

Several factors are likely to contribute to the disproportionate rate of HIV infection among Black MSM:

1) Low frequency of HIV testing resulting in a high proportion of Black MSM who are unaware of their HIV status.
2) High HIV prevalence and incidence rates within sexual networks resulting in increased likelihood of exposure to HIV during sex.
3) High prevalence of other STIs, which facilitates HIV transmission and acquisition.
4) Barriers to health care access and HIV/STI treatment resulting in high levels of undiagnosed and untreated HIV infection.

Two factors that are not unique to Black MSM, but that have been shown to be associated with increased risk of HIV infection among MSM as a whole, are substance use and mental health issues, such as depression.[4]

Low awareness of HIV status and high prevalence of STIs could be addressed with increased counseling, testing, and treatment. Barriers to health care and treatment could be reduced through the use of PHNs, who are trained participant advocates that help participants meet their health care and other service needs in a fragmented system of care. Disrupting the spread of HIV within networks in which HIV and other sexually transmitted infections (STIs) are highly prevalent (and highly incident) could be accomplished through interventions that target network members of Black MSM who are newly diagnosed with HIV or who were previously diagnosed but are not in care. Inviting participants to discuss their substance use or mental health issues with a counselor, and then providing referral for care and HIVrisk reduction counseling could reduce the effect these issues have on participants' risk-taking behavior.

Thus, we will gather data on the feasibility and acceptability of an intervention comprised of the following components:

1) Enrollment of sexual network members of Black MSM who are newly diagnosed with HIV or have been previously diagnosed but are not in care ("in care" being

defined as having engaged with a health-care provider for HIV-related care in the last six months).
2) Counseling and testing for HIV.
3) Counseling and testing for other STIs.
4) Inviting participants to discuss issues such as substance use and mental health problems with a counselor after completion of confidential screeners for these issues in an ACASI interview, and providing referral for care and risk reduction counseling for these issues, as appropriate.
5) Facilitating access to HIV and STI treatment, health care, and other services by PHNs.

The hypothesized impact of the intervention is two-fold. At the individual level, the intervention is designed to decrease a participant's individual risk of acquiring or transmitting HIV by addressing his personal risk factors, by, for example, identifying and treating undiagnosed HIV or STI infections, or by helping participants reduce risk-taking behaviors influenced by drugs or alcohol. At a population level, the intervention is designed to lower the viral load in HIV infected men by identifying those who qualify for HIV treatment (some of whom may be newly aware of their status) and intervening to increase treatment and access to health care. By lowering both the proportion of men with undiagnosed HIV infection, and the viral load among those with chronic, untreated infection, we expect to reduce HIV transmission within networks of Black MSM.

Description of Possible Future Community Randomized Trial (CRT)

The study described in this protocol is a feasibility study. It will provide estimates about the potential efficacy of this intervention to reduce HIV incidence rates among Black MSM. These estimates will inform the protocol team whether a larger, community-randomized efficacy trial of the intervention, with HIV incidence as the endpoint, is warranted. In such a trial, cities, or possibly sub-sections of cities, would be randomized to intervention or control conditions. The intervention would be delivered on a community-wide basis for a period of time (e.g., two to three years) in the intervention cities. At the end of the intervention delivery period, a cross-sectional survey of Black MSM would be conducted in each intervention and control city, using the methodology of venue-based, time-space sampling described in more detail in Section 1.2.1 [7,8]. HIV incidence rates would be estimated from the cross-sectional surveys by application of the most up-to-date HIV testing algorithms for identifying recent infections. The efficacy of the intervention would then be determined by comparing HIV incidence rates among Black MSM in intervention versus control cities.

This feasibility study will generate specific information on sites' recruitment capability with this population, demonstrate the acceptability and feasibility of intervention components, and produce data to estimate the intervention effect through mathematical modeling. Furthermore, the feasibility study will provide specimens to assist in the efforts to improve laboratory algorithms to identify recent infections from cross-sectional surveys. Qualitative research methods will provide data on contextual and geographic factors that influence the willingness of Black MSM to participate in research and to accept the components of the study intervention, as well as the degree to which stigma and discrimination influence HIV testing and access to care. The information from this feasibility study will inform the design of the CRT.

Illustrations of the Efficacy Trial and Feasibility Study

Preliminary calculations have been done to estimate the number of communities necessary for the community-randomized trial based on various values for these parameters, presented in Table 1. It is clear that in a scenario in which incidence and the effect of the intervention are both low, the number of communities needed for the community-randomized trial would be prohibitively high, at around 30 communities per arm. However, a more effective intervention would necessitate only 8-15 communities per arm, or 16-30 communities for the full trial. This lower number of communities would be feasible, since the protocol team believes that many cities with substantial Black MSM populations can be identified. Census data show that there are in fact over 60 metropolitan areas in the US with greater than 100,000 Black residents (with an estimated 2500 MSM per 100,000 people, assuming 5% prevalence of MSM among males).

Table 1: Potential Sample Sizes for a Community Randomized Trial
HIV Incidence of 3/100 Person-years (PY) in the Control Arm Number of communities needed with 300-500 Person-years in Each Community, and ranging from 30-50% effectiveness. (kappa = 0.25; power=90%; alpha=0.05)

Control Incidence	**Person-years per Community per Arm**	**Number of Communities per Arm**		
		Effect size = 50%	**Effect size = 40%**	**Effect Size = 30%**
3/100 py	300 py	11	18	34
	400 py	10	15	28
	500 py	8	14	25

As illustrated in Figure 2 below, the number of sites required to conduct the efficacy trial is estimated to be between 16 and 30 cities. The final number of sites will depend on city-specific factors, such as rate of uptake of the intervention. The right side of the figure highlights the components of the recruitment strategy and the intervention itself. Before making the significant investment of time and resources that would be required to implement the efficacy trial, it is imperative to understand whether Black MSM can be recruited successfully from both the community and from participant referrals, whether Black MSM will accept the intervention components, and whether uptake of the components can reasonably be expected to affect HIV incidence. HPTN 061 will answer these questions.

Figure 3 (on the page following Figure 2) shows the six sites that have been selected to complete HPTN 061. The first step at each site is to recruit participants; this will help answer the question of whether recruitment of Black MSM for this sort of intervention is possible. The next step is to offer HIV/STI testing, which will provide the first indication of the acceptability of this critical part of the intervention, and will provide data to help estimate HIV incidence. Each of the subsequent steps (offering counseling and referral for issues arising during post-ACASI counseling, offering PHN services, and participant follow-up) will answer questions critical to the design of an efficacy trial in the areas of intervention acceptability, estimated intervention effect on HIV incidence, and estimation of HIV incidence among Black MSM. The components shown are only a subset of the planned intervention components for HPTN 061. The feasibility study will also answer whether

uptake of the intervention varies among cities. This variability would influence the number of cities needed for an efficacy trial, as described more fully in Section 1.2.6.

Figure 2- Design of the Future I Intervention Trial

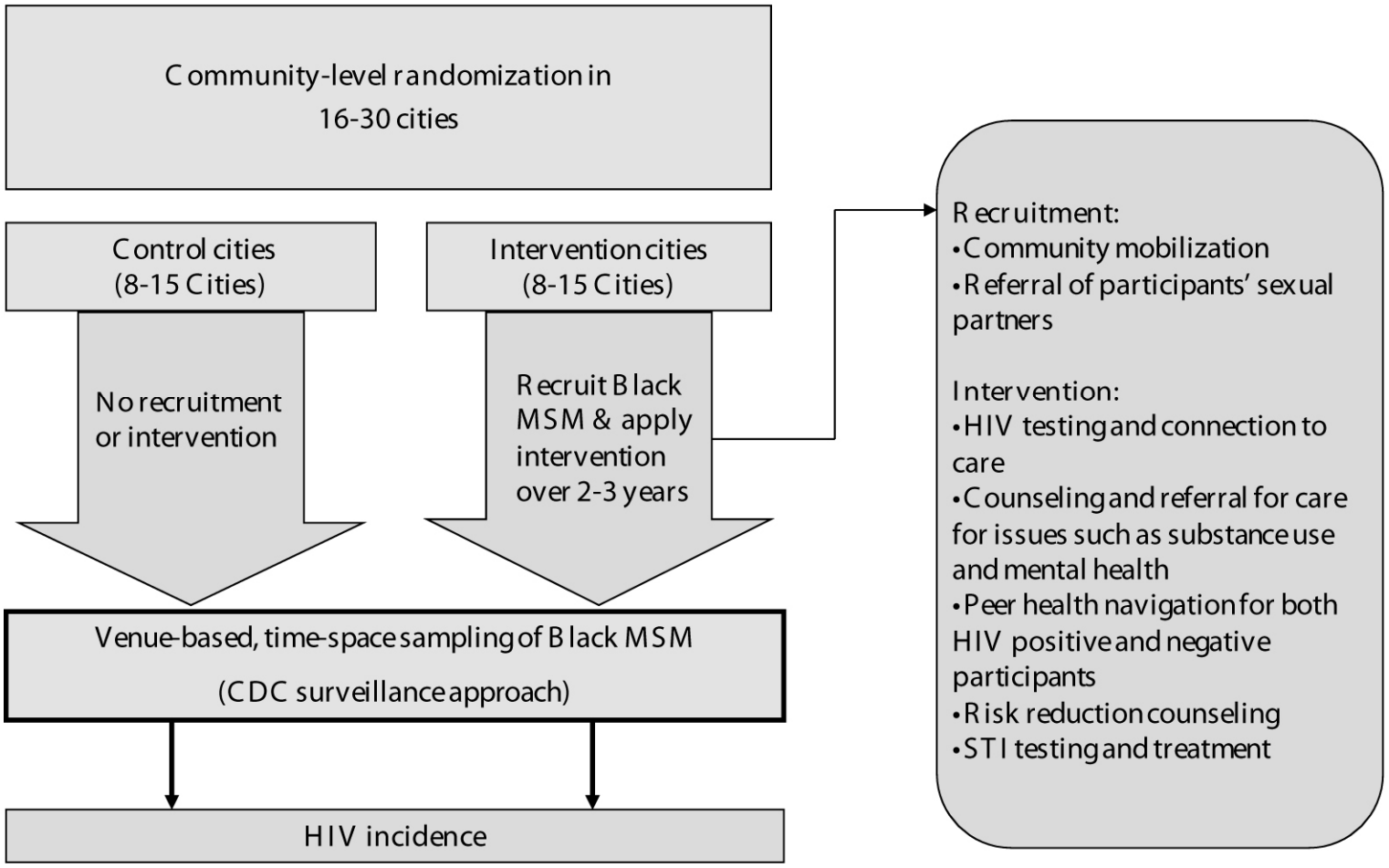
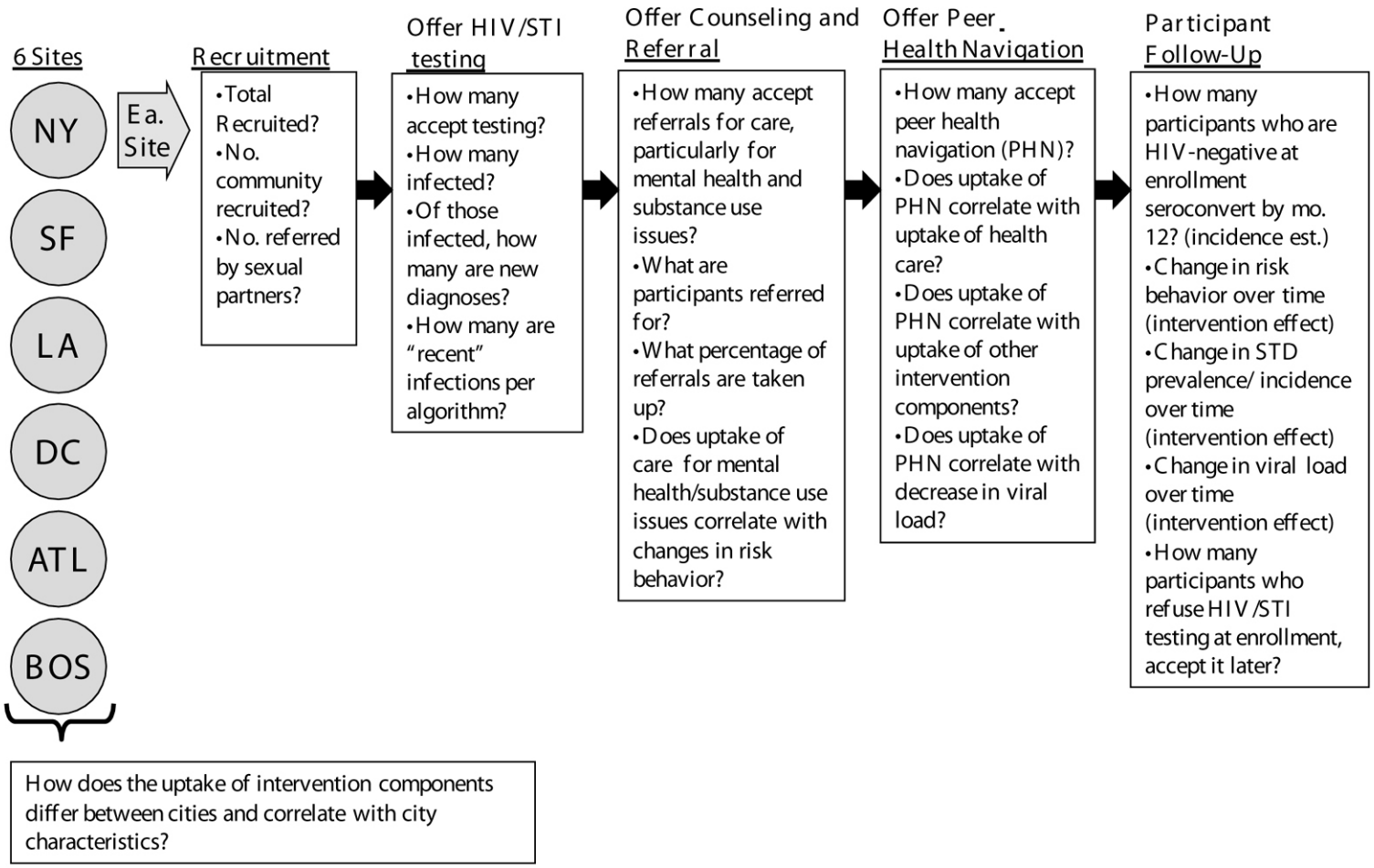


Figure 3- Design of the Feasibility Study (HPTN 061)



1.1.1 What is Known about the Epidemic in Black MSM

Black MSM are infected with HIV at dramatically disproportionate rates. In the US, MSM continue to comprise the largest proportion of new HIV infections, accounting for 49% of HIV/Aquired Immunodeficiency Syndrome (AIDS) cases in 2005, with at least a third of these new infections reported in Black MSM.[9] The disproportionate effect of HIV among Black MSM also is illustrated by multi-city surveys conducted among MSM who attend public venues (Young Men's Survey [YMS] Phase 1 and Phase 2 and National HIV Behavioral Survey [NHBS]). Among young MSM (15- to 22-year-olds), substantially higher HIV prevalence and incidence was found among Black compared to White MSM (prevalence: 14% vs. 3%; annualized incidence: 4.0% vs. 2.4%). Even larger race/ethnic disparities were found among older (23-29 year old) MSM with an HIV prevalence of 32% among Black MSM compared with 7% among White MSM; annualized HIV incidence was 14.7% among Black MSM vs. 2.5% among White MSM.[10] Data from NHBS conducted in 2004-2005 confirms this disturbing differential: HIV prevalence among MSM at least 18 years old was 46% among Black MSM compared to 21% among White MSM.[1 2]

Differences in sexual-risk behaviors and substance use do not explain the disproportionate HIV rates by race among MSM. In recent surveys, race/ethnicity differences in HIV prevalence and incidence among MSM persisted after controlling for drug and sexual risk behaviors. In most of these studies, the proportion reporting sexual risk behaviors, such as unprotected sex or high numbers of partners, was less or no different among Black men than White men.[3 4 5 6] Analysis of data from the EXPLORE Study, a large-scale behavioral intervention trial among MSM conducted between 1999 and 2003, found that HIV incidence was significantly higher in Black than White MSM, even when controlling for sex and drug risk behaviors, STIs, and other covariates (Harm Ratio (HR) = 2.0; 95% CI: 1.3, 3.1).[4] Thus, in the aggregate, Black MSM are not more risky in their sexual behaviors than other MSM, but they are more likely to become infected with HIV.

Biological factors could possibly explain some of the differences in HIV prevalence and incidence between Black and non-Black MSM. For example, immunogenetics in the form of variations of the chemokine (C-C motif) receptor 5 (CCR5) allele could play a role, although this will not be explored as part of this study. As well, Black men are less likely to be circumcised than White men; up to one-third of Black men are uncircumcised.[11 12] Some studies suggest that a lack of circumcision may be a risk factor for HIV infection among MSM.[13] However, data on MSM are inconsistent in this regard and no studies have been done to demonstrate the efficacy of circumcision on reducing HIV acquisition or transmission among MSM. Thus, this study will collect data on circumcision, and will inform participants about data from heterosexual studies, but does not propose to include circumcision as an intervention or to offer circumcision to participants.

The most likely explanations, however, for the disproportionate HIV infection rates among Black MSM are low frequency of HIV testing, high HIV prevalence within sexual networks, high prevalence of other STIs, and barriers to health care access and HIV/STI treatment. These result in later diagnoses of HIV-infected men, more STIs, and fewer infected men having their viral loads reduced with effective therapy, making them more likely to transmit

HIV if they have sex. Given that Black MSM are more likely to have sex with other Black MSM, their risk-per-sexual encounter may be higher as a consequence of this risk matrix.

Low frequency of HIV testing among Black MSM. Knowledge of HIV status among Black MSM is particularly low, with 67-91% of infected men found to be unaware of their HIV infection in several surveys.[1,14] Studies also have shown that among Black MSM who believed they were HIV-uninfected and disclosed this to new sex partners, 24% were actually HIV-infected; this percentage was considerably lower for White men (3%) and Latino men (5%).[14 15 16] Furthermore, men who are unaware that they are HIV-infected are more likely to engage in sexual risk behaviors compared to men who know they are HIV infected.[17 18] Individuals who are unaware of their HIV infection are estimated to contribute to about half of the new infections acquired each year through risky sexual activities in the US.[19] Although they comprise a small proportion of HIV infections, individuals who are recently infected and unaware of their HIV status may be particularly likely to transmit HIV to new partners, as shown in studies in Africa and North America.[20 21] Thus, there is a strong rationale and public health justification for identifying previously undiagnosed infections.

High HIV prevalence in Black MSM sexual networks. Black MSM may be having sex with a group of partners with high prevalence and incidence of HIV, who also may be unaware that they are likely to transmit HIV to their partners. High prevalence within a sexual network would create a higher risk of infection with each sexual act and thus amplify HIV prevalence within a network. This hypothesis is supported by findings that indicate that 1) Black MSM are more likely than other MSM to have Black sexual partners, and 2) anal intercourse with Black male partners among Black MSM explains part of the race differential in HIV prevalence.[22 23] An intervention that can interrupt this amplification within networks could be successful in lowering the risk within the Black MSM population.

High prevalence of other STIs facilitating HIV transmission. Many studies have shown that infection with another STI increases acquisition and transmission of HIV.[17 24] Several studies have found that some STIs, (i.e., gonorrhea, syphilis, and *Herpes simplex* virus (HSV) type 2) are more prevalent among Black MSM compared to other men.[25 26] The only significant predictor of HIV prevalent infection among young Black MSM in YMS was a history of a prior STI.[5]

Barriers to health care access and HIV/STI treatment. Several measures indicate that Black MSM are less engaged in the health care system than others. Among HIV-infected MSM, Black MSM are less likely to have access to private clinics[27] or to express HIV-related health concerns to their medical providers.[28] Several studies have shown racial disparities in use of HAART, with Black MSM less likely to receive recommended levels of antiretroviral care[29 30] or to adhere to HAART treatment.[31] Declines in AIDS incidence and in death rates have been small for HIV-infected Black MSM compared to HIV-infected MSM of other racial/ethnic groups. [32] For Black MSM who have not been diagnosed with HIV, health care engagement also appears to be low- a higher proportion of HIV-infected Black MSM test late in their HIV infection compared to White MSM.[33] This disparity may be partly due to differential access to care, lower use of outpatient care, and racial bias in the care setting for Blacks in general.[34 35 36 37] Lower engagement with the health care system likely contributes

to higher rates of untreated STIs, lower awareness of HIV infection status, and higher viral loads among Black MSM, all of which can contribute to higher HIV incidence.

Risk Factors for all MSM. Although the focus of this study is on HIV risk factors that affect Black MSM, the intervention will also address multiple issues known to affect MSM in general. Research has shown that these risk factors include substance use, depression, and housing insecurity.[38]

1.1.2 Other Recent or Current Studies in the Field

There are several research efforts underway, sponsored by Centers for Disease Control (CDC) and NIH, that are relevant to this study and to the future randomized trial of the intervention. We hope that this feasibility study, along with these other efforts, will facilitate the design of the future community-randomized study and will inform other research or interventions with Black MSM. Some of the most relevant CDC and NIH research initiatives are: 1) determining best outreach strategies for identifying the largest number of undiagnosed Black MSM; 2) evaluating whether characteristics of networks affect HIV infection rates among Black MSM; 3) using network-based approaches to recruit Black MSM for behavioral intervention studies; and 4) determining best estimates of HIV incidence among Black MSM.

1) Identifying best outreach strategies to identify Black MSM with undiagnosed HIV infection. In 2006, the CDC funded a follow-up study to the Network Demonstration projects. The purpose of the new study is to compare the relative effectiveness of three strategies — alternate venue testing, social networks, and partner counseling and referral services (PCRS) — for reaching Black MSM with undiagnosed HIV infection. Four sites — Atlanta, District of Columbia, Baltimore and New York City — have been funded by a three-year cooperative agreement, and the sites began data collection in early 2008.
2) Characterizing the impact of social networks on HIV infection among Black MSM. Analyses are now underway that use data across the 25 funded NHBS metropolitan statistical areas (MSAs).[39] NIH has also recently funded a network-based study in which principal investigator Kyung-Hee Choi will recruit Black, Latino, and Asian MSM and compare the characteristics of social networks, sexual risk behaviors, and HIV infection for each racial/ethnic group of MSM. Results from the project are anticipated within the next two years.[40]
3) Using network-based recruitment methodology to recruit Black MSM into HIV prevention interventions. A recent CDC-funded demonstration project adapted Jeffrey A. Kelly's Popular Opinion Leader intervention for Black MSM in North Carolina.[41] Opinion leaders were recruited to discuss safer sex with members of their network. Cross-sectional assessments of sexual risk were collected from a total of 1190 Black MSM (nearly 300 Black MSM during each data collection wave) at baseline, 4 months, 8 months and 12 months. Significant reductions were observed for receptive unprotected anal intercourse (UAI) at 4 months (by 23.8%, n=287) and 8 months (by 24.7%, n=299), and for insertive UAI (by 35.2%), receptive UAI (by 44.1%), and any UAI (by 31.8%) at 12 months (n=268). [42] The CDC has also funded a network-based intervention targeting Black MSM in Baltimore. The study, led by Carl Latkin, will implement a seven-session, group-level intervention that includes a

peer network strategy to evaluate dissemination of the intervention through social networks. Results from the study will be available in 2009.

4) Determining HIV incidence among Black MSM. The CDC's NHBS expanded the number of sites that tested MSM in its latest round of data collection. New estimates by the CDC of HIV incidence among MSM of various racial/ethnic groups were reported in August 2008, revealing that HIV incidence in the US was higher than previously reported, at approximately 56,300 per year (instead of 40,000). Importantly, 45% of infections were among Blacks and 53% were among MSM.[43] A meta-analysis currently submitted for review by Ron Stall and colleagues has calculated an HIV incidence of 2.39% for MSM in the United States, but 4.0% for Black MSM, based on data published by the CDC in 2001 (R. Stall, unpublished data). Additionally, ongoing discussions are taking place between the CDC and NIH to fund jointly a prospective study targeting Black MSM.

HPTN 061 is an important opportunity to take the best of what is known about HIV among Black MSM and prepare for evaluating an innovative, multi-component intervention with a wide geographic reach. We know that:

- Black MSM are infected with HIV at disproportionate rates.
- Risk behaviors do not fully explain the infection differential.
- HIV testing rates are low among Black MSM.
- Certain STIs occur at higher frequency among Black MSM.
- Black MSM experience barriers to health care.

The studies described above focus on single issues (e.g., determining HIV incidence or describing social networks) that will add to the knowledge base for the final design of the multi-component intervention. The strength of HPTN 061 is its capability to test the feasibility of the multiple intervention components at the same time, as would be delivered in the ultimate community-randomized trial. This approach will provide the best information about feasibility of the combination of the intervention components. Most importantly, HPTN 061 will provide data on the potential effect of this multi-component intervention on HIV incidence, a critical piece of information for determining whether this approach has the potential to have an impact on the HIV epidemic among Black MSM in multiple cities in the US.

1.2 Rationale

This feasibility study is focused on a population that represents a quarter of the new HIV infections each year and for which few interventions are available. This study, which will collect information about recruitment and the uptake of intervention components, will facilitate design of a full interventional trial. Another objective will be to use the samples, behavioral data, and HIV test results from this study to improve laboratory methods for determining HIV incidence from cross-sectional surveys. To explain more clearly the rationale for this feasibility study, a description of the future proposed intervention trial is provided below.

1.2.1 Description of the Planned Future Intervention Trial

If this feasibility study meets its objectives, a future trial is proposed in which urban communities would be randomized to intervention or control conditions. The intervention would be implemented on a community-wide basis for a period of time (e.g., two to three years) in the intervention communities. At the end of the intervention delivery period, HIV incidence rates would be measured in each intervention and control community. HIV incidence rates would be determined by conducting cross-sectional surveys of Black MSM in each community using venue-based, time-space sampling. Blood specimens from these surveys would be tested using appropriate HIV-testing algorithms to identify recent infections. The efficacy of the intervention would be determined by comparing the HIV incidence rates among Black MSM in intervention communities compared to control communities.

We face two principal challenges in assessing the outcome of a full intervention trial that measures the HIV incidence in communities of Black MSM: 1) lack of proven methods for sampling the Black MSM community; and 2) lack of optimized laboratory methods for measuring HIV incidence rates in cross-sectional studies.

To address the first challenge, community-randomized trials that use geographical location to define communities can use survey sampling methods to obtain random samples. However, in a community defined by behavior and race that is geographically diffuse, such methods are not feasible. A sampling frame of Black MSM does not exist. Household or telephone surveys would be unlikely to find a sufficient number of Black MSM, and clinic-based samples of Black MSM would be biased.[7] Respondent-driven sampling has also been proposed for representative sampling of "hard to reach" populations, although this approach does not yield a reproducible sample in some settings.[44 8] An alternative approach is venue-based, time-space sampling developed by the CDC and used in multiple surveys of MSM, including NHBS.[7 39] This methodology can produce a sample that is representative of men who attend venues in the sampling frame and emphasizes the need to produce a sampling frame of venues that is comprehensive for the population. This is the approach that would be used in the community-randomized trial for selecting a sample in each community at the end of the intervention delivery period to measure the study outcome of HIV incidence.

With regard to the second challenge, methods for assessing the community outcome (HIV incidence) could either use a sentinel cohort that would be sensitive to the intervention effect, or a cross-sectional sample. To measure HIV seroincidence in a sentinel cohort, it would be necessary to enroll and follow an at-risk HIV-negative cohort, tested before and after the intervention. However, a major component of the Black MSM intervention involves increasing the uptake of HIV testing. So, to the degree that HIV counseling and testing would be implemented among both randomized arms within a sentinel cohort, the effect of this increased testing on incidence would not be measurable. Thus, using a sentinel cohort may not be feasible. A cross-sectional survey at the end of the intervention delivery period would avoid the problems of a sentinel cohort approach, but would require a method for estimating HIV incidence from cross-sectional surveys. This requires accurate laboratory assays for identification of recent (i.e., within the previous six months) HIV infection,[45 46 47] a field that is still under considerable development and to which this feasibility study is designed to contribute.

Data from this feasibility study will also be used to inform the decision about the level of randomization that will be required for the future randomized trial. The randomization unit in this future trial is expected to be the metropolitan area. This level of randomization is likely to be necessary because the intervention will require broad mobilization within a metropolitan area to increase access to and acceptability of HIV testing, and recruitment of social and sexual networks is expected to extend the reach of the intervention throughout the metropolitan area. Data from venue-based sampling indicates that Black MSM frequenting a certain venue often reside at ZIP codes throughout the metropolitan area, thus location of residence does not provide a mechanism for identifying smaller communities for randomization. For example, CDC's NHBS in New York City found that 74% of Black MSM recruited at Manhattan-based venues resided in the outer boroughs of New York City or farther (22% in the Bronx, 27% in Brooklyn, 11% in Queens, 14% outside New York City) (B.Koblin, unpublished data). On the other hand, multiple, non-overlapping communities of Black MSM may exist in some metropolitan areas, which allows for independent randomization of these communities. One objective of this feasibility study is to describe the social and sexual networks of Black MSM within cities to inform decisions about what constitutes a randomizable unit for the intervention trial.

Before implementation of the community-randomized trial envisioned for this intervention, it will be important first to demonstrate that Black MSM can be successfully recruited for this intervention, particularly those subgroups of greatest interest: those who are HIV-uninfected, but at high risk of infection; those unaware of their HIV infection; and those who know that they are HIV-infected, but who are not in care and have sex with men who are uninfected or of unknown status. It will also be critical to know that Black MSM will accept the intervention, as will be revealed through the uptake of intervention components and participant satisfaction with the components. Another prerequisite for the randomized trial will be that the availability of laboratory methods for identification of recent HIV infection in a cross-sectional study. Evaluation of all of these requirements are components of this feasibility study.

1.2.2 Rationale for Intervention Components

This intervention emphasizes enrollment of HIV-negative and HIV-positive Black MSM, and their networks of Black MSM sexual partners. As the intervention components are rolled out to these networks, and act to reduce the rate of HIV transmission on the one hand and the viral load of already infected participants on the other, the risk of HIV acquisition and transmission can be expected to decrease.

The rationale for providing HIV counseling and testing among Black MSM is a simple one, in that diagnosis of HIV infection is the first step toward managing an individual's viral load and, therefore, infectiousness. As well, knowledge of infection status can lead to safer sexual practices, such as condom use, and disclosure of HIV status to partners. Because one of the aims of the study is to determine the uptake of HIV testing, HIV testing will not be a requirement for enrollment.

Testing for specific STIs in this study is based on prior research that has shown an association between STIs and increased HIV risk. Research to date has not proven that treatment of STIs lowers the risk of HIV transmission or acquisition, though the Mwanza trial in Tanzania suggested benefit of treating bacterial STIs promptly to reduce HIV

seroincidence in heterosexuals.[48] None of these studies, however, has been conducted in this population (Black MSM). The question remains whether treatment of STIs can help slow the spread of HIV within these communities. Providing counseling, testing, and treatment for syphilis, Chlamydia, and gonorrhea among populations of Black MSM will be a tangible health benefit for the enrolled participants and offers an opportunity for more effective sexual risk reduction counseling and behavior change. Furthermore, the change in prevalence of these STIs during follow-up can also serve as a surrogate measure for change in HIV risk behavior.

Inviting participants to discuss with a counselor issues such as substance use or mental health issues and then providing referral for care and risk reduction counseling addressing these issues, should help to reduce the contribution of these known risk factors to HIV acquisition and transmission.

Prior research has shown that Peer Health Care System Navigators (PHNs) are effective at improving health care uptake by HIV-positive MSM, by helping clients overcome obstacles to accessing care. A novel feature of this study will be the provision PHNs to both men who are HIV-uninfected and those who are infected. Since Black MSM are believed to have greater-than-average obstacles to care, the use of PHNs to connect Black MSM to HIV and STI treatment, health care, and assistance with other practical needs such as housing can be expected to be effective in lowering the viral load of those with HIV infection, and reducing the risk of infection of those who are HIV-uninfected. PHNs will work to provide culturally appropriate referrals whenever options for referral are available.

1.2.3 Rationale for Qualitative Component

The primary objective of the overall study is to obtain information needed to design a full community-randomized trial to reduce HIV incidence among Black MSM. Toward this objective, it is essential that HPTN 061 examine the individual, interpersonal, cultural, institutional, and geographic (by site location) processes that influence uptake of the study interventions by Black MSM — a group rarely addressed by population-specific studies. Therefore, HPTN 061 will conduct qualitative focus groups and individual interviews to explore how these conditions contribute to study participation and intervention uptake, and to examine how stigma, discrimination and other emergent themes influence HIV testing and access to care. Qualitative methods provide an efficient and effective strategy for gathering contextually and geographically specific data on Black MSM regarding their beliefs, attitudes, and practices that relate to the use of and access to HIV prevention services.[49]

The formative phase of this research investigation will include focus groups, which will be followed by in-depth, individual qualitative interviews conducted with Black MSM. This combined qualitative methodology has been used in studies to enhance the depth of inquiry and the richness of "new" information regarding the area being studied.[50] Within this context, little qualitative research has examined salient contextual factors related to HIV/STI testing patterns, including access to and utilization of HIV/STI prevention services, in community-based samples of Black MSM.[51 52 53 54]

To obtain information needed to design a full community-randomized trial to reduce HIV incidence among Black MSM, knowledge of the perspectives and experiences of Black

MSM is needed. The qualitative component of HPTN 061 is a means of systematically collecting information about individual and contextual factors that affect study uptake, HIV testing, health services, utilization and other emergent themes.

A novel feature of the qualitative component of the study is that it will allow for the examination of the particular conditions under which HIV risk increases in a population-specific sample. Qualitative methods, such as the ones that we will use in this study, are particularly well-suited to this research because 1) they can yield an in-depth understanding of social processes and cultural meanings that are hard to capture in survey research, 2) they facilitate analysis of the complex personal factors and social relations influencing the HIV-risk outcomes, 3) they have proven to be effective in fostering the formulation of theoretical frameworks, and 4) they are effective in generating data that directly reflect the voices, interpretations, logic, and lived experiences of people for whom the intervention is intended.[55 56 57 58 59] HPTN 061 will benefit from the strengths of qualitative research methodologies used.

1.2.4 Rationale for Enrolling Both HIV-Positive and HIV-Negative MSM

The goal of this intervention is to lower HIV incidence among Black MSM. Accordingly, it targets both the prevention of acquisition of new infections among HIV-negative individuals, as well as reduction of transmission of new infections from HIV-positive individuals.

1.2.5 Rationale for Follow-Up Visits

Follow-up visits at 26 and 52 weeks are included in the feasibility study to assess changes in behavior (e.g., condom use), viral load, and occurrence of HIV or STIs. These data are needed to estimate the potential effect of the intervention through mathematical modeling. Note that follow-up visits are not part of the design of the planned community-randomized intervention trial.

1.2.6 Rationale for Enrolling at Multiple Sites

This feasibility study will be executed at six sites in different cities distributed across the US: San Francisco, Los Angeles, Boston, New York, Atlanta, and Washington, DC. Collectively, the metropolitan areas in which these six sites are located represent nearly 20% of the Black population of the US. It is assumed that MSM are over-represented in urban centers, so these six sites should provide a robust sample of the Black MSM population. The inclusion of multiple and diverse sites is a critical component of the study because Black MSM communities are not monolithic. The protocol team will need to determine how communities may be alike or different (e.g., in terms of intervention uptake). Differences among cities may exist because of differences in city structure, historical patterns of segregation, differences in venues attended by Black MSM, and varying levels at which MSM have been given recognition and power.[60 61] Some of the questions that these data may address include:

- Whether uptake of PHNs varies by city characteristics, such as population size, geographic area, and extent of public transportation.
- Whether uptake of HIV testing varies by city.
- Whether the structure and composition of social and sexual networks of Black MSM vary by city.

Through the feasibility study, the team will learn about potential differences in the cities and determine how these differences might influence the success of the intervention. The team will also learn how to most effectively adapt the intervention to accommodate these variables, which will be critical for implementation of the community-randomized trial.

The cities chosen were selected in part because their diverse characteristics should provide the team with a good idea of how well the intervention will be accepted by a cross section of community types. For example, the geographic distribution of the cities intentionally covers the West Coast, East Coast and South/Mid-Atlantic. As well, a larger (New York, Los Angeles) and a smaller city (Boston, San Francisco) were chosen on both East and West coasts to elucidate the differences that city size may play in intervention penetration. The sites chosen also vary in terms of the population density, from highly concentrated populations in New York City to less-concentrated populations like Atlanta. Although the study sites are different from one another in the ways listed above, they are similar in that all are urban environments with substantial Black populations. The study team cannot predict *a priori* what community characteristics will affect the uptake of this intervention, but qualitative interviews with participants during the study, as well as responses to study questionnaires administered during follow-up visits, will help the study team identify what the critical issues are for each site, knowledge that can then be applied to preparation of the future study.

The feasibility study will also inform the protocol team about how to randomize the full trial. If analysis of the multiple sites shows that they are very similar to one another on intervention uptake and effect parameters (e.g., if all sites have similar rates of HIV testing, or if all sites observe a similar decrease in viral load among men who start ART), then the team can plan to randomize all cities in the full trial without any matching. However, if there is variability between cities, and if that variability is correlated with some other factor on which cities can be matched (e.g., condom use is correlated with city size, or uptake of PHNs is low in West Coast cities), then cities will need to be randomized with matching.

Cities participating in the feasibility study will be eligible to participate in the CRT in either the intervention or control arm. There is little concern that exposure to the intervention during the feasibility study would bias results at that site during the CRT because the number of participants enrolled in the feasibility study will represent a small proportion of the number of Black MSM in any of these cities. As well, a time lag of approximately two years is expected between the conclusion of the feasibility study and the initiation of the CRT.

2 STUDY OBJECTIVES AND DESIGN

2.1 Primary Objective

- To obtain information needed to design the full community-randomized trial, particularly in the areas of:
    - Recruitment of Black MSM
    - Uptake of the intervention components by Black MSM, including the proportion of enrolled participants who:

- Agree to HIV testing.
- Agree to STI testing.
- Utilize peer navigation.

- Estimating the following in the course of the study
  - Proportion of participants who are newly diagnosed with HIV at enrollment.
  - Increase in condom use from enrollment to week 52.
  - Decrease in viral load at week 52 among HIV-infected participants who initiate HAART during their study participation.
  - Decrease in prevalence of STIs from enrollment to week 52.
- Satisfaction of Black MSM with intervention components.

2.2 Secondary Objectives

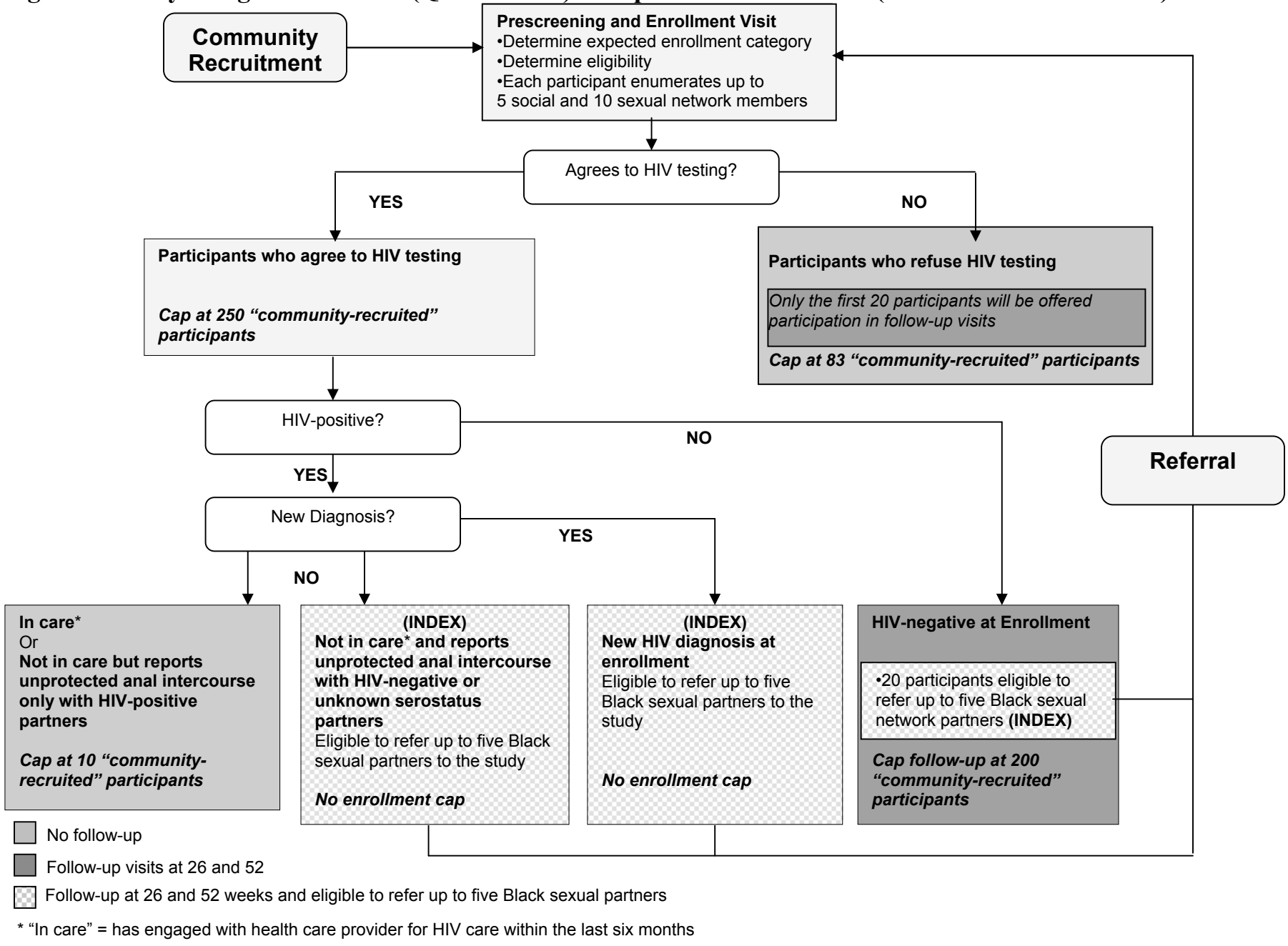
- To collect samples, behavioral data, and HIV test results to improve laboratory measures of HIV incidence in cross-sectional surveys.
- To estimate the HIV incidence rate under intervention conditions.
- To estimate the effect of the intervention on HIV incidence through mathematical modeling.
- To describe social and sexual networks of Black MSM based on individually self-reported network data.
- To describe risk behaviors of sexual network members of Black MSM, especially of those who are newly diagnosed with HIV infection, or previously diagnosed but not in care.
- To assess attitudes of Black MSM toward other HIV prevention interventions.
- To use qualitative research methods to:
  - Examine individual, interpersonal, cultural, institutional, and geographic-specific processes that influence study participation and uptake of intervention components.
  - Understand how and to what extent stigma and discrimination (and other emergent themes) influence HIV testing and access to care by geographic region.

2.3 Study Design: Main (Quantitative) Component

This study is a multi-site, community level feasibility study. As described below, most participants will be enrolled into longitudinal follow-up; a small proportion will only complete an enrollment visit. Participants will be Black MSM recruited at six cities in the US. Participants will be identified as either "community-recruited" or "referred" participants. As well, both community-recruited and referred participants could be "index"

participants. A basic diagram of this study design is provided below in Figure 4. Definitions of these categories are provided below.

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

Community-recruited participants meet the study inclusion criteria and are recruited directly from the community, i.e., have not been referred to the study as sexual network members of an index participant.

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).

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. HIV-negative participants are being included as index participants so that a participant's HIV status will not be automatically disclosed if he is referring participants to the study.

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.

Referred participants are those who have been referred to the study as one of the five Black sexual network members of an index participant. Referred network participants must meet the study eligibility criteria to be enrolled. Referred participants may also be index participants if they meet the index participant criteria.

"Community-recruited," "index," and "referred" distinctions are illustrated in the following example:

At the beginning of the study, a participant ("Robert") is recruited to the site by outreach work or an advertisement and enrolls. Robert is a "community-recruited" participant because he was not referred as a sexual partner of someone already in the study. If Robert qualifies as an "index participant," he may refer up to five Black sexual partners to the study. When one of those partners ("Damien") enrolls in the study, Damien will be in the first wave of "referred" participants. If Damien qualifies as an index participant as well, he may refer up to five of his Black sexual partners. If Damien's partners enroll, they will be considered to

be in the second wave of "referred" participants. This will continue until the waves of referral self-extinguish, or two months after the last community-recruited participant has been enrolled.

It should be noted that there will be enrollment caps, by site, on the various categories of community-recruited participants, but not on the number of referred participants. This is explained in more detail in Section 3.3. The caps are intended to ensure that the study population is diverse and not disproportionately skewed to one category of community-recruited men or another. As well, limiting the number of community-referred participants will allow the team to focus on and assess feasibility of enrollment of referred sexual network partners, believed to be the group in which the intervention may have the greatest impact.

Each site will develop its own plan for recruitment, but it is expected that in each city, outreach staff will work closely with community-based organizations or other groups with ties to the community to build connections with the Black MSM population and to generate enthusiasm for the study. Individuals interested in participating in the study will be asked a small number of questions as a prescreening activity. These questions will address their knowledge of their HIV status, their willingness to have an HIV test, their sexual behavior in the last six months, and, for those who report they are HIV positive, the status of their recent sexual partners, and recent HIV care history. Prescreening will be conducted orally and will not be documented. If the prescreening shows that the participant would be eligible for the study, they will be invited to undergo informed consent for enrollment. As detailed in Section 3.3, however, enrollment of certain sub-categories of community-recruited participants will be limited.

Enrollment Visit

All participants will have an enrollment visit (however not all will have follow-up visits, as described below). At the enrollment visit, each participant will complete a questionnaire using the Audio Computer-Assisted Self Interview (ACASI) system covering topics such as sexual risk behaviors, drug/alcohol use, current and prior engagement with the health care system, structural and personal/cultural barriers to receipt of HIV care, unmet service needs, venues frequented, and attitudes about race, sexual history, research, and health care. The ACASI system is the preferred interview modality because of its advantages in terms of confidentiality and for low literacy or illiterate participants. Demographics and locator information will be collected by interviewer. Interviewers will also ask each participant to enumerate (using initials or nicknames) up to 5 social and 10 sexual network partners and provide basic information about these partners such as race, age, and HIV status. These data will be used to describe and understand the characteristics of Black MSM social and sexual networks. It is important to note that the referral of up to five sexual network members by index participants is a different activity than the enumeration of up to 5 social and 10 sexual network members at enrollment, which will be solicited from all enrolled participants.

Participants will be offered HIV and STI testing and counseling. Participants with reactive HIV rapid test results will have HIV infection confirmed by Western blot (WB) and will have a CD4 cell count and viral load test performed. Counselors will provide post-test HIV

counseling to those who have had HIV rapid tests performed and will schedule all participants to return to the clinic approximately two weeks later to receive additional test results, i.e., WB confirmation of reactive HIV rapid test results and/or STI test results. For participants meeting the criteria to be allowed to refer participants (i.e., "index" participants), the counselor will explain the referral process and will provide a brief training to the participant in techniques for motivating referred partners to come in for screening. The counselor will discuss with index participants whether there could be a risk of social harm or partner violence in referring partners to the study.

After the participant has completed the ACASI questionnaire, the counselor will meet with the participant and invite him to talk about any issues raised by the topics covered in the interview session. The counselor will provide pre- and post-test counseling and risk reduction counseling, including focus on substance use/mental health issues, if appropriate. If acute and serious substance use/mental health issues are suspected or apparent, the participant will be referred for a clinical evaluation and for available care.

Study participation will end at this point for three groups of participants (those who will not be seen for follow-up after the enrollment visit, and will not receive peer health care system navigation): 1) participants with an HIV-positive diagnosis prior to screening for HPTN 061 who are either in care (have seen a health care provider for HIV-related care in the last six months) or who have unprotected anal sex only with HIV-positive partners, 2) HIV-negative participants enrolled after the site's 200-person cap for this category has been filled, and 3) participants who refuse HIV testing after the site's first 20 participants in this category have been enrolled. Thus, these three groups of participants will provide only baseline cross-sectional data.

All other participants (index participants, the first 200 community-recruited HIV negative participants, the first 20 community-recruited participants who refuse HIV testing) will then have the counselor explain about peer health care system navigation and determine if the participant is interested in peer health navigation. If possible, the PHN will meet the participant during the enrollment visit and either conduct an initial discussion that day, schedule for a later day, or, if the participant does not have any need for navigation, will plan to call after a few weeks to check for any emerging needs. From this point forward, the PHN will interact with the participant on a schedule determined by the participant's needs that is independent of the study visit schedule. The PHN will help the participant overcome his particular barriers to health care (including engagement and retention in HIV care for HIV-positive participants and care and resources for substance use/mental health issues) through a number of activities described more fully in Section 4.

Follow-Up Visits

The infrequent follow-up visit schedule creates a risk of retention challenges. Sites will be required to have a retention plan, including strategies such as contacting participants periodically between visits to stay in touch and to acquire updated locator information. In addition, participants will be interacting frequently with the PHNs after enrollment, which will both strengthen the participant's ties to the study and provide opportunities for the PHNs to remind the participant about upcoming study visits.

Follow-up visits will include completion of a questionnaire by ACASI, and HIV testing for those who were not HIV-positive at the prior visit. HIV testing will be offered to those who previously refused testing. Those with a first time reactive HIV rapid test at a follow-up visit will be confirmed by WB and will have a CD4 cell count performed. All HIV-positive participants will have a viral load test performed at the time of diagnosis and at the 52-week visit. All participants will receive STI counseling and testing at 26- and 52-weeks. Participants will receive counseling to include risk reduction counseling and pre- and post-test counseling, as well as referrals to available services. Participants will be asked to report any STI or HIV diagnoses they receive between visits and to provide (or provide permission for study staff to request) documentation of diagnoses.

Plasma specimens for testing at the HPTN Network Laboratory (NL) will be collected at all visits for all participants.

2.4 Study Design: Qualitative Component

HPTN 061 represents a unique opportunity to learn more about Black MSM, a group about which few reliable data are available. Therefore, HPTN 061 will use two methods to collect qualitative information: qualitative interviews and focus groups.

Focus Groups: Three to five focus groups will be conducted at each of the six sites participating in HPTN 061 with the goal of recruiting 24 participants total at each site, providing a robust sampling of approximately 6% of the total participants. The intent of this activity is to elicit subjective accounts from a variety of Black MSM; therefore, a non-random purposive sampling will be used to over-sample among Black MSM from hard-to-reach groups (e.g., men who do not identify themselves as gay, men under the age of 21, and men born outside of the US). The team will also strive to include participants not willing to receive HIV testing in the focus groups. Men will be invited to participate in a focus group on a "rolling basis." As men enroll, some will be offered the opportunity to participate in a focus group. The nature and intent of the group will be explained, and interested participants will be offered pre-established focus group dates to choose from. Participants who agree to participate in a focus group will be asked to provide contact information so that staff can provide reminders closer to their focus group date). Staff will strive to enroll three focus groups of eight participants each, but may have a greater number of smaller focus groups depending on enrollment.

The focus group meetings will be approximately 1.5 to 2 hours long. Focus groups will be conducted as soon as possible after enrollment, a process further described in the study-specific procedures manual (SSP). The focus groups will take place at locations identified by study staff to ensure adequate privacy and confidentiality, most likely at the site or at a local community organization. Participants will receive compensation for participation in the focus groups.

The focus groups will be led by experienced, trained, local facilitators, and will explore issues related to 1) the men's overall perceptions of life in their local area; 2) contextual factors associated with HIV/STI testing patterns, service uptake, and health care utilization;

and 3) stigma and social norms among Black MSM and between Black MSM and the larger community. Focus group facilitators will be culturally matched to participants whenever possible.

A semi-structured interview guide (included in the SSP manual) will guide the discussions for the focus groups, and probes will be used to obtain in-depth data about the concepts not initiated by the men but identified *a priori* for exploration by the HPTN 061Qualitative Working Group (QWG), described below.

Participants will be addressed by first names or nicknames during the groups to safeguard confidentiality. Demographic data collected as part of the main study will be used to describe the composition of the group and to compare and contrast analyses locally and across sites, based on group demographics.

Focus groups will be digitally audio-recorded and transcribed by trained transcriptionists. Participant identifiers will be removed from transcripts and replaced by participant identification numbers. The audio files from the digital voice recorders will be maintained in a password-protected subdirectory of the project director (PD) in the respective sites. These files will be uploaded by the PD to the secured and encrypted website of the professional transcription service for the purpose of transcription. Trained personnel from the respective sites will verify the accuracy of the transcription by listening and making comparisons from the digital audio files to the transcriptions. This will capitalize on site-specific familiarity and knowledge that the interviewers will have developed regarding their own interviews and study participants. The "cleaned" transcript will be securely forwarded to the QWG for initial analyses.

Qualitative Interviews: Each of the six communities participating in HPTN 061 will conduct between 10 and 30 semi-structured individual interviews among participants who are recruited for, and consent to, this component of the study. After the focus group analyses have been completed, a qualitative interview guide will be developed to address major study domains, including: 1) knowledge, attitudes, and behavior regarding HIV/STI testing patterns, service up-take, and health care utilization, 2) stigma and discrimination related to HIV, homosexuality, and race; 3) themes that emerged from the focus groups; and 4) themes that arise spontaneously during the interviews.

Participants enrolling in the main HPTN 061 study will be asked to participate in the qualitative component. This convenience sampling frame will allow interviews to be completed in a timely manner, so that enough time is allotted to code and analyze the data before the end of the study. Some data suggest that not identifying as gay may increase HIV-risk among some MSM;[62] therefore, we will purposely select participants from the main study so that up to half the participants identify as "other than gay" and approximately half identify as "gay" in order to explore whether our findings vary by sexual identity. To the extent possible, within each of these two groups, we will purposely sample for diversity by age (half <35 and half >35), and socioeconomic status (SES) (half high school or less and half more than high school). The team will also strive to include participants who refuse

HIV testing into the qualitative interviews, to gain insight into reasons Black MSM refuse HIV testing.

Trained study staff will conduct 60- to 90-minute individual qualitative interviews. The interviews will be audio recorded and transcribed for analysis. Interviews will be conducted within 30 days of participants' study enrollment date and will take place at a location identified by study staff to ensure adequate privacy and confidentiality. Participants will be provided with a separate reimbursement for participation in an interview. Each site is expected to interview at least ten participants, to allow for cross-study analysis. Sites that plan to perform site-specific analyses on interview data are expected to interview a total of 30 participants, however this number may be reduced on a site-by-site basis if data show that no new trends are emerging, if costs or site capacity do not allow for conduct of all the interviews, or for other reasons.

Qualitative Study Coordination and Leadership

Qualitative study components of this protocol will be directed by a QWG consisting of HPTN 061 investigators, consultants, and local site representatives selected by the protocol team. The QWG will elect leaders responsible for coordinating various aspects of the qualitative study, including:

- An administrative leader responsible for convening the QWG, setting meeting agendas, and keeping minutes that reflect key decisions and action items (with responsible parties and target dates).
- A focus group leader and a leader of individual interviews who will be responsible for maintaining the respective coding matrices developed by the QWG, documenting the code domains and construct core ideas, creating domain-based reports, documenting code lexicons, and ensuring cross-site comparability in both data collection and analysis.
- A quality control leader who will oversee the analysis process including development of transcription protocols and coding protocols, review of face sheet content, establishment of inter-coder agreement procedures and checks against subjective bias/over-interpretation, and all aspects of training.
- A reports leader responsible for producing reports with clearly substantiated recommendations for the intervention trial.

The QWG will use the Handbook for Team-based Qualitative Research as a guide for conducting the study and analyses.

3 STUDY POPULATION

3.1 Inclusion Criteria

Participants who meet **all** of the following criteria are eligible for inclusion in this study:

- Self-identify as a man, or male at birth.
- Self-identify as Black, African American, Caribbean Black, or multiethnic Black.
- Report at least one instance of UAI with a man in the past six months.

- At least 18 years old.
- Provide informed consent for the study.
- Reside in the metropolitan area and do not plan to move away during the time of study participation.

3.2 Exclusion Criteria

- Co-enrollment in any other HIV interventional research study or have been enrolled in an HIV vaccine trial in which they were either in the active arm or do not know the arm in which they were enrolled.
- Would be enrolled as a community-recruited participant in a category that has already reached its enrollment cap.
- Any medical, psychiatric, or social condition, or occupational or other responsibility that, in the judgment of the investigator, would make participation in the study unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives.

3.3 Participant Categories and Enrollment Caps

This study endeavors to maximize the potential impact of the intervention by focusing on two groups: men who are HIV-positive but unaware of their status, and men who are HIV-infected but are not in care and are having unprotected sex with uninfected partners or partners of unknown status. In studies where community word-of-mouth is a vital engine for recruitment (as is expected for HPTN 061), men who meet the criteria for a single category (e.g., HIV-positive and in care) may already be in contact with one another through support groups and may enthusiastically refer one another to the study. Although this rapid recruitment would be ideal for quickly meeting enrollment targets, it has the potential to result in a monolithic sample that would undermine the goals of the study. Therefore, enrollment in this study will be limited in each city by category-specific enrollment caps. Figure 4 depicts graphically how the enrollment caps will be applied to participant categories at one site. Recruitment of all community-recruited participants will cease when 250 community-recruited participants who agree to HIV testing have been enrolled. In an effort to limit the number of HIV-uninfected participants, enrollment of this category will be capped at 200 participants. Because it will be impossible to identify participants who will be uninfected prior to enrollment and HIV testing, the enrollment cap in this case will mean exclusion from follow-up visits only. HIV-negative participants who are enrolled after the 200-participant cap is reached will not count toward the overall cap of 250 community-recruited participants who agree to testing. An enrollment cap of 83 participants will apply to those willing to enroll in the study but not consenting to HIV testing. An enrollment cap of 10 community recruited participants will apply to those with a prior diagnosis of HIV infection who are already in care or report only having unprotected anal sex with HIV-positive partners.

3.4 Note on Recruited Populations and Nomenclature

The population of Black men in the US who engage in sex with other men is diverse. Black MSM may identify as gay, straight, bisexual, transgendered, or none of these. Because this study would like to enroll and understand the broad spectrum of Black MSM practices,

identities, and prevalences of those practices and identities, this study targets all Black MSM and uses that term throughout. It is expected that recruitment for this study at various sites may need to be conducted in different ways for different communities of Black MSM. For example, one approach will speak to and validate gay Black men, while others seek to recruit men who do not consider themselves gay, but nonetheless have sex with men.

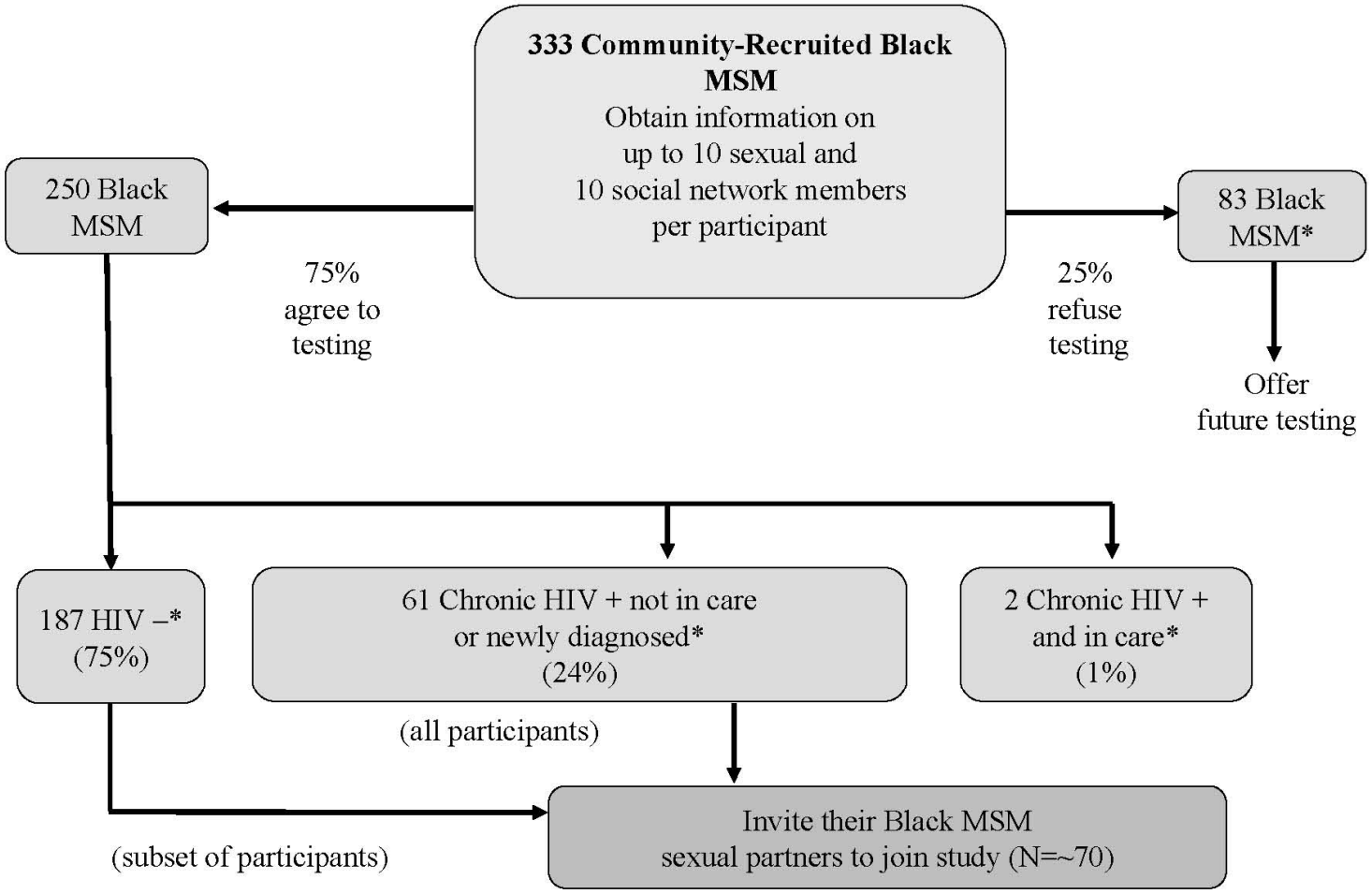
3.5 Recruitment Process

Recruitment will begin through outreach efforts of site staff to recruit community-recruited participants. Community-recruited participants meeting certain criteria ("index" participants) will be asked to recruit members of their sexual network to the study ("referred" participants). This recruitment and referral scheme is presented in Figure 5.

Each site will be asked to enroll 250 community-recruited Black MSM who agree to HIV testing over a 12-month period. Since one of the aims of the study is to determine the uptake of HIV testing, HIV testing will not be a requirement for enrollment. Therefore, the sites should expect to enroll approximately 333 index participants through community recruitment to reach 250 men who agree to testing, based on the assumption that approximately 25% of men will refuse HIV testing. Recruitment methods will be developed at each site and could include community outreach, engagement of key informants and local community-based groups, advertising, and use of online strategies including the placement of banner ads, text ads, chat room outreach, and social networking sites. The methods will be focused on maximizing the identification of Black MSM with undiagnosed HIV infection. Data will be collected to determine if enrollment differs by recruitment strategy or place of recruitment. As an example of enrollment varying by place of recruitment, in the NHBS survey in New York City, the acceptance of enrollment into the survey by Black MSM varied by venue type: 63% of Black MSM approached at bars enrolled in the survey, 78% of Black MSM approached at street locations enrolled, and 82% of Black MSM approached at retail businesses enrolled (B.Koblin, unpublished data).

Index participants (those who meet the criteria enumerated above for being eligible to refer partners to the study) will be asked to refer up to five of their Black MSM sexual network members for screening. If these referrals meet the enrollment criteria for referred participants, they will be enrolled into the study as "wave one referred" participants. Any referred participants who meet the criteria to be index participants will also be asked to refer up to five of their Black MSM network members for enrollment into the study as "wave two referred" participants. No limit on the number of waves of referral is planned, because it is believed the waves will be self-limiting. Enrollment of referred partners will cease at a site two months after the last community-participant has been enrolled. It should also be noted that the goal is to enroll several referred partners for each index partner. However, conservative estimates have been made (i.e., that most index participants will enroll only one partner). Thus, it is predicted that each site will enroll at least 70 referred participants over the entire study period. In total, each site would expect to enroll approximately 403 participants: 250 community-recruited participants who agree to testing, 83 who do not, and at least 70 referred participants.

Figure 5- Recruitment/Referral Scheme for HPTN 061 (For One Site)



*The number of participants enrolled in these categories will depend on variables such as HIV incidence in the local population of Black MSM, and the effectiveness of recruitment strategies among the various groups. However, to ensure diversity among the enrolled participants, enrollment caps on certain categories will be enforced. For example, no more than 200 HIV-uninfected participants will be followed up, and no more than 10 chronically infected participants already in care for HIV or only having sex with HIV+ men will be enrolled. See Section 3.3 for details.

3.6 Participant Retention

For those participants who are scheduled to participate in follow-up visits, the study staff will make every reasonable effort to retain them for the entire study period. The follow-up visit burden of this study is low compared to other studies, since there are only two visits after enrollment, at 26 and 52 weeks. However, the long period of time between visits could make it difficult for participants to remember their visits and increase the likelihood that a participant's locator information would become out-of-date between visits. Therefore, outreach staff will stay in touch with participants between scheduled visits to remind participants of their visit schedules and to inquire about anticipated changes in locator information. Participants will also be working with PHNs on an ongoing basis after enrollment on a schedule that is separate from the study visit schedule. PHNs will have the opportunity to remind participants of their upcoming study visits, and the ongoing interaction between the participants and the PHNs will strengthen the connection of the participants to the study.

Study site staff are responsible for developing and implementing local standard operating procedures (SOPs) to achieve high levels of follow-up, including use of dedicated retention personnel who will stay in contact with participants between visits to quickly follow-up with participants who have missed visits. As in any study, effective retention should begin by thoroughly explaining the study visit schedule and procedural requirements during the informed consent process, and by collecting extensive locator information during the screening visit. The retention target is for no greater than 5% loss-to-follow-up of enrolled participants at the 26-week visit and 10% at the 52-week visit.

For each participant, clinic staff will obtain confidential contact information. Each study site will develop its own locator form and will determine the best way to collect this information for its own study population. This information will be updated during each study visit. If a participant misses a scheduled appointment, clinic staff will try to establish communication with the participant through all possible means (e.g., telephone, e-mail, mail contact, and home or workplace visits). The importance of attending all scheduled follow-up visits will be emphasized to study participants at each visit. Participants may be unable to report to the clinic for a study visit for a variety of reasons. Therefore, a provision has been made for sites to conduct off-site visits when all other options for scheduling the visit have been explored (e.g., earlier or later office hours, weekend visits). Further details about off-site visits are provided in Section 5; of note, off-site visits will only be conducted at sites that have an approved SOP in place for doing so, when prior consent has been obtained for off-site visits from the participant, and when the visit can be conducted in a place and manner that would not compromise the confidentiality of the participant or the safety of the participant or the research team.

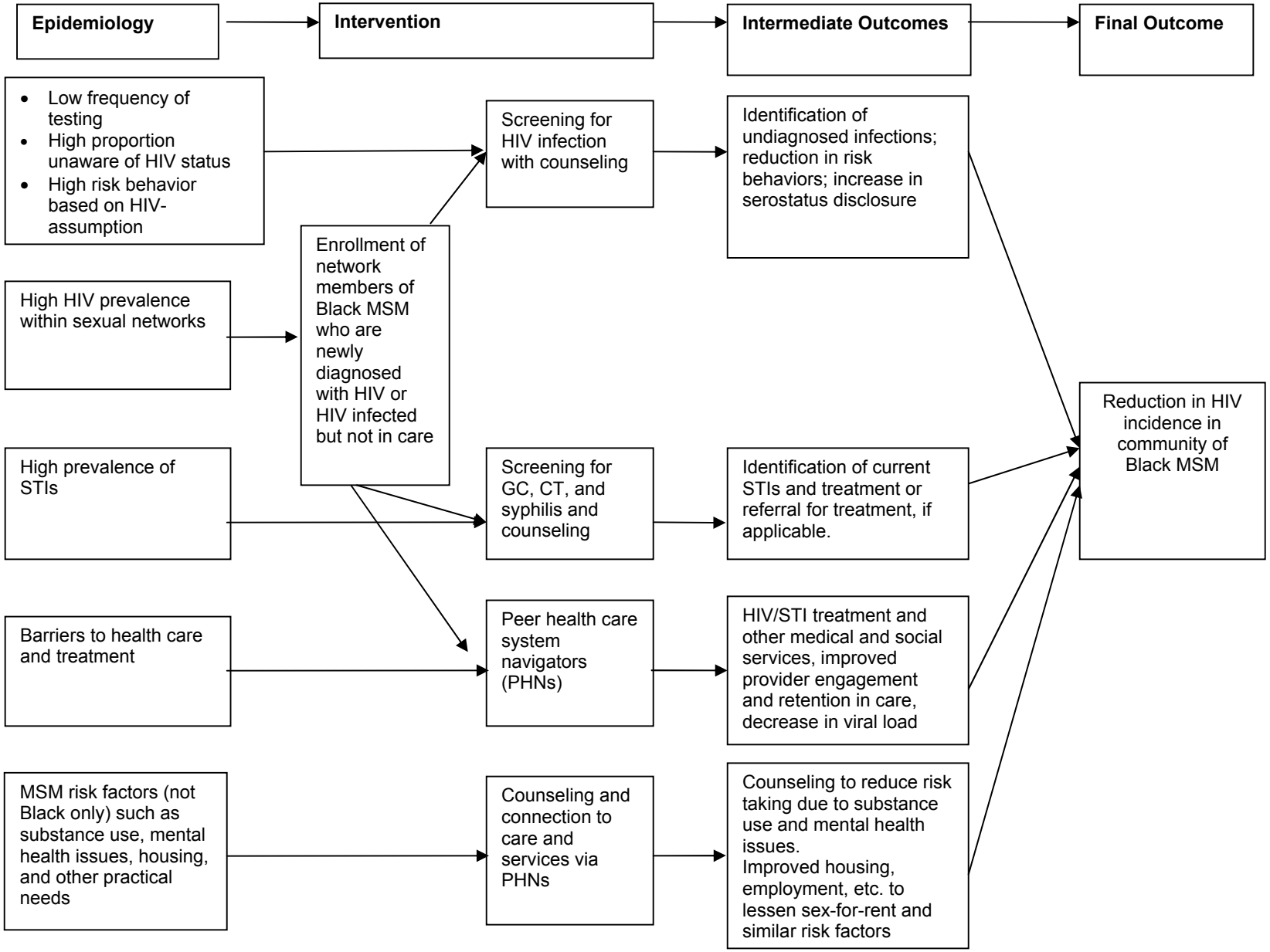
3.7 Participant Withdrawal

Participants may voluntarily withdraw from the study for any reason at any time. The site investigator also may withdraw participants from the study, after consultation with the protocol co-chairs, lead biostatistician, and the chair of the Study Monitoring Committee (SMC) (or the Network PI if the SMC Chair is unavailable) in order to protect the participants' safety and/or the safety of study staff. Participants also may be withdrawn if the study is terminated prior to its planned end date. No participants should be withdrawn from the study solely for non-attendance at study visits or refusal of study procedures. Study staff will record the reasons for all withdrawals from the study in participants' study records.

4 STUDY INTERVENTION

This study will examine the feasibility and acceptability of an intervention to address factors likely to be contributing to high rates of HIV infection among Black MSM using multiple components, both proven and innovative. Two factors (low awareness of HIV status and high prevalence of STIs) will be addressed by increased provision of counseling and testing. However, the interplay of sexual networks in which HIV and other STIs are highly prevalent (and highly incident) in an environment in which critical barriers to health care are commonplace, creates a more complicated picture and leads to the innovative components of the intervention. Figure 6 presents the key epidemiologic explanations for the disproportionate impact of HIV upon Black MSM, the related intervention components, the expected intermediate outcomes, and the expected final outcome of reducing HIV incidence. After Figure 6, we provide the rationale for each of the intervention components.

Figure 6- Epidemiologic Causes of High Prevalence among Black MSM, Intervention Components, and Outcomes



4.1 Network Recruitment

The high prevalence of undiagnosed HIV within Black MSM networks and the higher likelihood that Black MSM have Black male sexual partners create a feedback system in which amplification of infection is expected.[26] To maximize the intervention effect, while addressing practicality and feasibility of intervention delivery, we have chosen to focus the network recruitment on the Black sexual network members of participants who are newly diagnosed with HIV or who are previously diagnosed, but are not in care. Therefore, any reductions in transmission dynamics at the network level have the potential for a proportionally larger impact at the population level (of Black MSM). Specifically, increased voluntary counseling and testing (VCT) and knowledge of HIV status, improved access to care, and increased adherence to antiretroviral medication among seropositive men may reduce viral load in a large enough proportion of Black MSM in a given community that uninfected men will be at less risk. Lower risk would be even more likely if these seronegative men also began to reduce their high-risk behaviors at the same time (a benefit of testing, counseling, and care among seropositive MSM). Although recruitment will include a network component, the intervention will be delivered individually to participants.

Community-recruited participants will be recruited through multiple strategies developed by the local sites (e.g., street outreach, engaging key informants and local community-based groups, and advertising). Information about the sexual and social networks of each participant will be solicited. The goals of collecting this information are many-fold, and include characterization of the size of Black MSM networks, understanding the role of race and gender in the networks, and understanding the influence the networks have on a participant with regard to risk-taking behavior. This information will be crucial to tailoring the intervention and developing the randomization approach for the community-randomized trial.

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 061will have his HIV status disclosed, up to 20 randomly selected HIV-uninfected 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.

The protocol team considered enrolling sexual network members who were not Black MSM (e.g., non-Black MSM or female partners). Although there may be risk associated with partners who are not Black MSM, the epidemiologic evidence shows that the higher HIV prevalence among Black MSM is, in part, explained by having partners who are also Black MSM.[20] Therefore, intervening with Black MSM themselves may have the best potential to affect HIV incidence in this group.

At least one study has shown that it is possible to recruit social and sexual networks of Black MSM.[63] Furthermore, the "Social Network Demonstration Project" sponsored by CDC used a social network strategy to identify people with undiagnosed HIV infection in seven cities.[64] This demonstration project illustrated that networks can be recruited, and that Black and Latino MSM were particularly good recruiters of other network members.[64]

4.2 HIV Counseling, Testing, and Referral for Care

A major component of this intervention is finding men with undiagnosed HIV infection. Licensed HIV antibody tests (e.g., licensed rapid HIV antibody tests with follow-up of reactive tests with WB assays) will be used to identify HIV-infected men who are unaware of their HIV status. Participants will be provided pre- and post-test counseling. Participants who are identified as being HIV-infected (whether this is a new diagnosis or confirmation of a prior diagnosis) will be assisted in obtaining care by a PHN. As described in Section 4.4 of this protocol, the assistance of a PHN goes well beyond traditional referral for care, since PHNs will not only be aware of local resources for care, but will work with participants over time to overcome whatever barriers they may have to accessing that care.

In addition to standard HIV testing, laboratory assays that have not yet been United States Food and Drug Administration (FDA)-cleared will also be performed by the HPTN NL to address the special contribution of acute and recent infection to the HIV epidemic in Black MSM. These assays may include pooled HIV ribonucleic acid (RNA) testing (also generically known as nucleic acid amplification testing [NAAT]), [65] assays that combine p24 antigen screening with antibody testing, assays that profile the evolution of HIV antibodies during seroconversion (e.g., the HIV subtypes B, E and D (BED) assay, Avidity assays), and other tests. Since these assays are not yet FDA-cleared for clinical use, they would be used retrospectively in the feasibility study to determine if acute or recent infections were identified. Community representatives consulted in the development of this protocol expressed concern that the protocol team planned to perform HIV NAAT testing retrospectively, only at the week 52-visit, and not to communicate results of a positive test back to the participant. The team's decision was based on considerations of cost, expected benefit, and the possibility that pooled HIV RNA testing would be performed using an assay that is not FDA-cleared for this purpose.

Providing real-time NAAT testing for clinical care at multiple visits would require shipping samples frequently from each site to the NL where they would have to be tested individually using an FDA-cleared assay. This would be very expensive, and, based on incidence estimates at these sites, would likely only identify perhaps one acute infection during the entire study, or perhaps none. Nonetheless, the protocol team acknowledged that the retrospective HIV NAAT testing performed in HPTN 061 may indeed identify a participant who was acutely infected at the time of his 52-week visit, and recognized that there was an ethical issue in not providing that information to him. Therefore, if any participant tests positive for HIV RNA during the retrospective pooled NAAT analysis, the protocol team will attempt to confirm the positive result. To do this, the protocol team will obtain a stored sample from the study subject, and perform an HIV RNA test using an assay that is FDA-cleared for HIV diagnosis; this testing will be performed in a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory at the HPTN NL. The study team

would only attempt to contact a study participant in the event that the FDA-cleared test result was reactive. Participants so contacted would be advised to have HIV diagnostic testing performed in a setting that could provide appropriate post-test HIV counseling. It is noted that pooled HIV RNA test results might not be available for a year or more after the close the study, and that additional time would be needed to perform the FDA-cleared test on a new sample.

4.3 STI Testing and Referral for Care

The risk of HIV acquisition and transmission has been shown to be increased by the presence of other STIs, in particular, ulcerative STIs.[17 66 24] This is particularly relevant for this population, since several studies have found that STIs such as gonorrhea, Chlamydia, syphilis, and HSV-2 are more prevalent among Black MSM compared to other men.[67 68 26] Participants diagnosed with gonorrhea, Chlamydia, and/or syphilis will be offered treatment or referred for treatment. Participants will be encouraged to return to the clinic between study visits for testing and treatment (or referral for treatment) if they suspect they have acquired an STI. Because chronic HSV-2 infection cannot be eradicated, and because recent research found that suppressive therapy for HSV-2 does not decrease the risk of HIV infection,[69] participants will not be tested for HSV-2 in this study; however, symptomatic HSV-2 infections will be referred for care.

Other STIs were considered for inclusion based on prior reports of high prevalence and incidence among Black MSM, association with unprotected intercourse, epidemiological associations with increased HIV incidence, and feasibility of providing curative treatment. Because Human Papillomavirus (HPV) can be transmitted without unprotected intercourse and is untreatable, participants who have evidence of HPV disease will be triaged to medical care; if the HPV vaccine is found to decrease anal HPV infections among MSM, participants will be referred for vaccination. Likewise, since the majority of MSM have either developed natural infection with Hepatitis B and/or received the vaccine, they will not be screened for this infection as part of the trial; individuals who have not been vaccinated will be referred to screening and vaccination programs. Hepatitis C is primarily transmitted by blood contact with shared injection paraphernalia, although MSM may acquire the infection via traumatic sexual intercourse. However, given the relative low prevalence and incidence of Hepatitis C among MSM and the lack of highly effective treatment with limited toxicity, Hepatitis C infection will not be assessed in this study.

It is notable that only one of five community-based interventions that focused on bacterial STI control resulted in decreased HIV incidence.[48] The rationale for testing and treating STIs in this protocol is not that it is a proven effective strategy for reducing HIV risk. Rather, the protocol team believed that treatment of STIs, as one interventional component among others, may contribute to reducing HIV risk for Black MSM. Also, STI testing and treatment may be seen as a health benefit by the participants, which could build participant rapport with the study and staff, and in turn provide opportunities for more effective risk reduction counseling and behavior change. The prevalence and incidence of STIs can also act as surrogate markers for self-reported changes in risk behavior.

4.4 Peer Health Care System Navigators

The first reported patient navigation program was developed at Harlem Hospital for cancer patients by Dr. Harold Freeman in 1990.[70] Patient navigators were culturally matched with patients and often were cancer survivors themselves. Their principal role was to assist patients in fulfilling multiple service needs within a fragmented system of care, and to maintain continuous care by increasing patients' confidence and their support networks. This program was highly regarded by patients and effective in increasing access to and continuity of care for African American women and has been widely adopted across the US and Canada for multiple population groups.

Patient navigation has recently been described as an emerging model of care coordination within HIV care.[71] [72] In the recent Health Resources and Services Administration (HRSA) Special Projects of National Significance (SPNS) Outreach Initiative, four sites across the US implemented navigation-like models to identify HIV-infected individuals who were not receiving adequate HIV care, and to assist them to become engaged and retained in appropriate, continuous HIV care.[73] These navigators used similar strategies as advocates, health educators, case managers, and social workers to work with minority and underserved individuals. After participation, their clients had reduced access and stigma barriers, improved engagement with health care providers, and reduced viral load at 6- and 12-month follow-up assessments, compared to baseline.[73] [74] Study outcomes demonstrated that SPNS Initiative navigators helped HIV-infected individuals gain access to health care resources and use them more effectively.[75]

One of the sites involved in the SPNS Initiative was the Fenway Community Health Clinic. Staff from this organization worked with the Multicultural AIDS Coalition (MAC) to develop a manualized intervention from the patient navigation model used in the SPNS initiative. This Health System Navigation (HSN) model incorporated skills-building that had been effective in HIV prevention and substance abuse treatment, including motivational interviewing and Stages of Change. A particular focus of the training was to teach navigators how to increase clients' self-confidence and communication skills as a way to improve relationships with their case managers and HIV providers. Navigators were given extensive training on the local systems of HIV services, social programs, and other ancillary service providers, such as job training and housing agencies. This training prepared navigators to work with African American MSM, Latino and Caucasian gay men, individuals returning from incarceration, and substance abusers.

HPTN 061 will incorporate navigation as a key component of the intervention. PHNs at each site will receive comprehensive training that is overseen by site leadership. Site navigation staff will be in regular communication with, and when possible will be trained by, Dr. Judy Bradford and a member of her staff who assisted with development of the HSN manual.[76] Most PHNs will be from the target population or will have demonstrated competency in working to facilitate the ability of Black MSM to participate in research.

During the HPTN 061 study, PHNs at each site will conduct an assessment of participants' health care history (including HIV care for positive participants), unmet service needs, and barriers to health care, and they will answer any questions participants have about what

navigation will be like. They will exchange contact information, discuss expectations for what they will work on together, begin developing an action plan, and decide how they will stay in touch with each other.

Evaluation of the interventions in the SPNS Initiative demonstrated that the number and type of navigator-client contacts had a significant impact on health outcomes.[77] When participants received nine or more contacts with their navigators during the first three months, they were only half as likely to have a gap of four months or more in primary care during the first 12 months after enrollment, a finding that remained after controlling for baseline CD4 cell count. Participants who had two or more contacts that included accompaniment to primary care visits had a significantly lower risk of a four-month gap in HIV primary care. Despite the overall success of these interventions, active illicit drug users were less likely than others to show significant improvement in HIV care over the 12-month period, emphasizing the need to include substance abuse treatment options in HIV prevention and care programs.[75]

Consistent with these findings, the HPTN 061 study will establish frequent contact between PHNs and clients in the first months of navigation, tapering to less frequent contact, and transitioning to a sustainable care plan in later months. The frequency and longevity of contact between clients and PHNs will depend upon the extent of the client's needs. For HIV-infected participants, transition to a stable care plan and a regular (non PHN) case manager will likely take up to 12 months. Clients will be encouraged to contact their PHNs as needed, especially during the first weeks and months of the relationship. When the PHN-client relationship is well-established with a consistent action plan and progress toward removing barriers, PHNs will encourage their clients to become more independent, but will invite them to initiate contact if they need guidance or support.

PHNs will complete an encounter form after each contact with their clients, including supplemental notes to capture the nature of the contact and further detail about experiences reported by the clients. A limited amount of data concerning the frequency of contacts and the types of navigation utilized will be extracted for inclusion into the study database. Clients will have the opportunity to provide their feedback on the PHNs and the navigation process as part of the questionnaire at follow-up visits. Although the work between the PHN and the client will occur independently of the study's follow-up visit schedule, and often off-site from the clinic, the PHN will still be an integrated member of the study team, working with counselors, retention coordinators, and other site staff on a day-to-day basis. PHNs will work to provide culturally appropriate referrals whenever options for referral are available.

The fact that PHNs will work off-site, and will interact on the participants' behalf with health care providers and others who are not members of the study staff, may increase the risk of a breach in confidentiality of participant information. PHNs will therefore receive extensive training and follow strict procedures to safeguard confidential information.

4.5 Assessment and Care for Substance Use and Mental Health Issues

Previous research has shown that stimulant use, heavy alcohol use, use of drugs/alcohol during sex, and mild-to-moderate depression are risk factors for HIV infection among MSM.[4]

Although these risk factors do not appear to be a larger problem for Black MSM than for other MSM,[26] a holistic approach to lowering the HIV risk of Black MSM and enhancing their connections to care should include substance use and mental health strategies. Incorporating assessment and care for substance use and mental health into this study will also provide an opportunity to investigate the acceptability of interventions in this population, an area in which little is known.

In this study, three different mechanisms will address substance use and mental health issues among participants: 1) collection of data through ACASI, 2) counseling and referral to care through study counselors, and 3) exploration of participant needs and connection to care through peer health navigators.

1) Collection of Data Through ACASI- All participants will complete a survey through ACASI that will collect information on their experience with a variety of issues, including use of drugs and alcohol, depression, childhood sexual abuse, post-traumatic stress disorder (PTSD), and experience of homophobic or partner violence. For depression, alcohol use, and PTSD, data will be collected through validated screeners (CES-D, AUDIT and SPAN, respectively). These data will be entered into the study database and will allow a thorough analysis of the prevalence of these issues among Black MSM in these six cities, including the associations of these factors with risk behavior and HIV status. The study team exhaustively discussed the merits of reporting these data out to the clinic for participant care, or having the counselor repeat these assessments in their face-to-face discussion with the participant after completion of the ACASI. It was decided that to repeat the assessments would be overly burdensome to the participants, and to report ACASI data to clinic staff would compromise the ACASI system's guarantee of confidentiality among a population historically suspicious of research. It was felt that the critical issue was to allow participants to ensure that there was no negative mental health impact due to the experience of completing the visit, and that to proactively probe for these issues was likely to do more harm than good. It was felt that allowing the participants to bring up issues that they wanted help with during the counseling session was the best solution, with the staff alert for and responding to anyone appearing to be in acute distress, as described below. Analysis of the ACASI-collected data is expected to help inform the planned community-randomized trial.

2) Counseling and Referral to Care- At the conclusion of the ACASI session, all participants will meet with a counselor, and will be invited to discuss any issues that the interview session has raised. The counselor will use a low-pressure, empathetic approach and will respect the wishes of the participant, allowing him to open up or keep to himself, as he needs to. The participant and counselor will then complete HIV/STI pre- and post-test counseling (for those consenting to testing) and risk reduction counseling based upon the Project RESPECT manual. This counseling will include discussion of the effects of substance use and mental state upon the participant's sexual risk behavior, and ways to reduce the effect of a substance use or mental health problem on their sexual risk. Counselors will make the participant aware of locally-available resources for help with problems that have been identified during counseling, and will offer to help arrange a referral. The counselor will provide the participant with a comprehensive list of all available resources so that the participant can

follow up on issues that he may not feel like discussing during the visit, or that reveal themselves at a later time.

At the end of each study visit, the counselor will perform a final check-in with the participant to assess their emotional state. If at this time or any other during the visit a participant appears to have acute and serious issues, he will receive a clinical evaluation by a licensed mental health provider (masters-level social worker, clinical psychologist or psychologist), who will be available on call or as part of the care team at the site facility so that the evaluation can take place the same day and not as a referral. Based upon the results of that evaluation, the team will follow site-specific procedures for connecting the participant to appropriate care. This might mean immediate hospitalization for someone suffering from suicidality, or prioritized enrollment in a residential rehab program for those with a serious substance abuse problem.

3) Exploration of Participant Needs and Connection to Care Through Peer Health Navigators- For the estimated two-thirds of HPTN 061 participants who will be eligible to receive peer health navigation, PHNs will play a key role in connecting participants with substance and mental health issues to available care and treatment programs. As part of their work with participants, PHNs will assess participant health needs through dialogue and through use of an intake questionnaire and barriers-to-care assessment. Using this information , the PHNs and participant will determine the participant's health care priorities and determine an action plan. The PHN will refer the participant to appropriate care resources, and will also help the participants overcome barriers to accessing these resources, such as scheduling, transportation, prior negative experiences, etc. As described above for counselors, PHNs will have access to a licensed mental health provider in instances where a participant has issues that require evaluation or referral by a licensed professional. The work of the PHN will compliment and extend the counseling and referrals that are made by the counselor at the study visits.

Both counselors and PHNs will work together to maintain an up-to-date list of locally available services for referral programs, which may include support groups, drug treatment programs, and social services. Counselors and PHNs at all sites will receive clinical supervision by a licensed mental health provider (masters-level social worker, clinical psychologist or psychologist).

Although this study will strive to address the mental health and substance use needs of participants as they are uncovered, it should be noted that providing care for mental health and substance issues is not a primary focus of this protocol. Accordingly, the study will only take advantage of available resources and programs, and developing or providing counseling services beyond short risk reduction counseling will not be part of this study.

5 STUDY PROCEDURES

An overview of the study visit and procedures schedule is presented in Appendix I. Additional detail on visit-specific study procedures is presented below. Detailed instructions to guide and standardize study procedures across sites will be provided in the SSP.

5.1 Prescreening

There will be no formal screening procedures for HPTN 061; however, prescreening will be performed either in person or over the telephone. Potential participants who express interest in the study will be asked a small number of questions to determine whether they are eligible for the study and to determine the enrollment category into which they would be enrolled. Those who are eligible for enrollment into an open category based on prescreening will be scheduled for an enrollment visit. Please note that prescreening is a verbal procedure only; no documentation will be made of answers to the prescreening questions.

5.2 Enrollment Visit

Because no record of prescreening will be maintained, participants reporting to the study site for enrollment will be re-screened for eligibility by answering a few short questions before informed consent procedures are initiated. Written informed consent for the study will be obtained before any further study procedures are initiated.

Note that procedures below are grouped by category, but are not necessarily arranged in the order in which they should be performed. A suggested order of procedures is included in SSP Section 6, the visit checklists. It is imperative that completion of the ACASI interview take place before pre-test and risk-reduction counseling so that these messages will not influence participants' answers.

Administrative, Behavioral, and Regulatory Procedures

- Obtain informed consent for enrollment. Invite participants to participate in qualitative component of study (if applicable) and solicit consent for specimen storage and testing (optional).
- Obtain locator and demographic information.
- Administer eligibility checklist.
- Collect data by ACASI on topics such as sexual risk behaviors, drug/alcohol use, health care/HIV testing history, incarceration history, structural and personal/cultural barriers to receipt of HIV care, unmet service needs, venues frequented, and attitudes toward race, sexual identity, other prevention strategies, research, and health care.
- Collect information about 5 social and 10 sexual network members for descriptive purposes.
- If participant qualifies (index participant):
    - Request referral of up to five Black MSM sexual network members.
    - Provide training on techniques for motivating network members to come to the study site.
    - Administer questionnaire about motivators or barriers to referring sexual network members.
- Schedule next visit. If the participant has agreed to qualitative component of study, schedule the visit for that activity, if appropriate.

Clinical/Counseling Procedures

- Provide counseling for issues raised during completion of ACASI questionnaire.
- Provide HIV and STI pre-test counseling.
- Provide risk reduction counseling, and referrals for care (or professional assessment) for issues such as substance use and mental health problems.
- For HIV-positive participants, obtain HAART history.
- Collect samples for HIV/STI assessments:
    - Blood draw for laboratory tests and sample storage.
    - Urine for gonorrhea/Chlamydia trachomatis (GC/CT) testing.
    - Swabs for rectal GC/CT testing.
- Examine for circumcision, unless participant identifies that they have had gender reassignment surgery.
- Provide STI test results and post-test counseling. Offer STI treatment or referral for treatment, if applicable.
- Provide HIV rapid test results and post-test counseling.
- For participants receiving reactive HIV rapid test results, explain procedural implications for WB confirmation, CD4 cell count, and viral load testing, and the necessity of returning to the site to receive these results.
- If participant qualifies, introduce health care navigation. Begin work with the PHN or complete questionnaire about reasons for refusal of health care navigation.
- Offer condoms and lubricant.

Laboratory Procedures

- HIV rapid test.
- HIV WB for participants to confirm reactive HIV rapid test.
- CD4 cell count testing for participants with a reactive HIV rapid test.
- Syphilis serology (including titer).
- GC/CT NAAT from urine.
- HIV viral load for subjects with a positive WB result.
- Prepare rectal swabs for shipment to NL.
- Plasma sample storage, for subsequent shipment to NL.

5.3 Follow-up Visits (26 and 52 Weeks After Enrollment)`

Administrative, Behavioral, and Regulatory Procedures

- Update locator information.
- Collect data by ACASI on topics such as sexual risk behaviors, drug/alcohol use, health care/HIV testing history, incarceration history, structural and personal/cultural barriers to receipt of HIV care, unmet service needs, venues frequented, feedback on the PHN experience, and attitudes toward race, sexual identity, other prevention strategies, research, and health care.
- Counselor will review and update the list of sexual network partners.
- Schedule next visit if applicable.

Clinical/Counseling Procedures

- Provide counseling for issues raised during completion of ACASI questionnaire.
- Provide STI pre-test counseling, and, if not previously confirmed HIV-positive, HIV pre-test counseling. If not previously tested, offer testing.
- Provide risk reduction counseling, and referrals for care (or professional assessment) for issues such as substance use and mental health problems.
- For HIV-positive participants, obtain HAART history.
- Solicit information about study-related social harms.
- Collect samples for HIV/STI assessments.
    - Blood draw for laboratory tests and sample storage.
    - Urine for GC/CT testing.
    - Swabs for rectal GC/CT testing (at 52 weeks only).
- Provide STI test results and post-test counseling. Offer STI treatment or referral for treatment, if applicable.
- Provide HIV rapid test results and post-test counseling.
- For participants receiving reactive HIV rapid test results, explain procedural implications for WB confirmation, CD4 cell count, and viral load testing, and the necessity of returning to the site to receive these results.
- If participant qualifies, introduce health care navigation. Begin work with the PHN or complete questionnaire about reasons for refusal of health care navigation. (at 26 weeks only)
- Offer condoms and lubricant.

Laboratory Procedures

- HIV rapid test, if participant was not confirmed HIV-positive at an earlier visit, or was not previously tested and agrees to be tested.
- HIV WB test to confirm reactive HIV rapid test result.
- CD4 cell count for participants with a reactive HIV rapid test, and for HIV-positive subjects at 52 weeks.
- Syphilis serology (including titer).
- GC/CT NAAT from urine.
- HIV viral load testing for participants with a positive WB result, and for HIV-positive subjects at 52 weeks.
- Prepare rectal swab samples for shipment to NL (at 52 weeks only).
- Plasma sample storage, for subsequent shipment to NL.

5.4 Additional Information about Study Procedures

Behavioral assessment using ACASI technology will be used to collect data on sexual risk behaviors; condom use; disclosure of status to partners; substance use; HIV testing history; access to and use of health care; perceptions of the health care system; feedback on PHN experience; psychosocial covariates (e.g., self-homophobia, racial and MSM-based

discrimination); venues where recruitment could take place; attitudes toward race, sexual identity, other prevention strategies, research, and health care; and, for known HIV-infected men, current HIV treatments. For participants who are unable or unwilling to use a computer, a counselor will administer the ACASI instrument to the participant, as described in the SSP manual. Participants will also be asked about their knowledge and attitudes about other HIV prevention interventions, including vaccines, circumcision, and pre- and post-exposure prophylaxis.

Subject to the enrollment caps previously described, some participants will be enrolled into the study who refuse HIV and/or STI testing. HIV/STI pre-test and risk reduction counseling will be based on Project RESPECT. Counselors will make the participant aware of locally-available resources for help with problems that have been identified during counseling, and will offer to help arrange a referral. Participants who appear to possibly have acute and serious substance use or mental health problems will be triaged for assessment by a licensed professional.

All participants will be asked to enumerate up to 5 members of their social and 10 members of their sexual networks, regardless of the members' gender or race/ethnicity. Sexual network members will include people with whom they had anal or vaginal sex within the prior six months. Social network members will include those people to whom participants report that they feel close, with whom they spend time talking or doing enjoyable things, who would be willing to loan them something valuable, whom they could stay with in an emergency, or with whom they party or socialize (this description may be modified as the study is operationalized). Data collected about each social network member will include information such as age, race/ethnicity, gender, nature of relationship to the participant, and frequency of interactions with each other, among others. For sexual partners, similar information will be collected as for social network members, as well as additional data related to such issues as whether this is a steady or non-steady partner, concurrency, partner serostatus, etc. These data will be used to better understand and describe Black MSM social and sexual networks. Index participants will be asked to refer up to five of their Black sexual network members. To maximize the impact of the intervention, index participants will only be asked to refer their network members who are Black MSM. A brief questionnaire will be administered to the index participants to assess motivators and barriers to referring network members to the study. The index participants will also be provided with brief training on techniques for engaging network members to come to the study site.

Network members (or "referred participants") will be asked to complete the same study activities as the "community-recruited" participants. Referral of sexual network members will continue through multiple waves until no more network members are referred, no more index participants are identified, or until two months have passed since the enrollment of the last community-referred participant.

All participants will be asked to either return to or expect contact from the study site to receive test results when they are available, about two weeks after the study visit. These results may include STI test results, HIV WB results (if the participant had a reactive HIV rapid test), CD4 cell count (if the participant had a reactive HIV rapid test), and HIV viral

load results (if confirmed HIV-positive by WB). Counseling and referrals for treatment will be provided as needed. STI results for participants who have a negative HIV rapid test may be provided over the telephone. Participants will be informed that they can return to the clinic between visits for STI testing if they think they have become infected. Participants in follow-up who have received a diagnosis of an STI or HIV from another clinic between study visits will be asked to bring documentation of their diagnosis to the study staff, or to provide permission for staff to solicit the documentation from their provider.

Individuals who have a reactive HIV rapid test will be counseled about the meaning of their WB result when they return to the clinic to receive that result. At that time they will have another blood sample drawn and a repeat (confirmatory) WB test performed . As appropriate, they will be counseled about clinical and social services for people who are HIV-infected and methods to reduce the likelihood of transmitting HIV to others. These participants will be given instructions from the study team about options for receiving the results of the second WB, according to local procedures. If the reactive HIV rapid test is not confirmed by two positive WB tests (or an indeterminate and then two positive WB tests), the site should contact the NL to determine whether additional HIV testing is needed to determine the subject's HIV infection status, and should contact the study participant to discuss the test results and to arrange for additional testing, if needed. Plasma specimens from each blood sample drawn for confirmatory testing will be stored for later use in incidence testing, if warranted.

Whenever participants return to the study site to receive test results and post-test counseling, or to have confirmatory tests performed, this is not considered a separate visit for purposes of CRF completion and visit numbering, but a continuation of the visit at which the first samples were collected. Blood draws for confirmatory testing will not count against the blood volume listed for the study visit, however, since confirmatory testing will take place on dates a week or more apart.

Qualitative Component: As described in Section 2.4, during enrollment for the main (quantitative) component of the study, some participants will be invited to participate in either a focus group or qualitative interview. Participation in the qualitative components will be optional, and recruitment for qualitative components will cease when adequate enrolment has been obtained. Informed consent for the qualitative component of the study will be solicited when the participant returns for a scheduled interview or focus group. A fuller description of the participant selection scheme can be found in Section 2.4 and the SSP manual. Both the qualitative interviews and focus groups will be conducted by trained and experienced staff. Qualitative interviews will be semi-structured, one-on-one interviews that will last about 1 to 1.5 hours. Focus groups will include up to eight participants, will be led by an experienced moderator, and will be expected to take about 1.5 to 2 hours of participants' time. Both qualitative interviews and focus groups will be recorded, transcribed, coded, and analyzed by study staff at the local and study-wide level.

5.5 Off-Site Visits

To maximize retention for the study, provision has been made to conduct off-site visits for follow-up. An off-site visit should only be conducted after all other options for scheduling

the visit at the clinic have been explored. Before off-site visits can be conducted, the site must have an SOP in place describing how this activity will be performed, and this SOP must be approved by both HPTN Coordinating and Operations Center (CORE) and the local institutional review board (IRB) or ethics committee (EC). As well, prior consent for conduct of off-site visits must be obtained from the participant. At off-site visits, study staff should attempt to perform all of the study procedures that would be conducted at the clinic for that visit, as long as the procedures can be correctly and safely performed and participant confidentiality maintained. If a participant refuses any protocol-specified procedures, this should be appropriately documented in the clinic/chart notes. Off-site visits should be performed at a location approved by the participant. Detailed procedures for the performance of off-site visits will be provided in the SSP manual.

6 SAFETY MONITORING AND ADVERSE EVENT REPORTING

Because this study includes no biomedical intervention or study product, standard adverse event reporting will not be undertaken and no adverse event data will be collected on case report forms for entry into the study database. However, in accordance with 45 CFR 46, unanticipated problems or serious adverse events that are judged to be related or possibly related to study participation will be documented and reported to the IRB/ECs according to their individual requirements and to the DAIDS Medical Officer. This reporting will be performed according to the timelines and definitions included in pre-established written procedures, such as the SSP manual, and the guidelines provided at www.hhs.gov/ohrp/policy/AdvEvntGuid.htm. Serious adverse events will not be reported to the DAIDS Regulatory Compliance Center (RCC).

"Social harms" will be monitored closely throughout the study. Information on social harms will be actively solicited from participants at follow-up visits, recorded on case report forms, and captured in the study database. Participants will also be encouraged to report any social harm on an *ad hoc* basis when it occurs. If a participant reports social harm, study staff will make every effort to provide appropriate care and counseling to the participant and offer referral to appropriate resources, as needed, for the participant's safety. Social harms that are judged by the Investigator of Record to be serious or unexpected will be reported to responsible site's IRB/EC at least annually, or according to their individual requirements. The nature and frequency of these social impact reports will be monitored by the protocol team on a regular basis. In addition, these data will be reviewed by the HPTN SMC.

7 STATISTICAL CONSIDERATIONS AND MATHEMATICAL MODELING

7.1 Review of Study Design

This is a multi-site longitudinal study to determine the feasibility and acceptability of a community-level, multi-component intervention for Black MSM that will eventually be used in a community-level, randomized intervention trial. The study will be conducted in six US cities with large Black MSM populations. A small proportion of participants will have only baseline cross-sectional data collected. The study aims to enroll 250 community-recruited participants who consent to HIV testing in each city over the course of 12 months, and may enroll additional participants as shown in Table 1. Comprehensive interventions (HIV/STI testing and counseling, peer health care system navigation, etc.) will be provided to

participants in all the cities. Follow-up assessments will be completed with the majority of study participants at 26 and 52 weeks post enrollment to assess any changes in risk behaviors, impact of the PHNs on health care access and use, and experience with the components of the intervention, as well as to detect any new HIV infections.

If the feasibility study indicates that a future community-level, randomized trial is feasible, the larger study will be conducted in communities (most likely metropolitan areas) that are randomized to intervention or control conditions. The community-wide intervention will be implemented in the intervention communities. At the end of the intervention delivery period, a cross-sectional survey of Black MSM will be conducted in each intervention and control community, using venue-based time-space sampling (not used in the feasibility study). HIV incidence rates will be estimated from the cross-sectional surveys by application of the most up-to-date HIV testing algorithms for identifying recent infections. The efficacy of the intervention will be determined by comparing HIV incidence rates among Black MSM in intervention versus control communities.

The feasibility study will provide specific information on recruitment capability, acceptability and feasibility of intervention components, and an estimate of the intervention effect on factors in the HIV transmission pathway, as diagrammed in Figure 7. Furthermore, the feasibility study will provide specimens to assist in the development of improved laboratory test algorithms to identify recent infections in cross-sectional surveys.

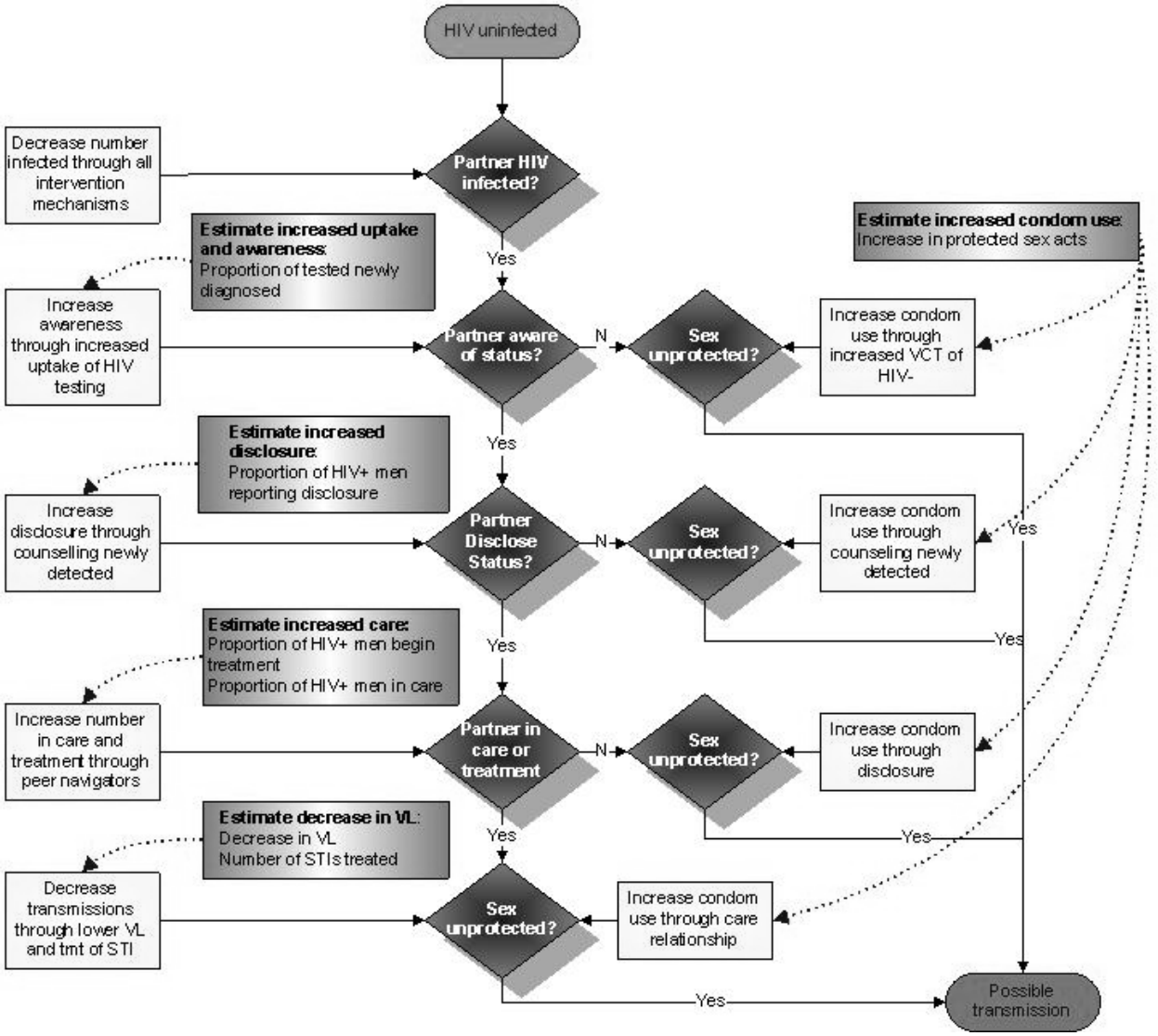


Figure 7- Estimates of Potential Intervention Effect upon HIV Incidence Available from the Feasibility Study

7.2 Study Endpoints

7.2.1 Primary Endpoints

The primary objective of the feasibility study is to obtain specific information needed to design the randomized trial. To that end, the following endpoints will be assessed:

- Recruitment – Assess the capability of each site to recruit Black MSM and their sexual network members.
    - Number of participants enrolled at each city within 52 weeks from the site activation date.
        - Proportion of index participants who refer at least one of their sexual network members.

- Uptake of intervention components
    - Proportion of participants who agree to HIV testing.
    - Proportion of participants who agree to STI testing.
    - Proportion of participants who use PHN.
        - HIV-infected participants: receive one or more HIV primary care visits every 26 weeks.
        - HIV-uninfected participants: accept referrals for unmet support or treatment needs.

- An estimate of the following in the course of the study:
    - The feasibility study is not designed to directly estimate the intervention effect on reducing HIV transmission. However, it will provide estimates of a number of factors that are in the transmission pathway, as diagrammed in Figure 7.
        - Proportion of participants who are newly diagnosed with HIV at enrollment.
        - Increase in condom use from enrollment to week 52.
        - Decrease in viral load at week 52 among HIV-infected participants who initiate HAART during their study participation.
        - Decrease in STI from enrollment to week 52.

- Satisfaction of study participants with the intervention components
    - Scores of the various intervention components on a satisfaction index collected via ACASI at follow-up visits.
    - Qualitative feedback provided to counselors at follow-up visits.

7.2.2 Secondary Endpoints

The following will be assessed or described, corresponding to the secondary objectives of the study:

- To collect samples, behavioral data, and HIV test results to improve laboratory measures of HIV incidence in cross-sectional surveys.

- Number of participants with recent HIV infection (as defined below in Section 7.4.2) at enrollment.
- Number of participants with acute HIV infection (as defined below in Section 7.4.2) at week 52.

- To estimate the HIV incidence rate under intervention condition
  - Number of seroconversions during follow-up among those who are HIV-uninfected at baseline.

- To estimate the effect of the intervention on the incidence rate through mathematical modeling, by analyzing HIV risk behaviors at enrollment, week 26 and 52:
  - Number of sex partners.
  - Number of sero-discordant or sero-unknown partners.
  - Type and frequency of anal intercourse.
  - Level of condom use.
  - Partner change rate.

- To describe social and sexual network characteristics of Black MSM based on individually self-reported network data:
  - Network size, composition, density (interconnectedness of members), multiplexity (multiple types of relationships), durability (duration of relationships), and homogeneity (similarity among members).
  - Overlap of a participant's sexual network with his social network.

- To assesses attitudes of Black MSM toward other prevention interventions (e.g., vaccine, circumcision, and pre- and post-exposure prophylaxis).

Please note that participants will fall into a number of enrollment categories, as described in Section 3 and below, that will provide interesting data for exploratory analyses and inter-group comparisons. For example, the differences in recruitment approach for "community-recruited" versus "referred" participants may yield differences in risk behaviors, network characteristics, or uptake of intervention components that will be interesting and informative. The number and types of exploratory analyses will depend on the data collected and will not be defined *a priori*, but are expected to be an important component of this feasibility study.

7.3 Accrual, Follow-Up, and Sample Size

Participants at each recruitment wave will fall into one or more of the following categories:

1) **Enrolled Not Tested: Do not agree to HIV testing**
2) **Enrolled Tested: Agree to HIV testing**
3) **Enrolled Index:** A subset of the Enrolled Tested participants who are selected to recruit their Black MSM sexual network members. There are three different types of Enrolled Index participants: 1) newly diagnosed

with HIV, 2) previously diagnosed, not in care, and report UAI with HIV-negative or unknown serostatus partners, and 3) HIV-uninfected.

Each participating city will target accrual of 250 community-recruited participants in the Enrolled Tested category. Men who do not consent to HIV testing will be enrolled as Enrolled Not Tested participants. Follow-up will take place with only the first 20 of the Enrolled Not Tested participants. Subsequent participants in this category will only be seen at enrollment.

Participants who are newly diagnosed with HIV or who were previously diagnosed but not in care, and 20 randomly selected HIV-uninfected 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.

Table 2. Per-Site Sample Size Calculation

Participant Category	Number of Participants			
	Community Recruited	**Referred Wave 1**	**Referred Wave 2**	**Total**
TOTAL	**333**	**61**	**9**	**403**
Enrolled Tested	**250**	**46**	**7**	**303**
HIV-infected	**63**	**12**	**2**	**77**
Index: Newly diagnosed[1]	32	6	1	39
Index: Previously diagnosed, not in care, and report unprotected anal sex with HIV-negative or unknown serostatus partners[1]	29	6	1	36
Previously diagnosed and in care, or not in care but reports unprotected anal intercourse only with HIV-positive partners	2	0	0	2
HIV-uninfected	**187**	**34**	**5**	**226**
Index: random sample[1]	20	0	0	20
With follow-up[3]	140	0	0	140
No follow-up[2]	27	34	5	66
Enrolled Not Tested[2]	**83**	**15**	**2**	**100**
With follow-up[3]	20	0	0	20
No follow-up[2]	63	15	2	80

[1] Index participants: Refer Black MSM sexual network members and follow-up at 26 and 52 weeks (highlighted in light gray).
[2] Do not refer Black MSM sexual network members; no follow-up.
[3] Do not refer Black MSM sexual network members; follow-up at 26 and 52 weeks (highlighted in heavier gray).

Each city will aim to retain at least 90% of enrolled participants through 52 weeks of follow-up. Participants who do not have planned follow-up will be excluded from the retention calculation.

The feasibility study is not designed to directly estimate the intervention effect on reducing HIV transmission. However, it will provide estimates of a number of factors that are in the transmission pathway. Table 3 shows the approximate number of enrolled participants anticipated in each category of the feasibility study, and the approximate precision we would have for selected estimates. For example, the proportion of Black MSM who agree to HIV testing will be estimated from all the enrolled participants. Row 1 of Table 3 shows the sample size used in the calculation (333 per site; 1998 overall), and the precision measured by the width of the confidence interval (CI) of the estimate.

In addition, from the separate estimates in each of the six communities, we would gain some insight into the variability of these factors between communities, though we do not expect to obtain a precise estimate of the coefficient of variation (CV) given the limited number of cities that could be allowed in the feasibility study (Table 4).

Table 3. Precisions of Selected Primary Endpoints and HIV Incidence Estimates

Participant Category	Measurement	Effect	Per-Site		Overall	
			Number[1]	Precision by Width of CI[2]	Number [1]	Precision by Width of CI[3]
Intervention Uptake						
Enrolled	% agree to HIV test		333	± 5.4%	1998	± 2.2%
	% agree to STI test					
HIV-positive with follow-up	% utilize PHN[5]		61	± 12.5%	366	± 5.2%
HIV-negative with follow-up	% utilize PHN[6]		160	± 7.7%	960	± 3.2%
Intervention Effect						
Enrolled, not diagnosed before enrollment	% newly diagnosed HIV-positive at enrollment	Increase in awareness	297	± 5.7%	1782	± 2.3%
HIV Incidence						
HIV-negative with follow-up	HIV seroincidence rate (per 100 PY)	Increase in condom; decrease in STI	160	1.9 (0.4, 5.5)[4]	960	2.0 (1.2, 3.1)[4]

[1] Because of uncertainties about enrolling participants in multiple waves, numbers from community-recruited participants are used, as listed in Table 2.

[2] Precision of estimate is calculated as $\pm 1.96 \times \sqrt{\frac{p(1-p)}{N}}$, where N is from the "Number" column. p is set to be 0.5 to give maximum width.

[3] Precision of estimate is calculated as $\pm t(0.975, df = N-1) \times \sqrt{\frac{p(1-p)}{N}}$, where N is from the "Number" column. p is set to be 0.5 to give maximum width. T distribution quantile is used to take account of variation between sites. If variation between sites is zero, the width of the CI will be smaller.

[4] Exact Poisson confidence limits for the estimated rate: $Y_l = \frac{\chi^2_{2Y,\alpha/2}}{2}$; $Y_u = \frac{\chi^2_{2(Y+1),1-\alpha/2}}{2}$, assuming a 2% annual incidence rate under intervention conditions.[83]

[5] For HIV-infected participants, utilization of peer health care system navigation is measured as receiving one or more HIV visits in every 26 weeks or having a medical case manager.

[6] For HIV-uninfected participants, utilization of peer health care system navigation is measured as accepting referrals for unmet support or treatment needs.

Table 4. Confidence Limits for Various Values of CV and Number of Cities

	Value of Coefficient of Variation (CV)[1]					
Number of Cities	0.05	0.10	0.15	0.20	0.25	0.30
4	(0.03, 0.19)[2]	(0.06, 0.37)	(0.08, 0.55)	(0.11, 0.73)	(0.14, 0.90)	(0.16, 1.07)
6	(0.03, 0.12)	(0.06, 0.24)	(0.09, 0.36)	(0.12, 0.48)	(0.15, 0.60)	(0.18, 0.70)
8	(0.03, 0.10)	(0.07, 0.20)	(0.10, 0.30)	(0.13, 0.40)	(0.16, 0.49)	(0.19, 0.59)
10	(0.03, 0.09)	(0.07, 0.18)	(0.10, 0.27)	(0.14, 0.36)	(0.17, 0.44)	(0.20, 0.53)

[1.] k is often ≤ 0.25 [84]

[2.] Lower limit: $\{[1+(S_n/\bar{x})^{-2}]\chi^2_{\alpha/2}/n-1\}^{-1/2}$

Upper limit: $\{[1+(S_n/\bar{x})^{-2}]\chi^2_{1-\alpha/2}/n-1\}^{-1/2}$ [85]

7.4 Data Analysis and Monitoring

7.4.1 Primary Analyses

- The study accrual process will be described by tabulating the number and rate of participants enrolled in the study by city and combined, by month, during the accrual period. The total number of "community-recruited" participants who agree to HIV testing will be compared with the accrual target of 250.
- The number of participants retained at 26 and 52 weeks will be tabulated for each study city and combined. The retention rate will be calculated as the number of participants who completed the week 26 or week 52 follow-up visit divided by the total number of participants who meet criteria for follow-up. The annual retention rate will be compared to the target of 90%.
- The proportion of participants who take up each of the intervention components listed in Section 7.2.1 will be calculated by city and combined. Ninety-five percent CIs of the per-city proportion estimates will be obtained by normal approximation to the binomial distribution. Correlation among participants from the same city will be taken into consideration when computing the CIs for the proportions across cities.
- The proportion of participants who are newly diagnosed with HIV at enrollment will be calculated by city and combined. HIV testing is offered at enrollment to all enrolled participants. The majority of participants will accept HIV testing. Some of them will be diagnosed with HIV for the first time and will be categorized as "newly diagnosed" participants at enrollment and used as the numerator in the calculation. Some of these "newly diagnosed" participants will be recently infected, while the others will be chronically infected. The intention of this estimate is to assess the proportion of Black MSM who would be newly diagnosed with HIV if HIV testing is offered in the community. The denominator is the number of participants enrolled (n=333) less the number of participants who had been diagnosed with HIV before enrollment (n=31 from Enrolled Tested category, 5 from Enrolled Not Tested category, total n=36), i.e., n=297. Ninety-five percent CIs of the per-city proportion estimates will be obtained

by normal approximation to the binomial distribution. Correlation among participants from the same city will be taken into consideration when computing the CIs for the proportions across cities.

- The intervention effect on reducing HIV viral load will be measured by the change in viral load from HAART initiation to 52 weeks post-enrollment on HIV-infected participants who initiated HAART. The mean difference of the viral load (log 10 transformed) will be estimated for each city and across cities. Correlation among participants from the same city will be taken into consideration when computing the CIs for the overall estimate.
- Generalized estimating equations (GEE) and robust variance estimates will be used to evaluate change over time in condom use and STIs, adjusting for baseline HIV status as an effect modifier, as the changes might be different among HIV-infected participants than uninfected ones. This approach will account for the within-subject correlation of the repeated measures. Since the feasibility study has no control arm, the observed "intervention" effect may be partially caused by the change in outcomes measured over time. We plan to compare the changes observed in HPTN 061 with results from the control arm of other studies, such as EXPLORE or meta-analyses.[86]

7.4.2 Secondary Analyses

Estimating HIV Incidence

Rapid HIV antibody tests and WB assays will be used to identify HIV-infected participants at enrollment and during study follow-up. In addition, the NL will perform testing to screen participants for acute and recent HIV infection, and to optimize algorithms for identification of recent HIV infection as described in Section 9.5. This will include BED testing and other assays (to be determined by the HPTN NL based on ongoing validation work). These assays, plus HIV rapid and WB test results, will be used to identify three groups of participants who have recent or incident HIV infection: 1) those testing HIV-positive at enrollment who are likely to have recent HIV infections, 2) those who are incident at week 26 or 52 (seroconverters), and 3) those with acute infection at week 52.

- Expected number of subjects with seroconversion: Only participants who agree to HIV testing and test negative at enrollment will be included in this analysis. Assuming approximately 960 HIV-uninfected participants at enrollment, 90% annual retention rate, and 2% "with intervention" annual incidence rate, we expect 960 participants×90%×2% = 17 seroconverters at the end of the study.
- Expected number of subjects with recent HIV infection at enrollment: Based on recent infection window period of approximately six months, the number of recently infected participants is approximately equal to the number of participants tested (excluding those with a history of HIV infection at enrollment) times person-years of follow-up (each participant contributes 6/12 = 0.5 years of follow-up) times the expected HIV incidence rate (3% at

baseline). Thus we expect approximately 20 recently infected participants at enrollment.

- Expected number of subjects with acute HIV infection at 52 weeks: For the purpose of this study, acutely infected participants are those who are HIV RNA positive and have one of the following: (1) a negative HIV rapid test, (2) a negative WB, or (3) an indeterminate WB. Based on a pre-seroconversion window period of three weeks, the number of acutely infected participants at week 52 is approximately equal to the number of participants retained at the end of study who do not have confirmed HIV infection times person-years of follow-up (each participant contributes 3/52 = 0.06 years of follow-up) times the expected HIV annual incidence rate (2% with intervention). We expect to confirm that pooled HIV RNA testing at the end of study will not identify any acutely infected participants, which will facilitate design of the future randomized trial.
- Estimated overall HIV incidence rate: An overall HIV incidence rate will be calculated from the total number of subjects with confirmed HIV seroconversion, plus the total number of subjects with acute HIV infection at 52 weeks (likely to be none). CIs will be calculated based on Poisson distribution assumptions.
- If BED is, or other assays are, deemed reliable for identification of recent infection, data from recently infected study subjects will be included in a separate analysis of HIV incidence prior to intervention. In that case, the pre-intervention HIV incidence rate will be calculated as the total number of subjects with recent HIV infection at enrollment, divided by the total number of person-years of follow-up (0.5 years times the number of negatives plus the recent positives). CIs will be calculated based on Poisson distribution assumptions.
- The coefficient of variation (standard deviation (SD)/Mean) of HIV incidence will be estimated. It is a measure of variation in the HIV incidence between cities and a key parameter in design of the future CRT. Given the relatively small projected baseline incident events (approximately 20) over all the cities, it will probably be necessary to combine information from the baseline recency estimate and the follow-up estimate of incidence.

Risk Behaviors and Network Characteristics

- The sexual risk behaviors of index participants enrolled in the study will be described by city and combined. At a minimum, the characteristics listed in Section 7.2.2 will be tabulated for all participants and separately for HIV-positive index participants and their sexual network members at enrollment, 26, and 52 weeks.
- Network characteristics listed in Section 7.2.2 will be reported by city and combined, for all enrolled participants, and separately for HIV-positive index participants and their sexual network members at enrollment, 26, and 52 weeks.

7.4.3 Data Monitoring

Close cooperation between the Protocol Chair, study site Investigators and Coordinators, NIAID Representative, HPTN Statistical and Data Management Center (SDMC), and other team members will be necessary to track study progress, respond to queries about proper study implementation, and address other issues in a timely manner. Rate of accrual, follow-up, social harm, and protocol compliance will be monitored closely by the study team. Each study site Investigator is responsible for ongoing monitoring of accrual and retention rates, and for ensuring the rapid deployment of additional or alternative procedures to address any shortfalls. The SDMC will provide accrual and retention reports to the study team on a regular basis.

The HPTN SMC will meet within the first four to six months of study implementation and approximately every six months thereafter throughout the study. The primary responsibilities of the SMC are to 1) periodically review and evaluate the accumulated data on study conduct and progress, and 2) make recommendations to the study investigators and DAIDS concerning the continuation, modification, or termination of the trial.

7.5 Mathematical Modeling

Mathematical models will be constructed to evaluate the epidemiologic impact of the interventions and to assess the feasibility of a community-level randomized trial to measure substantial efficacies in terms of reduction in HIV incidence. In part, the models will extend and adapt current deterministic and stochastic dynamic HIV transmission models[87-92] as well as statistical methods for the analysis of key epidemiologic data for Black MSM in the US. The biological and epidemiological input will be chosen according to the best available empirical data, and literature searches will be conducted to identify the most relevant and applicable data for MSM transmission in the US.

The data from the feasibility study will be a crucial element in the parameterization of the model, but will only provide some of the data needed. Other data will be extracted from the literature. The models will stratify the population into compartments according to HIV infection status and stage, diagnosis status, and the sexual risk activity class. HIV disease progression will be parameterized by the observed distributions from infection to AIDS to death using existing data such as that of the Multicenter AIDS Cohort Study. The impact of HAART will be parameterized by data on its coverage in the different cities and by HAART's effect on disease progression. Disease progression will be divided into discrete stages, such as the stages of acute, asymptomatic, and late disease. The transmission probabilities per anal contact will be determined from a literature search of data on MSM in the US. These transmission probabilities per anal contact will be adjusted based on HIV viral load. To do this, data from Rakai[20] that establishes the relationship between HIV transmission probability per coital act and HIV viral load will be used to adjust the MSM-specific transmission probabilities due to the impact of HAART and other interventions that reduce HIV viral load. The transmission probabilities per partnership will be derived from the transmission probabilities per coital act, frequency of acts, duration of partnership, presence of male circumcision, and level of condom use and unprotected sex. Given the variations of these attributes across partnerships, the models will allow for the formation of

different kinds of partnerships according to the nature of risk group and type of mixing among the groups.

The structure of the behavioral risk groups in the Black MSM populations of each city will be determined by the empirical data as measured in the feasibility study and other data extracted from the literature on the epidemiology of HIV among Black MSM. An analysis of the behavioral data will be done to determine the key behavioral measures, such as partner change rates, to be used to define each risk group. The mixing between the sexual activity classes will have assortative (choosing partners only from within their risk group) and proportionate (choosing partners with no preferential bias based on the kind of risk group) components. Observed biases in mixing, such as due to sero-sorting, will be incorporated. The models will allow different parameterizations of the role of risk factors either in terms of observed relative risk ratios (RR) or in terms of per-exposure cofactors. Supplementary data to the ones measured in the feasibility study including distribution of risk, partner change rates among different risk groups, mixing between risk groups, and condom use will be extracted from the literature.

The mathematical model is designed to include networks of Black MSMs with different risk profiles and mixing patterns but will not include non-Blacks or women. This choice reflects the kind of questions that the modeling will answer. The focus here is on the impact of the interventions on the risk of exposure within the Black MSM population. Also, several lines of data suggest that Black MSMs do not generally acquire HIV from female to male transmission.[17] Although Black MSMs could be infected by White MSMs, this transmission pathway is not the focus of the feasibility study. If this feasibility study determines that there is substantial mixing of Black with non-Black MSMs, then the model will have to be extended to include this population as well. The final structure of the model will depend on the data outcome and review of the epidemiology of HIV within this Black MSM population. Given that the complexity of the model grows combinatorially with each group included in the structure, inclusion of more population groups will be accommodated only if this would prove essential, such as through preliminary modeling analyses, for the questions that the modeling will answer.

Sensitivity and uncertainty analyses will be performed based on the ranges of the uncertainty in the epidemiologic data and measured efficacies of the interventions. The impact of the interventions as predicted in the model will be assessed with respect to structural changes in the model and assumptions. Three kinds of analyses will be investigated, in which the robustness of the predictions will be assessed: 1) with respect to variations in the biological, epidemiological, and behavioral input of the models, 2) with respect to the uncertainties in the measured efficacies of the interventions, and 3) with respect to variations in model structure.

For the measures that will not be precisely determined in the feasibility study (e.g., mixing between risk groups), a broad or full range of parameter estimates will be explored in the uncertainty analysis. The validation of the model will be done first by its ability to consistently and realistically describe HIV infectious spread in this population as gleaned from the literature review.

The models will attempt to describe spread of HIV infections in the six US cities studied. It will incorporate the data from the multi-site feasibility study in terms of changes to risk behavior and impact of PHNs and health care access. The endpoints of the feasibility study will facilitate model construction in order to simulate the impact of the interventions on transmission pathways. The modeling will also use other epidemiologic data from the feasibility study to parameterize the risk of exposure to HIV infection, including data on partnership change rates, fraction of sex partners who are infected, levels of condom use, type and frequency of sexual contacts, baseline levels of testing and diagnosis, STI incidence and prevalence rates, and HAART coverage.

The models will facilitate design and analysis of the community-randomized controlled trial and assess how the impact of the intervention will materialize in the trial setting. The dynamics of the interventions will be studied as they are rolled out. The implications in terms of statistical power will be delineated, and an assessment will be made about whether the trial will be powered to measure statistically significant efficacies within the suggested follow-up duration of the trial.

7.6 Qualitative Data Analysis

Focus Group Data

Analysis of the focus group data will be performed within 30 days of receipt of a clean transcript. Initial rapid content analysis will be completed using the Consensual Qualitative Research Method (CQR),[93] based on a grounded theory approach to qualitative data analysis.[94] The CQR method provides a reliable, systematic, and rigorous method in conducting qualitative data analyses, thus recognizing the importance of context, incorporating an inductive analytic process, using a team and making decisions by consensus, using auditors, and verifying results by systematically checking against the raw data. The key elements of conducting qualitative data analyses using the CQR method include: (1) develop and code domains, (2) construct core ideas, and (3) develop categories to describe consistencies across cases (cross analysis). The CQR method will be valuable in qualitative data analysis because research indicates that qualitative researchers should not impose "preconceived concepts, hypotheses, and theories on the data." [95]

The rapid analysis of focus group transcripts will provide the HTPN 061 protocol team with emerging themes (e.g., the role of economic incentives on research participation) and indicators (e.g., place of birth may play a role in up-take of health services) associated with the pre-identified domains and qualitative objectives. Analysis of the themes and indicators will continue to identify ranges of responses that can be used in addressing the overall study goal of increasing receptivity of protocol up-take. This process will provide immediate feedback to the trial team and will be used to identify attributes of interest for individual qualitative interviews. Additional analyses of focus group data will be conducted throughout the project. However, in order to identify attributes of interest and select men for individual interviews, timely identification of emerging themes and indicators is essential.

Qualitative Interview Data

Analyses of the interview narratives will focus on both the content and structure. Analyses will depend primarily on text transcriptions, although the audio data will be readily available and indexed in digital format to augment the textual analyses. All identifying information will be stripped from the transcripts, and only the research team and the transcribers will have access to the audio interview data. Audio recordings of interviews will be destroyed within three years of study completion.

Qualitative interview transcripts will be coded on two levels: by domains, also known as latent constructs (the characteristics that are determined to be significant organizing principles), and by indicators of the domains (what participants said).[96] These and other demographic characteristics are used in a "face sheet" for each study participant. This process is also useful because it helps demonstrate the range of experiences within each domain. For example, when an intervention is being developed, this process can help ensure it is not responding only to the most extreme case in each domain, but will be appropriate for a range of experiences encompassed in any one domain.

Once face sheets have been created, data coding by domain will begin. Data will be printed by domain and assigned to the each site's research team to develop codes. The data in each domain will be read and discussed, and a data coding system (coding lexicon) will be developed using an iterative process of applying linguistic markers.[96] For quality assurance (QA), we propose to double code 20% of transcripts to ensure 90% code-recode and inter-coder reliability.[58 97] Data will then be organized for directed content analysis.[58] Once all of the data have been coded, printouts of codes will be analyzed.[98] Finally, summary reports will be completed for each of the pre-identified domains (i.e., stigma and discrimination related to HIV, homosexuality, and race; knowledge, attitudes, and behavior regarding HIV and HIV-testing; and utilization of health care services) and any emergent domains related to the study objectives.

As described for focus groups, development/refining of the coding matrix, and coding and analysis of transcripts will be coordinated by the QWG. Through this approach, the qualitative data will be coded by representatives located centrally and locally, allowing the team to detect nuances specific to a geographical region as well commonalties among Black MSM.

As noted above, in addition to providing the basis for the individual interview guide, rapid analyses of focus group data will provide immediately useful feedback to the main study. This feedback will be used to make real-time adjustments of recruitment strategies and intervention components as early as two to three months after recruitment initiation. As additional focus groups and analyses are completed over the following few months, the teams will be able to make more nuanced adaptations to recruitment and intervention approaches.

The individual interviews will contribute deep descriptions of the individual, interpersonal, cultural, institutional, and geographic processes that influence the study intervention variables. Individual interviews are expected to begin one month after focus groups are concluded and to be completed within three months. The initial interview findings will be

used to refine follow-up and retention strategies of the main study. The team expects to complete formal analyses of the interview data within nine months of finishing the interviews and to complete a final report within a month after that. The analyses of data from focus groups and individual interviews will be used to adjust the feasibility study components in real time, and will provide a framework for implementation of the broader intervention trial.

8 HUMAN SUBJECTS CONSIDERATIONS

8.1 Ethical Review

This protocol, the template informed consent forms contained in Appendices II –V, and any subsequent amendments will be reviewed and approved by DAIDS Prevention Science Review Committee for scientific content and compliance with applicable regulations on research and human subjects.

The protocol, site-specific informed consent form, participant education and recruitment materials, and other requested documents — and any subsequent modifications —will be reviewed and approved by the ethical review bodies responsible for oversight of research conducted at the study site.

After initial review and approval, the responsible local IRBs/ECs will review the protocol at least annually. The Investigator will make safety and progress reports to the IRBs/ECs at least annually, and within three months of study termination or completion. These reports will include the total number of participants enrolled in the study, the number of participants who completed the study, all changes in the research activity, and all unanticipated problems involving risks to participants or others.

Questions and concerns may arise during this study about how to protect the rights of trial participants and their surrounding communities in light of the disparities in power, wealth, education, and literacy between those conducting this protocol and the communities where the trial is implemented. The community engagement process described in Section 8.2 will be used to ensure that all responsible for this study maintain the highest ethical standards possible.

8.2 Community Engagement

Community engagement and collaboration is central to the goals of the HPTN and successful public health practice. A growing body of work attests to the greater health and societal benefits, acceptability of interventions, and cost-effectiveness that result from such community-based approaches.[99 100]

Because this research affects Black MSM, members of this community will play an active, informed role, working throughout the trial with site research staff and the Principal Investigator, who is responsible for all aspects of a trial, including efforts to enhance community participation. This team will strive to overcome structural power imbalances by engaging researchers who themselves are members of the population of interest, key opinion leaders, and research site community advisory boards (CABs) in the design,

operationalization, and review of this protocol. This process is designed to ensure the best possible representation in terms of exclusivity and parity for the values, norms, and behaviors of those affected by the research process. This community engagement process is designed to build community capacity to understand and inform the research process, raise concerns, and help find solutions to unexpected issues that may emerge once the trial is underway.

Members of the community of interest have participated in the development of HPTN 061 since concept inception and are on the protocol team. Additional consultation has been conducted at each iteration with members of the community of interest who were familiar with HIV, community norms, current interventions, historic efforts, public policy, and public discourse on gaps in service. PHNs are an essential component of trial conduct. Most PHNs will be from the target population or have demonstrated competency in working to facilitate the ability of Black MSM to participate in research.

In January 2008, one of the Protocol Co-chairs presented design concepts and sought input from participants in a conference/skills-building retreat for Black MSM working in the HIV/AIDS field. Some members of the Black Gay Research Group (BGRG) were invited to provide specific comment on the trial design and to identify a strategy to ensure additional input from Black Gay researchers. Members of the group were appointed to the protocol team with the goal of incorporating expertise of target community-based academics. We hope that this will increase capacity for cultural competence as protocol implementation and data analysis progress.

Additional consultation will occur throughout conduct of this trial with other researchers who have demonstrated expertise in working with this population, or who come from the target communities. This will allow the team to maximize the community-public health-academic partnerships that are essential for translating network science into scientifically-accurate, culturally-relevant, and epidemiologically-effective HIV prevention messages.

Each trial site will have a CAB. Once trial sites are identified, the process of community consultation will engage members of those CABs and at least one key opinion leader or representative from a community-based organization serving the target population to participate in a protocol-specific community working group.

The HPTN 061 community working group will meet regularly by phone or Internet conference to ensure that communication is multi-directional and in a continuous feedback loop from site to community and community to site. Communications plans, community education materials, and deliberations related to this trial that are public knowledge will be made available in appropriate formats. Decisions taken at other levels, which might affect site trial conduct, will be communicated in a timely fashion. Plans for data analysis, interpretation of findings, and dissemination of results will be discussed and agreed upon at the onset; we will take into account, where necessary, the need to maintain confidentiality of proprietary and confidential information before any information is released to the public. The charge of the HPTN 061 community working group will be to raise issues with researchers and propose constructive suggestions for solutions to improve conduct of the trial.

The HPTN 061 community working group will work with protocol team leadership to develop a plan to foster buy-in from national leadership, research advocates, and public opinion leaders in the Black MSM community for community randomization and understanding of the information learned during this pilot.

The protocol team will consult with local and national Black MSM community leadership and public health officials to gauge whether the networks reached in the pilot phase of the study are representative of the networks of HIV-infected Black MSM in each of the cities where the feasibility study is being conducted.

In another initiative to build community support among those not already focused on Black MSM and/or the HIV epidemic, the Domestic Prevention Working Group (DPWG) of the HPTN has been engaged. The DPWG has begun to work with community, political, church, and business leaders in the cities where both HPTN 061 and HPTN 064 protocols will be conducted to solicit support and insight that could prove critical to the success of these studies (and those hoped to follow). The DPWG has begun collecting contacts for this effort and plans to hold an ongoing dialogue with these key opinion leaders throughout the length of the domestic prevention initiative.

8.3 Informed Consent

Written informed consent will be obtained prior to the initiation of study related activities. Written informed consent will be obtained from each study participant for specimen storage and possible future testing beyond what is required for HPTN 061, although consent for this additional specimen storage will not required for study participation. A sub-set of the participants in this study will be invited to participate in focus groups or semi-structured interviews to obtain qualitative data. Written informed consent will be obtained before beginning either of these activities as well. Some sites may require Health Insurance Portability and Accountability Act (HIPAA) consent. In obtaining and documenting informed consent, the investigators and their designees will comply with applicable local and US regulatory requirements and will adhere to Good Clinical Practices (GCP) and to the ethical principles that have their origin in the Declaration of Helsinki. Study staff must document the informed consent process in accordance with the Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials.

Each study site is responsible for developing study informed consent forms for local use (based on the templates in Appendices II-V) that describe the purpose of the screening and the study, the procedures to be followed, and the risks and benefits of participation, in accordance with all applicable local and US regulations. Sites should also refer to the DAIDS policy *Requirements for Informed Consent Development* when adapting the template consents for local use.[101] Community input will be sought for the development of the sample informed consent forms.

Before documenting their informed consent, participants will be given the opportunity to ask questions until they fully understand the study. They will be told that they can return at any

time to obtain more information or have additional questions answered. Participants will be provided with copies of the informed consent forms if they are willing to receive them. Study staff will document the informed consent process as instructed in the SSP manual.

The informed consent process will cover all elements of informed consent required by research regulations, including the following topics:

- The importance of adherence to the schedule of study visits and procedures
- The potential risks of study participation (and what to do if such risks are experienced)
- The potential social harms associated with study participation (and what do if such harms are experienced)
- The real yet limited benefits of study participation
- The right to withdraw from the study at any time

The informed consent process will include an assessment, before enrollment, of each potential participant's understanding of concepts identified by the protocol team as essential to the informed consent decision. Participants who are not able to demonstrate adequate understanding of key concepts after exhaustive educational efforts will not be enrolled in the study.

8.4 Risks

Venipuncture is sometimes associated with discomfort. Phlebotomy may lead to discomfort, dizziness, bruising, swelling, and rarely, an infection at the venipuncture site. Examination and swabbing of the genitals and rectum can also be associated with discomfort. Participants may become embarrassed, worried, or anxious when completing their HIV risk assessment and/or receiving HIV counseling. They also may become worried or anxious while waiting for their HIV and STI test results. Trained counselors will be available to help participants deal with these feelings. Individuals who learn that they have an STI or HIV infection may experience anxiety or depression related to their test results. Participants identified as newly diagnosed with HIV may become embarrassed or worried when asked to refer their sexual partners. Staff at sites may be obliged to comply with laws requiring partner notification in response to a diagnosis of an STI or HIV infection. Participants whose partners are informed in this way could have problems in their relationships with their sexual partners, including the possibility of violence.

Although study sites will make every effort to protect participant privacy and confidentiality, it is possible that participants' involvement in the study could become known to others, and that social harms may result (e.g., because participants could become known as HIV-infected or at "high risk" for HIV infection). For example, participants could be treated unfairly or discriminated against, or could have problems being accepted by their families and communities. This is discussed further in Sections 6 and 7.4.3.

8.5 Benefits

Participants in this study may experience no direct benefit. Participants and others may benefit in the future from information learned from this study. Specifically, results of this study may lead to understanding about how counseling, care, and treatment are best provided to Black MSM, and may ultimately lead to interventions that reduce HIV incidence in this population. Participants also may appreciate the opportunity to contribute to the field of HIV prevention research.

Participants will receive HIV and STI counseling and testing in this study. Participants will be provided STI treatment in accordance with CDC guidelines or referred for low or no-cost treatment by PHNs. Study participants will learn how to protect themselves from becoming infected with HIV and other STIs. HIV-positive participants will learn strategies for how to avoid infecting others and will receive highly interactive support from PHNs to access HIV-related medical care and psychosocial support services. For both HIV-infected and HIV-uninfected participants with other medical conditions (including substance use and mental health issues), peer health care system navigation will be provided to connect them to the sources of care available in their community. Participants will be offered condoms and lubricant at each study visit and will be encouraged to return to the site between visits for additional supplies.

8.6 HIV-Related Counseling and Care

8.6.1 Counseling

All risk reduction and pre- and post-test counseling will take place after behavioral data collection. At each visit, the health educator/counselor will provide the study participant with information on methods of HIV transmission and prevention, use of condoms, and pre- and post-test HIV counseling, if applicable.

HIV pre-test, risk reduction, and post-test counseling will be offered to all study participants who consent to HIV testing and to all enrolled participants at each follow-up. Testing will be performed in accordance with the algorithm in the SSP manual. Counseling will be provided in accordance with local standards of practice at each study site. In accordance with the policies of the NIH, participants who are tested for HIV must receive their HIV test results in order to take part in this study. The study site will document its counseling policies and procedures before the study is implemented for staff training and study monitoring.

8.6.2 Care for Participants Identified As HIV-Infected

This study will identify people who are infected with HIV, either at enrollment or during follow-up visits. Study staff will provide participants with their HIV test results in the context of post-test counseling. They also will refer people found to be HIV-infected to available sources of medical and psychosocial care and support.

8.7 Participant Reimbursement

Participants will be reimbursed for their time and effort in this study and for their travel to study visits. Index participants may be compensated for referrals that result in enrollment. Site-specific reimbursement amounts will be specified in the study informed consent form and approved by the IRB/ECs.

8.8 Confidentiality

All study procedures will be conducted in private, and every effort will be made to protect confidentiality and participants' privacy to the extent possible. Each study site will implement confidentiality protections that reflect the local study implementation plan. Also, study staff and community representatives will be encouraged to identify potential confidentiality issues and strategies to address them. In addition to local considerations, the protections described below will be implemented at all sites.

All study-related information will be stored securely at the study sites. All participant information will be stored in locked file cabinets and/or in lockable areas with access limited to study staff. All laboratory specimens; reports; and data collection, process, and administrative forms will be identified only by a coded number to maintain participant confidentiality. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored separately from study records identified by code number. All local databases will be secured with password-protected access systems. Forms, lists, logbooks, appointment books, and any other listings that link participant ID numbers to other identifying information will be stored in a separate, locked file in an area with limited access. PHNs will work with participants outside of the study site, but will follow strict procedures to limit the confidential information taken into the field and to safeguard any information collected outside of the site.

Participants' study information will not be released without the written permission of the participant, except as necessary for monitoring by:

- NIAID and/or its contractors.
- Representatives of the HPTN CORE, SDMC, and/or NL.
- Government and regulatory authorities.
- IRB/ECs.

The HPTN has obtained a Certificate of Confidentiality from the US Department of Health and Human Services that will be applicable for this study. Sites may register under the Certificate through the HPTN CORE once they have obtained local IRB approvals for the study. This Certificate protects study staff from being compelled to disclose study-related. information by any US Federal, State or local civil, criminal, administrative, legislative, or other body.

All protected health information (PHI) will be protected according to the provisions of the HIPAA and will only be used or disclosed as allowed by the privacy rule pursuant to relevant waivers or authorizations, or as required by federal law.

8.8.1 Confidentiality in Qualitative Research

The focus groups and qualitative interviews conducted as part of HTPN 061 raise different confidentiality issues from the main research study.

During focus groups, participants will share information about themselves and their experiences, some of which may be quite personal, for example their HIV status or experiences with discrimination. All participants will be counseled before the beginning of the focus group that they are expected to respect personal information shared by other participants during the session and to not share or discuss this information after the focus group is over. As well, participants will be asked to use only first names or nicknames during the focus group session to safeguard their own and others' confidentiality.

Another potential concern in conducting the qualitative components of this research is the security and confidentiality of the audio recordings and transcripts. To protect participants' confidential information, participant names will not be used during the qualitative interviews and (as noted above) only nicknames and first names will be used in focus groups. All recordings will be identified by session number or participant identification number only, and not by participant name. Recordings of all interviews and focus groups will be kept in a locked storage cabinet or in a password-protected computer file, accessible only to designated staff. Any inadvertently captured identifying information will be stripped from the transcripts, and only the research team and the transcribers will have access to the audio interview data. Audio recordings of interviews will be destroyed within three years of study completion.

8.9 Communicable Disease Reporting Requirements

Study staff will comply with all applicable local requirements to report communicable diseases identified among study participants to local health authorities. Participants will be made aware of all reporting requirements during the screening and study informed consent process.

8.10 Study Discontinuation

The study may be discontinued at any time by NIAID, the HPTN, the OHRP, site IRBs/ECs or other US or local government or regulatory authorities.

9 LABORATORY SPECIMENS AND BIOHAZARD CONTAINMENT

9.1 Local Laboratory Specimens

The following types of specimens will be collected for testing or processing at the local laboratory (LL):

Subjects who agree to testing:

- Blood for HIV rapid testing using an FDA-cleared kit (all subjects at enrollment, including those reporting a history of HIV infection).*
- Sera for syphilis serology.

- Urine for GC/CT NAAT testing.
- Swab for rectal GC/CT testing.
- Plasma for future NL testing and storage.

Subjects with a reactive HIV rapid test:

- Plasma for WB testing using an FDA-cleared kit.*
- Blood for CD4 cell count* (CD4 cell counts must be performed at a laboratory that is CLIA-certified; laboratories that are certified through the DAIDS/Immunology Quality Assurance (IQA) program are preferred).
- Additional plasma for future NL testing and storage.

***NOTE**: *HIV rapid testing and WB are not required at the 26- and 52 week visits if a subject was previously confirmed to be HIV seropositive. Consult SSP Section 11 for detailed algorithm. CD4 cell count is not required at the 26 week visit if subject was previously confirmed to be HIV seropositive..*

All subjects with positive WB test result:

- HIV viral load (at time of on-study diagnosis, HAART initiation, and at 52 weeks)

A diagram of the HIV testing algorithm for HPTN 061 is provided in the SSP manual.

Each study site will adhere to standards of good clinical laboratory practice, the HPTN Manual of Laboratory Operations[102], and local SOPs for proper collection, processing, labeling, transport, and storage of specimens to the LL. Specimen collection, testing, and storage at the LL will be documented using the HPTN Laboratory Data Management System (LDMS).

9.2 HPTN Network Laboratory (NL) Specimens

The following types of specimens will be collected for testing at the HPTN NL:

All subjects:

- Rectal swab for GC/CT NAAT, frozen at –70°C (enrollment and 52-week visits only).

All subjects with a reactive HIV rapid test or previous positive WB:

- Plasma for HIV incidence testing (see below).

All subjects with a negative HIV rapid test:

- Plasma for pooled HIV RNA testing (52-week visit only, pooling performed at the NL).

Special Cases: Plasma for resolution of Discordant or inconclusive HIV diagnostic test results. The NL may request a stored sample for further HIV diagnostic testing, in which case results may be provided back to the site for clinical management of the participant.

Note: No host genetic testing will be performed on samples collected for this study, either as part of this study or on samples for which consent is obtained for long term storage and testing.

HIV Incidence Testing:
The HPTN NL will perform testing to optimize algorithms for identification of recent HIV infection. If an algorithm is successfully validated, the NL will use the algorithm to identify participants who tested HIV-positive at study enrollment and were likely to have been recently infected. The algorithm is likely to include BED testing, CD4 cell count results, and other assays to be determined by the NL. Some specialized assays may be performed at a commercial laboratory or at the CDC. Testing for HIV incidence will be batched to reduce cost and maximize consistency of test procedures. Assays used by the NL for determining HIV incidence (including HIV-1 RNA assays) are not currently FDA-cleared for diagnosis of HIV infection. All testing will be performed retrospectively. Results from these tests will not be provided to study sites, clinicians, or study participants, and will not be used for clinical management. However, as noted above, if a participant has a positive HIV NAAT result at 52 weeks, the NL will require a stored sample from the participant to test using an FDA-cleared HIV RNA assay. If such testing also indicates acute infection at the time of sample collection, attempts will be made to contact the participant and direct him to local resources for a diagnostic HIV test and appropriate counseling (see Section 4.2).

Each study site will adhere to standards of good laboratory practice and the HPTN Manual of Laboratory Operations for proper collection, processing, labeling, and transport of specimens to the NL. All specimens will be shipped in accordance with International Air Transport Association (IATA) specimen shipping regulations. All shipments will be documented using the HPTN LDMS.

9.3 Quality Control (QC) and Quality Assurance (QA) Procedures

The clinical sites will document that their clinical laboratories are CLIA-certified and that they perform the appropriate external QA testing. NL staff will conduct periodic visits to each site to assess the implementation of on-site laboratory QC procedures, including proper maintenance of laboratory testing equipment and use of appropriate reagents. NL staff will follow-up directly with site staff to resolve any QC or QA problems identified through proficiency testing and/or on-site assessments.

9.3.1 Shipping of Specimens for QA Testing

All specimens will be shipped in accordance with the HPTN Manual of Laboratory Operations and IATA specimen shipping regulations. All shipments will be documented using the HPTN LDMS.

9.3.2 Specimen Storage for QA Testing and Protocol-Related Testing

Storage of specimens for protocol-related testing (required for all study participants who agree to be tested for HIV infection)

Study site staff will store plasma collected in this study until all protocol-related testing is complete. Note that some testing will be performed retrospectively, after the last participant completes the final study visit. Protocol-related testing at the NL using plasma collected at the study sites will include:

- QA testing.
- Determination of HIV incidence, including comparison of BED results to those obtained with other assays.
- Characterization of HIV viruses (e.g., HIV genotyping, HIV subtyping, HIV sequencing and phylogenetics, HIV tropism) and other immunologic studies; note that some specialized assays may be performed at a commercial laboratory.

9.4 Specimen Storage for Possible Future Research Testing

In addition to the required consent for storage of samples for QA and protocol-related testing described in Section 9.3, participants will be asked to consent to long-term storage for other possible future research testing. This consent is optional. Samples from participants who do not provide this consent will be destroyed after all protocol-related testing has been completed.

9.5 Classification of the Infection Status of Study Participants For Analysis

When the pertinent data are available, participants will be classified into three categories for analysis purposes: chronically infected subjects, recently infected subjects, or acutely infected subjects. This is a different from how the pool of participants will be divided for enrollment purposes.

A. Chronically infected participants

A number of participants will be classified as chronically infected based on self-report of a prior positive HIV diagnosis. These participants will have blood drawn for testing and for sample storage. Chronically infected participants will include those who are in the enrollment categories of "HIV-infected and in care, or not in care but only having UAI with HIV-positive partners" or "HIV-infected, not in care, and having UAI with HIV-negative or unknown serostatus partners."

B. Recently infected participants

Participants will be classified as recently infected if:

- BED and other laboratory data are consistent with recent HIV infection, based on the best available laboratory algorithms.
- They are HIV-seronegative or HIV-indeterminate at one visit and HIV seropositive at a subsequent visit (HIV seroconversion).

Recently infected participants will be drawn from those who are in the enrollment categories of "New HIV diagnosis at enrollment" and "HIV-negative at enrollment."

C. Acutely infected participants

HIV-1 RNA testing will be performed retrospectively on selected participants to clarify their HIV infection status (e.g., for those with indeterminate WB). Pooled HIV-1 RNA testing will also be

performed to identify participants who have acute HIV infection at 12 months. If a sample pool is HIV-1 RNA positive, individual samples will be tested.

Participants will be classified as acutely infected at a visit if they have a positive test for HIV-1 RNA and either (1) a negative rapid test, (2) a negative WB, or (3) an indeterminate WB. If a participant is found to have acute and/or recent HIV infection at more than one study visit, the participant will be counted as a single incident infection. Acutely infected participants will be drawn from those who are in the enrollment category of "HIV-negative at enrollment."

D. Determination of HIV infection status in other study participants

The HIV infection status of all participants who do not meet any of the criteria above will be determined based on the results of BED testing, other HIV incidence testing, and other clinical and laboratory data, if possible.

If necessary, and in accordance with HPTN Network Policy, an Endpoint Adjudication Committee will be convened and will provide guidance to the protocol team in the event that one or more study participants' final HIV status is not unequivocal, or if the point at which one or more participants became infected is not clear.

9.6 Biohazard Containment

The transmission of HIV and other blood-borne pathogens can occur through contact with contaminated needles, blood, and blood products, appropriate blood and secretion. Precautions will be employed by all personnel in the drawing of blood and shipping and handling of all specimens for this study, as currently recommended by the CDC.

10 ADMINISTRATIVE PROCEDURES

10.1 Study Activation

Prior to implementation of this protocol and any subsequent full version amendments, sites must receive protocol and protocol consent form approval from their local IRB. After ethical review and approval, study sites and CORE staff will submit required regulatory documentation — as listed in the SSP manual — to the DAIDS Regulatory Compliance Center (RCC) in accordance with DAIDS procedures. Protocol documents must be registered with and approved by the DAIDS (RCC) Protocol Registration Office before the site can enroll any subjects into the study. Sites should refer to the DAIDS Protocol Registration Policy and Procedure Manual located on the RCC website for requirements and guidance on the registration process.[103]

Pending successful protocol registration and submission of all required documentation, CORE staff will issue a "site activation notice." The study may not begin until a study activation notice is received at the site.

10.2 Study Coordination

Study implementation at all sites will be directed by this protocol and by a common SSP manual. The SSP manual will outline procedures for conducting study visits, collecting and submitting study data, collecting and shipping specimens, and other study operations.

Study case report forms will be developed by the study team and HPTN SDMC. Data will be recorded on site and transferred to the HPTN SDMC, where they will be entered and cleaned using the DataFax data management system. Quality control reports and queries will be routinely sent to the site for verification and resolution.

Close cooperation among the study site investigators and coordinators, DAIDS representative, protocol coordinator, biostatistician, data managers, and other study team members will be necessary to track study progress, respond to queries about proper study implementation, address issues in a timely manner, and ensure consistent participant management, documentation, and information sharing. Rates of accrual, follow-up, and protocol compliance will be monitored closely by the study team. Representatives of the HPTN CORE and SDMC also will evaluate these rates on a regular basis.

10.3 Study Monitoring

On-site study monitoring will be performed in accordance with DAIDS policies. Study monitors will visit the site to:

- Verify compliance with regulations and guidelines related to human participants and other topics.
- Assess adherence to the study protocol, SSP manual, and local counseling practices.
- Confirm the quality and accuracy of information collected at the study site and entered into the study database.

Site investigators will allow study monitors to inspect study facilities and documentation (e.g., informed consent forms, clinic and laboratory records, other source documents, case report forms), as well as to observe the performance of study procedures. Investigators also will allow inspection of all study-related documentation by authorized representatives of the HPTN CORE, SDMC, NL, DAIDS, and government and regulatory authorities. A site visit log will be maintained at the study site to document all visits.

10.4 Protocol Compliance

The study will be conducted in full compliance with the protocol. The protocol will not be amended without prior written approval by the Protocol Chair and DAIDS Program Officer. All protocol amendments must be submitted to and approved by the relevant IRB(s)/ECs and DAIDS before implementing the amendment.

10.5 Investigator's Records

The study site investigator will maintain and store in a secure manner complete, accurate, and current study records throughout the study. The investigator will retain all study records for at least two years after study closure, unless otherwise specified by DAIDS or the HPTN CORE. This minimum storage requirement is often superceded by other DAIDS policy. Retention or destruction of essential documents must be in accordance with local institution/IRB/EC policies and procedures. No clinical research files will be destroyed without approval first being obtained from the DAIDS Program Officer.

Study records include administrative documentation — such as site registration documents and all reports and correspondence relating to the study — as well as documentation related to each participant screened for and/or enrolled in the study — such as informed consent forms, locator forms, case report forms, notations of all contacts with participants, and all other source documents.

10.6 Use of Information and Publications

Publication of the results of this study will be governed by HPTN policies. Any presentation, abstract, or manuscript will be submitted by the investigator to the HPTN Manuscript Review Committee and DAIDS for review before submission.

10.7 Dissemination of Results

The study team acknowledges the importance of having a dissemination plan in place before the study is initiated. This plan will describe the procedures and timelines for distributing the results to the many stakeholders in the study, and the media outlets that would report on these findings. These stakeholders include participants, the communities at the study sites from which participants are recruited, Black MSM in the IRBs, researchers in the field of HIV/AIDS research, the HPTN leadership, advocacy groups, and others. It is important to have the dissemination plan in place at the beginning of the research, because studies can be halted before their expected completion date, leaving protocol teams unprepared to communicate critical messages about the study in a coordinated and timely way. The dissemination plan for HPTN 061 will be included in the SSP manual.

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APPENDIX I: SCHEDULE OF STUDY VISITS AND PROCEDURES FOR HPTN 061

PROCEDURES	Enroll Visit [1]	26 Week Follow-up Visit[1]	52 Week Follow-up Visit[1]
ADMINISTRATIVE, BEHAVIORAL, AND REGULATORY PROCEDURES			
Administer eligibility checklist.	X		
Obtain informed consent for enrollment. Solicit consent for storage of specimens for future testing. Describe and solicit participation in qualitative components of study, if appropriate. Schedule qualitative visit.	X		
Obtain/update locator information.	X	X	X
Collect demographic information.	X		
Complete ACASI questionnaire.	X	X	X
Collect information about up to 5 social and 10 sexual network members.	X		
Update information about sexual network members.		X	X
For index participants, request referral of up to 5 Black MSM sexual network members. Provide training on techniques for motivating network members to come to the study site. Administer questionnaire about referral motivators & barriers.	X		
Schedule next visit, if applicable	X	X	
CLINICAL/COUNSELING PROCEDURES			
Provide HIV pre-test counseling, if participant willing to undergo HIV testing. [3]	X	X	X
Collect information about HAART history from HIV positive participants	X	X	X
Provide STI pre-test counseling, if participant willing to undergo STI tests.	X	X	X
Provide risk reduction counseling.	X	X	X
Invite participant to discuss substance use, mental health or other issues raised in completion of ACASI questionnaire. Provide counseling and/or refer for further assessment or care, as needed.	X	X	X
Provide HIV test results and post-test counseling, if applicable. [4]	X	X	X
Provide STI test results, post-test counseling, and treatment/referral for treatment, if applicable. [4]	X	X	X
Introduce peer health care system navigation. Begin work with peer health care system navigator or complete questionnaire about reasons for refusal of peer health care system navigation.	X	X	
Collect venous blood draw for HIV rapid test.[6]	X	X	X
Collect venous blood draw for syphilis test, WB, [7] CD4 cell count, [8] HIV viral load, [9] and plasma storage.[10]	X	X	X
Collect urine for GC/CT NAAT testing.	X	X	X
Collect rectal swab for GC/CT NAAT testing. [11]	X		X
Confirm circumcision status by examination, unless participant identifies that they have had gender reassignment surgery.	X		
Offer condoms and lubricant	X	X	X
LOCAL LABORATORY PROCEDURES			
HIV rapid test [6]	X	X	X
HIV WB [7]	X	X	X
CD4 cell count [8]	X	X	X
HIV viral load [9]	X	X	X
Syphilis serology (including titer)	X	X	X
Urine NAAT for GC/CT	X	X	X
Store plasma and rectal swab samples for shipping to NL when requested by the SDMC.	X	X	X

[1] Note that participants may be asked to return to the clinic to receive test results about two weeks after the study visit. These visits are considered part of the visita t which the samples are collected.

[2] Staff will solicit participation in the study's qualitative component at the enrollment visit from appropriate main study participants. . Consent for the qualitative components will be obtained when the participant returns for this activity at a visit separate from the study's regular visit schedule.

[3] HIV pre-test counseling and HIV testing is not necessary at follow-up visits for participants with a prior HIV-positive diagnosis.

[4] HIV WB and STI test results will be provided at the post-test visit after the study visit, scheduled for a time soon after the results are expected to be available.

[5] Participants refusing PHN at enrollment can choose to begin navigation at the week 26 visit.

[6] HIV rapid test is peformed at enrollment for all study subjects consenting to HIV testing, even if they provide a history of prior HIV diagnosis; HIV rapid testing is not performed at 26 or 52 weeks if HIV infection was confirmed at a prior visit. The HIV rapid test will be performed at the clinic site. Testing at the clinic site must be performed under the oversight of the study coordinator for the CRS.

[7] A WB is performed at any visit where a reactive HIV rapid test result is obtained. A WB is not performed at the 26- or 52-week visits if HIV infection was confirmed at a prior visit.

[8] A CD4 cell count is performed at any visit where a reactive HIV rapid test result is obtained. A CD4 cell count is not performed at the 26- week visit if HIV infection was confirmed at enrollment. A CD4 cell count is obtained at 52 weeks for all subjects with confirmed HIV infection.

[9] HIV viral load is performed at the first visit at which the participant receives a positive WB result during the study and 52-week visits for any participant with a previously confirmed HIV infection.

[10] Plasma is stored for all participants at all study visits. The HPTN SDMC will provide the sites with instructions for shipment of selected plasma samples to the NL for testing.

[11] Rectal swabs are shipped to the NL for testing and are obtained at the enrollment and 52 week visits only

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APPENDIX II: SAMPLE INFORMED CONSENT FOR ENROLLMENT

TITLE OF THE RESEARCH:

HPTN 061- A Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men in Preparation for a Community-Level Randomized Trial to Test the Efficacy of the Intervention in Reducing HIV Incidence Among Black Men Who Have Sex with Men

HPTN 061, Version 2.0 02 April 2009
DAIDS ID: 10666

SPONSOR: NIAID, NIDA, NIMH, NIH

INVESTIGATOR OF RECORD: [*insert name*]
PHONE: [*insert number*]

INTRODUCTION:

You are being asked to take part in this research study to see if we can design a new and better way to try to slow the spread of HIV (human immunodeficiency virus, the virus that causes AIDS) among Black men who have sex with men (MSM). This study is sponsored by the US National Institutes of Health (NIH). The person in charge of the study at this site is **(*insert name of Principal Investigator*)**. Before you decide if you want to be a part of this study, we want you to know about the study.

This is a consent form. It gives you information about this study. We will explain the purpose of the study and the kinds of activities that are part of this study. We will describe the risks and benefits of the study. We will describe what is expected of you, and what you should expect of us if you decide to participate. This consent form might contain some words that you do not know. Please ask us to explain anything that you do not understand. After we tell you about the study we will ask if you want to be part of the study. If you agree to take part, you will be asked to sign this consent form, or make your mark in front of a witness. You will be given a copy to keep; you do not need to take that copy if you do not want to. This process is called informed consent.

Please note that:

- Your participation in this research is entirely voluntary.
- You may decide not to take part or to withdraw from the study at any time without losing the benefits of your standard medical care.
- If you decide not to take part in the study, you can still join another study later, if one is available and you qualify.

PURPOSE OF THE STUDY:

The purpose of this study is to see if we can design a new and better way to try to slow the spread of HIV among Black MSM.

Studies show that Black MSM are much more likely to become infected with HIV than other groups. We are not sure why this is, but the studies suggest several possible reasons. First, many Black MSM have never been tested for HIV. Second, it can be hard for Black MSM to get the medical care they need. Third, the people Black MSM hang out with and have sex with may think and act in ways that make it hard to stay healthy and free of HIV.

We have ideas about how to deal with these problems. In this study, we will try out some of our ideas. Based on what we learn, we may do another larger study to see if these ideas can slow the spread of HIV among Black MSM.

Some of the ideas we will try out in this study are to:

- Offer Black MSM free HIV testing and help those who test positive for HIV to get the care they need.
- Connect Black MSM with a trained person called a "peer health care system navigator" (PHN) who can help them get medical care, whatever their HIV status.
- Talk to Black MSM about whom they hang out with and have sex with, and invite some of their sexual partners to join the study if they are willing.

To test these ideas, we will enroll about 2418 people from six cities in the United States. It will take about one year to enroll all people at each site. About 403 people will be enrolled at this site.

PROCEDURES:

If you agree to take part in the study, you will enroll today. If you qualify to take part in follow-up visits, you will be asked to return to the clinic for another visit in six months and then another visit six months after that. If you are enrolled in the study but do not qualify for follow-up visits, today will be your only visit.

Enrollment Visit (Today):
Today's visit will last about three and a half hours. You will be asked questions about where you live, your health, and your previous experiences with health care. You will be asked about your sexual history. You will be asked how you feel about race, sexuality, and research. You may choose not to answer any of the questions if you wish. You will use a computer to answer most of the questions. Some questions will be asked by an interviewer.

A counselor will talk to you about protecting yourself and your partner(s) from HIV and other diseases passed during sex (sexually transmitted infections, or "STIs"). We will offer you condoms and lubricant and counsel you on how to use them safely.

The counselor will ask you about some of your friends and sexual partners, for example what race they are and how long you have known them. We will not ask their names. This information will help us better understand the social world of Black MSM. We may ask you to refer some of your sexual partners to this study; if so, we will offer you some tips on how to bring this up with them.

We will draw a small amount of blood from you (up to about 40 ml, or about 3 tablespoons). If you agree, we will test your blood for HIV and syphilis. Some of your blood will be stored in case it is needed later for tests related to this study. These tests may not be done for a year or more after you have had your last study visit.

We will collect a swab from your rectum and also collect a urine sample to test for two other infections passed during sex, Chlamydia and gonorrhea. We will also look to see if you have been circumcised, unless you have had gender reassignment surgery (also known as a sex change operation).We will ask if you prefer to have a male or female staff member perform these procedures and will do our best to accommodate your preference.

You may be asked to come back to the clinic in a couple of weeks to receive results from some of the tests.

If we find you have any STIs, we will either treat you or refer you to a clinic where you can be treated.

If your HIV test today is positive, we will do other tests to make sure that you really are infected, to check how much HIV is in your blood, and to see the effects HIV has had on your immune system. You will need to come back to the clinic to receive the results of these tests when they are ready. When you come back, the staff will discuss your test results with you. They will refer you for care if the tests confirm that you are infected. Sometimes an HIV test result is not clearly positive, but is also not negative. In that case (and also if your HIV test results are positive), we will collect some more blood (about 20 mL, or a little more than 1 tablespoon) and test it again until we know for sure whether or not you are infected with HIV. We will also save some of this blood for additional testing at the end of the study. If you are infected with HIV and get treatment for it, we would like to find out from your health care provider what treatment you are getting and how long you have been getting it. At the end of this form we will ask your permission to contact your health care provider for this information.

You may qualify to have two follow-up visits after today, or this may be your only visit. If you qualify for the follow-up visits, you will be eligible to be introduced to a peer health navigator today. The peer health navigator is a member of the research team who can help you get connected to health care services or people to help you with other needs you may have, such as mental health issues or drug or alcohol use. You do not have to work with a PHN if you do not want to. If you do work with the PHN, you will meet with him or her several times over the coming months at times that are convenient for you and the PHN. Although a PHN will work to connect you with health care services in your area, a PHN will never share any of your study information with someone who is not a member of the research team without your permission.
If you are going to have follow-up visits, we will schedule your next visit for six months from today.

Six-Month Visit

If you qualify for follow-up visits, you will be scheduled to come back to the clinic in about six months. This visit will last about three hours. At the six-month visit:

- We will ask you where you live and update our records if your address has changed.
- We will ask you questions about your health and health care, about your sexual activity since the last visit, and about your experience with the peer health care system navigator.
- We will also ask you questions about your feelings about race, research, and sexuality.
- We will ask you to update your list of sexual partners collected at the enrollment visit (we will not ask you to list them by name, but only by nickname or initials).
- We will collect urine from you to test for infections passed through sex (gonorrhea and Chlamydia). We will schedule a time for you to receive these results when they are available, about two weeks after the visit. If you have any sexually transmitted infections, we will either treat you or refer you to a clinic where you can receive treatment.
- We will draw a small amount of blood from you (up to about 40 ml, or about 3 tablespoons).
    - We will test this sample for syphilis.
    - A small amount of your blood will be stored in case it is needed later for tests related to this study.
    - If you did not have a positive HIV result at the enrollment visit, we will test this blood sample for HIV. If this HIV test is positive, we will perform more tests to be sure that you have HIV, to check the effects that HIV has had on your immune system (CD4 cell count), and (if you really do have HIV) to see how much HIV is in your blood. When you come back to the clinic for your results, we will collect some additional blood and test it again to make absolutely sure that you are infected with HIV..
- We will talk to you about protecting yourself and your partner(s) from HIV and other STIs and offer you condoms and lubricant.
- We will schedule your 12-month visit.

If you think you may have become infected with an STI, you may come back to the clinic anytime between the enrollment visit and the end of your participation in the study and we will test you for HIV, syphilis, gonorrhea, or Chlamydia. We will explain the results of the tests to you and if you are positive, we will either treat you or refer you to a clinic where you can receive treatment. If you go to another doctor between study visits and find out that you have an STI or HIV, we will ask you to tell us about it. We will also ask you to bring in the report from your doctor or give us permission to ask for that report from your doctor.

Twelve-Month Visit

If you were scheduled for a follow-up visit at six months, you will also be scheduled for a follow-up visit at 12 months. This visit will last about three hours. The activities at the 12-month visit are nearly the same as those at the six-month visit, with a few differences:

- We will collect a swab from your rectum to test for STIs. You will be provided the results and, if you have an infection, we will either treat you or refer you to a clinic where you can be treated.
- If you had a positive HIV test at this visit, ***or at any other visit***, we will perform two more tests to see the effects that HIV has had on your immune system, and to see how much HIV is in your blood. The results of these two tests will be given to you when you come back to the clinic, about two weeks after this visit. If you have a positive HIV test for the first time at this visit, we will collect some additional blood from you when you come back for your test results and test it again for HIV to make absolutely sure that you are infected with HIV.
- Many weeks or months after your twelve-month visit, we plan to test the blood of all participants in the study using an extra-sensitive HIV test. We expect that this test may show that one or maybe two participants out of all the participants in the study had an HIV infection so new that regular HIV tests could not detect it. We will attempt to contact you if your blood is positive by this extra sensitive test, but the test results may not be available until long after you have finished the study. For this reason we ask that you always let the study staff know how to get in touch with you, even after your study visits are over.

Each time we collect blood from you; we will freeze and store some of the blood that is leftover for other study-related tests. These tests may be done a year or more after your last study visit. We would also like to keep your frozen blood samples after the study is over, and possibly test them in the future to answer questions that are not directly part of this study. A separate form asks for your permission to do this.

We may also ask if you would be willing to participate in an extra, less formal interview soon after today's visit, or if you would be willing to join in a group discussion called a focus group. We will explain these extra procedures separately to you and you will have the chance to ask more detailed questions about them. If you are interested in participating in the activities we describe to you, you will be asked to sign a separate consent form for them.

Contact Outside of the Clinic
If you miss a study visit or are not able to come to the research site, someone from the study staff may be able to visit you at your home or another location of your choosing to complete the visit if you give us permission to do so. The site staff can explain the steps we would take to protect your confidentiality if they visit you outside the clinic. At the end of this form you will be asked whether or not you agree to let us contact you outside of the clinic.

RISKS and DISCOMFORTS:
Some people feel discomfort when they are checked for circumcision or when their rectum is swabbed. Some people feel discomfort when blood is drawn and may feel dizzy or even faint. You may have a bruise or swelling where the needle goes into you. Some people may develop an infection where the needle goes in, but this is very rare.

You will be asked questions about your sexual history. You may be embarrassed by these questions. You may choose not to answer the questions, if you wish.

The counseling about HIV and other STIs may cause you to worry or become anxious. If the tests show that you have HIV or other STIs, you may become depressed or feel anxious. ***[To be modified by site**:* If tests show that you have (***local staff to identify appropriate reportable diseases***), we are required by law to report this to (***state or municipal agency***), and (***state or municipal agency***) will contact your partners who might also be infected. You could have problems with your partners if they are notified in this way because they might feel that you have put them at risk.***]*** You may become embarrassed or worried when asked to describe your sexual partners or refer them to the study. You might also have problems with your partners if you try to recruit them into this study. Depending on your partner, these problems could include the possibility of violence.

We will make every effort to protect your confidentiality during the study. However, it is possible that others might learn of your participation and think you are infected with HIV or are at high risk for infection with HIV. Because of this, you could have problems being accepted in your family and community.

POTENTIAL BENEFITS:

There may be no direct benefit for you as a result of participating in this study. However, what we learn from this study may help us find new ways to prevent the spread of HIV in the future. Results of this study may help us understand how counseling, care, and treatment to prevent HIV are best provided to Black MSM. You will receive information about your HIV status and how to protect yourself and your partner(s) from HIV and STIs. You will receive treatment or referral for STIs and free condoms and lubricant. If you qualify to participate in follow-up visits, you will receive help in accessing health care and related services available in your community. If you agree to HIV testing, knowing your HIV status may help you make good decisions to protect your health.

NEW FINDINGS

We will tell you about new information from this or other studies that may affect your health, welfare, or willingness to stay in this study. At the end of the study, you will be told when the study results may be available and how to learn about them.

REASONS WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT:

You might not complete the study, even if you would like to, if:

- The study is cancelled by the sponsor of the study (US National Institutes of Health (NIH)), by a government or regulatory agency, by the HPTN, or by the Institutional Review Board (IRB). An IRB is a committee that watches over the safety and rights of people who participate in research.
- If the team that oversees the study feels that withdrawing you from the study is necessary in order to protect the safety of you, other participants, or the study staff.

ALTERNATIVES TO PARTICIPATION:
If you choose not to take part in this study, it will have no effect on the regular medical care that is available to you at this clinic or elsewhere. There may be other research studies in your area for people who are HIV-positive or at high risk for HIV.

COSTS TO YOU:
There will be no cost to you for study-related visits, examinations, laboratory tests, or other procedures.

REIMBURSEMENT:
At each visit you will receive **(*insert site-specific compensation*)** to pay for your transportation costs and time. If study staff ask you to refer some of your sexual partners to the study, you will receive (***insert site-specific compensation***) for each partner who enrolls in the study.

CONFIDENTIALITY:
We will do everything we can to keep your personal information confidential. To help us keep your personal information confidential, we have obtained a Certificate of Confidentiality from the US Federal Government. This certificate protects researchers from being forced to tell people who are not connected with this study, such as the court system, about your participation. Any publication that results from this study will not use your name or identify you personally.

Some people may review your records to ensure that this research is done properly; these include: (insert name of site) IRB, National Institutes of Health (NIH), Government or regulatory authorities, study staff, and study monitors. Also, the Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study. The Certificate cannot keep the United States Government from auditing or evaluating federally-funded projects such as this one.

Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse or neglect, or a risk of harm to you or others, we will tell the proper authorities**. (*Use next sentence only at sites where this applies*)** As well, we are also obligated by local law to report any new cases of ***(insert disease names here*)** to local public health authorities, who may follow-up with you to identify your recent sexual partners.

RESEARCH-RELATED INJURY:
If you are injured as a result of being in this study, you will be given immediate necessary treatment for your injuries. However, you may have to pay for this care. There is no program for compensation either through this institution or the US National Institutes of Health (NIH). You will not be giving up any of your legal rights by signing this consent form.

LOCAL COMMUNITY INVOLVEMENT IN THIS STUDY
A local community advisory board (CAB) is also involved in this study. CAB members are drawn from the local area and may include Black MSM, people who work for local community groups, clergy, teachers, or others. CAB members helped design and review this study. The CAB will not have access to medical information that can identify you. The CAB

makes us aware of issues in this study that may be important to the community. CAB members also help to share research information with the community.

PEOPLE TO CONTACT FOR PROBLEMS OR QUESTIONS:

If you have questions about this study or a research-related injury, contact:

- **(*site insert name of the investigator or other study staff*)**
- **(*site insert telephone number and physical address of above*)**

If you have questions about your rights as a research subject, contact:

- **(*site insert name or title of person on the Institutional Review Board (IRB) or other organization appropriate for the site*)**
- ***(site insert telephone number and physical address of above*)**

SIGNATURE PAGE

If you have read this consent form (or had it explained to you), all your questions have been answered and you agree to take part in this study, please sign your name or make your mark below.

_____	_____
Participant's Name (print)	Participant's Signature and Date
_____	_____
Participant's Legal Guardian (As appropriate)	Legal Guardian's Signature and Date
_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature and Date
_____	_____
Witness' Name (print) (As appropriate)	Witness' Signature and Date

Please initial one of the boxes below to say whether site staff can visit you outside of the clinic, for example if you miss a visit or are unable to come to the study clinic. Your choice will not affect whether you can participate in this study or the kind of care you will receive as part of this study.

_____ **Yes, you may visit me outside of the clinic**
(initials)

_____ **No, you may not visit me outside of the clinic for any reason**
(initials)

Please initial one of the boxes below to say whether site staff can obtain information from health care providers if you have received care from them for HIV or sexually transmitted infections (STIs). Your choice will not affect whether you can participate in this study or the kind of care you will receive as part of this study.

Yes, you may contact my health care provider for medical information and/or records about my diagnosis and treatment for:

_____ **HIV (initials)** _____ **STIs(initials)**

No, you may not contact my health care provider for medical information and/or records about my diagnosis and treatment for:

_____ HIV **_____ STIs**
(initials) **(initials)**

APPENDIX III: SAMPLE INFORMED CONSENT FOR THE STORAGE OF SPECIMENS OBTAINED WHILE PARTICIPATING IN A RESEARCH TRIAL

TITLE OF THE RESEARCH:

Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men in preparation for a Community Level Randomized Trial to Test the Efficacy of the Intervention in Reducing HIV Incidence Among Black Men Who Have Sex with Men

HPTN 061, Version 2.0 02 April 2009
DAIDS ID: 10666

INVESTIGATOR OF RECORD: [*insert name*]
PHONE: [*insert number*]

SPONSORS: NIAID, NIDA, NIMH, NIH

INTRODUCTION:
You have decided to take part in a research study sponsored by the United States' National Institutes of Health (NIH). While you are in this research study there may be some blood samples taken from you that might be useful for future research that is not directly related to this study. You are being asked to agree to the storage of these blood samples. This consent form gives you information about the collection, storage, and use of your blood samples. The study staff will talk with you about this information. Please ask the study staff any questions you might have. You will be asked to sign this form to indicate whether you agree to have your blood samples stored and tested for other future research. You will be offered a copy of this form to keep.

HOW WILL YOU GET THE BLOOD FROM ME?
You have agreed to have blood drawn, tested, and stored as part of the research study. During the study, your stored blood may be tested to check on your health. It also may be tested for HIV. The research doctors would like to keep any blood that is leftover, after the research study is done, to use for future research. If you agree to this, no additional blood will be taken from you. Only leftover blood samples will be kept and used for future research.

HOW WILL YOU USE MY BLOOD SAMPLES?
Your blood samples will only be used to look for additional evidence of infection with HIV or other agents, damage caused by infection, or your body's response to infection (such as examining cells, proteins, and other chemicals in your body).

The researchers do not plan to contact you or your regular doctor with any results from tests done on your stored blood samples. This is because research tests are often done with

experimental procedures, so the results from one research study are generally not useful for making decisions on managing your health. Should a rare situation come up where the researchers decide that a specific test result would provide important information for your health, the researchers will notify your study doctor and your study doctor will try to contact you. If you wish to be contacted with this type of test result, you must give the study doctor or nurse any change to your address or phone number. If you want your regular doctor to be told about this type of test result, you must provide the study doctor or nurse with your regular doctor's name, address, and phone number.

Your blood samples will not be sold or used directly to produce commercial products. Research studies using your blood samples will be reviewed by the National Institutes of Health and a special committee at the researcher's institution (an Institutional Review Board or IRB).

HOW LONG WILL YOU KEEP MY BLOOD SAMPLES?
There is no time limit on how long your blood samples will be stored.

HOW WILL MY BLOOD SAMPLES BE STORED?
Your blood will be stored here at this clinic, [at another facility at this institution] or at the Network Laboratory where your blood can be kept safely and securely. The storage facilities are designed so that only approved researchers will have access to the blood samples. Staff at these locations will not have information that directly identifies you. Your stored blood samples will have an ID number on them but not your name or any other personal information. An IRB will oversee the storage facilities to protect you and other research volunteers from harm.

DOES STORAGE OF MY BLOOD SAMPLES BENEFIT ME?
There are no direct benefits to you. The benefit of doing research on stored blood samples includes learning more about HIV infection.

WHAT ARE THE RISKS?
There are few risks related to storing your blood samples. When tests are done on the stored blood samples there is a small but possible risk to your privacy. It is possible that if others found out information about you that is learned from tests it could cause you problems getting a job or insurance.

WHAT ABOUT CONFIDENTIALITY?
In order to keep your information private, your blood samples will be labeled with a code that can only be traced back to your research clinic. Your personal information (name, address, phone number) will be protected by the research clinic. When researchers are given your stored blood samples to study they will not be given your personal information. The results of future tests will not be included in your health records.

Any publication about the results of future tests will not use your name or identify you personally. The researchers will do everything they can to protect your privacy. To help us keep your personal information confidential, we have obtained a Certificate of

Confidentiality from the US Federal Government. This certificate protects researchers from being forced to tell people who are not connected with this study, such as the court system, about your participation. However, it is not always possible to guarantee confidentiality. Your personal information may be disclosed if required by law. Also, the Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.

Your records may be reviewed by:

- The United States National Institutes of Health (NIH)
- Government or regulatory agencies
- ***(insert names of applicable IRBs/ECs)***
- Study staff
- Study monitors

WHAT ARE MY RIGHTS?

Allowing your blood samples to be stored for future research that is not directly related to this study is completely voluntary. If you decide not to have any blood samples stored other than what is needed to complete this study, you can still remain in this research study or any future study. If you decide now that your blood samples can be stored for future research, you may change your mind at any time. You must contact the study staff and let them know that you do not want your blood samples used for future research. Your blood samples will then not be used.

WHAT DO I DO IF I HAVE QUESTIONS?

For questions about the storage of your blood samples, contact (***insert the name of the investigator***) at (***insert telephone number***).

For questions about your rights related to the storage of your blood samples for research, contact (***insert the name or title of person on the Institutional Review Board***) at (***insert telephone number***).

SIGNATURE PAGE

Please carefully read the statements below and think about your choice. No matter what you decide, it will not affect your care.

I agree to have my left over blood samples stored and tested for future research related to HIV infection.

_____Yes

_____No

_____	_____
Participant's Name (print)	Participant's Signature and Date
_____	_____
Participant's Legal Guardian (As appropriate)	Legal Guardian's Signature and Date
_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature and Date
_____	_____
Witness' Name (print) (As appropriate)	Witness's Signature and Date

APPENDIX IV: QUALITATIVE INTERVIEW INFORMED CONSENT

TITLE OF THE RESEARCH:

HPTN 061- A Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men in Preparation for a Community-Level Randomized Trial to Test the Efficacy of the Intervention in Reducing HIV Incidence Among Black Men Who Have Sex with Men

HPTN 061, Version 2.0 02 April 2009
DAIDS ID: 10666

SPONSOR: NIAID, NIDA, NIMH, NIH

QUALITATIVE INTERVIEW INFORMED CONSENT
INVESTIGATOR OF RECORD: (*insert name*)
PHONE: (*insert number*)

Introduction
You have been asked to take part in a one-on-one interview with a study counselor as an extra activity to your participation in the HPTN 061 study. What you tell us in the interview will help us understand more about Black men who have sex with men (MSM). We want to know how Black MSM feel about HIV testing, about problems they face in getting health care, how well they feel they are treated in their community, and other issues. Between 10 and 30 men from this site will be asked to participate in these interviews. We hope that what we learn from these interviews will help us slow the spread of HIV among Black MSM in the future.

What Will Happen During This Study?
During the interview you and a counselor will talk about questions about a number of different topics, such as:

- How do you, and the people you know, feel about testing for HIV or other diseases passed during sex?
- What difficulties have you had in getting health care?
- How do you feel about participating in research studies?
- Have you felt discriminated against because of your race or sexuality?

To protect your privacy, you will meet with the counselor in a private area where others cannot overhear you. We hope that you will feel comfortable to answer all of the questions openly and honestly, but you may refuse to answer any of the questions, or stop the interview completely, at any time. If any of the questions make you very upset, the interviewer will stop the interview. You will also be provided with contact and referral information if any of the questions raise issues that you would like to talk about further, at this or some later time.

To make sure that we can learn the most from what you have to say, **your interview will be recorded**. After the interview is finished, a professional typist will type up what is on the recording, producing a document called a transcript. Your name will not be included on the transcript. After all of the interviews are done, your answers will be combined with the answers provided by others who have been interviewed. The transcripts of the interview recorded here will be reviewed by staff at this clinic and also by staff working on this study at other research sites in the US We will study the answers from different participants to look for common patterns.

- The interview **will take approximately 1 to 1 ½ hours** to complete.
- There will be **no cost to you** to participate in the interview.
- **You will receive *(insert local compensation amount)*** for your time and effort.

What Are the Potential Benefits?
There may be no direct benefits to you for participating in this interview. We hope that information from these interviews will help find new ways to reduce the risk of HIV for Black MSM in your community. You may feel a benefit from telling your story and sharing your experiences with someone who is interested in hearing what you have to say.

What Are the Possible Risks or Discomforts?
It is possible that answering the interview questions may make you embarrassed or upset. You may refuse to answer any of the questions, or stop the interview completely, at any time. The greatest risk may involve your privacy. The steps that the study team has taken to protect your privacy are described below.

How Will Your Privacy Be Protected?
Every effort will be made to keep your personal information confidential. Your personal information (name, address, phone number) will be protected by the research clinic. This information will not be used in any publication of information about this study.

If you participate in the interview, your session will be recorded. After the interview is finished, the recording will be typed (called a transcript) by qualified personnel. All identifying information will be removed from the transcript. Your name will not be included on the transcript.The recordings of the interview will be kept in a locked cabinet, or password protected computer file accessible only to authorized personnel. All audio recordings will be destroyed within three years of the study completion.

To help study staff keep your personal information confidential, we have obtained a Certificate of Confidentiality from the US Federal Government. This certificate protects researchers from being forced to tell people who are not connected with this study, such as the court system, about your participation. Any publication that results from this study will not use your name or identify you personally.

People who may review your records include ***(insert name of site)*** IRB, National Institutes of Health (NIH), government or regulatory agencies, study staff, and the study monitors. Also, the Certificate of Confidentiality does not prevent you from releasing information about

yourself and your participation in the study. The certificate cannot keep the United States Government from auditing or evaluating federally funded projects such as this one.
Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, we will tell the proper authorities.

Your participation in this interview is voluntary. You are not required to participate in this interview in order to remain in the rest of the 061 study. You may refuse to answer any of the questions, or stop the interview completely, at any time without reducing or affecting any care that you receive at this site.

What are Some Reasons Why You May Be Withdrawn From This Activity without Your Consent?
You may be withdrawn from the study without your consent for the following reasons:

- The research study, or this part of the study, is stopped or canceled before you participate.
- The study staff feels that completing the study or this part of the study would be harmful to you or others.

What Happens If You Are Injured by This Activity?
Because this activity only involves answering interview questions, it is very unlikely that you could be injured. However, if you are injured as a result of being in this study, you will be given immediate treatment for your injuries. However, you may have to pay for this care. There is no program for compensation either through this institution or the US National Institutes of Health (NIH). You will not be giving up any of your legal rights by signing this consent form.

Persons to Contact for Problems or Questions
For questions about this study or a research-related injury, contact:

- ***(site insert name of the investigator or other study staff)***
- ***(site insert telephone number and physical address of above)***

For questions about your rights as a research participant, contact:

- ***(site insert name or title of person on the Institutional Review Board (IRB) or other organization appropriate for the site)***
- ***(site insert telephone number and physical address of above)***

SIGNATURE PAGE

If you have either read or have heard the information in this consent form, if all of your questions have been answered and if you agree to take part in the qualitative interview, please sign your name on the line below.

_____	_____
Participant's Name (print)	Participant's Signature and Date
_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature and Date
_____	_____
Witness' Name (print) (As appropriate)	Witness's Signature and Date

APPENDIX V: FOCUS GROUP INFORMED CONSENT

TITLE OF THE RESEARCH:

HPTN 061- A Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men in Preparation for a Community-Level Randomized Trial to Test the Efficacy of the Intervention in Reducing HIV Incidence Among Black Men Who Have Sex with Men

HPTN 061, Version 2.0 02 April 2009
DAIDS ID: 10666

SPONSOR: NIAID, NIDA, NIMH, NIH

FOCUS GROUP INFORMED CONSENT

INVESTIGATOR OF RECORD: (*insert name*)
PHONE: (*insert number*)

Introduction
You have been invited to take part in a "focus group," which is a discussion among a small number of people about a few specific topics. The focus group you are being asked to join will be with other participants in the HPTN 061. A trained member of the study staff will lead the focus group. This discussion will help us learn more about Black MSM, so we can better understand such topics as:

- How Black MSM feel about life in their community.
- What issues shape whether Black MSM get tested for HIV or make use of health care.
- What kind of stigma Black MSM experience.

We expect that between six and eight participants will participate in each focus group. We expect to conduct three to five focus groups in each of the communities where HPTN 061 is taking place. We hope that in time, this information will help to reduce the spread of HIV among Black MSM.

Procedures
The focus group will be led by a member of the research team, the "focus group leader." The leader will ask the group to give their opinions and to describe their experiences as Black MSM living in this community. Everyone in the focus group will be encouraged to add to the discussion, and to respond to the questions or comments from other members of the group.

(To be modified to reflect site practices: The focus group is taking place in a location that the study staff have determined will provide you with privacy and confidentiality during the study visits, such as the clinic***.)***

To make sure that we learn the most from what you and the other members of the focus group have to say, **the focus group discussions will be recorded**. After the focus group is finished, a professional typist will type up what is on the recording, producing a document called a transcript. No names will be included in the transcript to protect your confidentiality. The transcripts of the focus group recorded here will be reviewed by staff at this clinic and also by staff working on this study at other research sites in the US.

- The focus group **will take between 1 ½ and 2 hours** to complete.
- There will be **no cost to you** to participate in the focus groups.
- **You will receive** (***insert local compensation amount***) for your time and effort.

What Are the Potential Benefits?
There may be no direct benefits to you for participating in this focus group. We hope that the information from these focus groups will help find new ways to reduce the risk of HIV for Black MSM in your community. You may feel a benefit from telling your story and sharing your experiences with others who are interested in hearing what you have to say.

What Are the Possible Risks or Discomforts?
The focus group will be led by a member of the research team. We will ask everyone in the focus group to respect each other's privacy. Everyone will be asked not to talk about what anyone in the group said to other people. But we cannot promise that people in the focus group will do this. You should share only those things you do not mind other people knowing. Participants will also be asked to use a made-up name during the focus group. The focus group leader may ask people to leave the room, or may stop the focus group altogether, if participants do not obey the ground rules or become very upset, but this is not expected. You will also be given contact and referral information if the discussions raise issues that you would like to talk about at a later time.

The greatest risk may involve your privacy and confidentiality. The steps that the study team has taken to protect your privacy are described below.

How Will Your Privacy Be Protected?
Every effort will be made to keep your personal information confidential. Your personal information (name, address, phone number) will be protected by the research clinic. Your name, or anything else that might identify you personally, will not be used in any publication of information about this study.

If you participate in the focus group, your session will be recorded. After the focus group is finished, the recording will be typed (called a transcript) by qualified personnel, but your name will not be included on the transcript. The recordings of the focus group will be kept in a locked cabinet, or password protected computer file accessible only to authorized personnel. All audio recordings will be destroyed within three years of the study completion.

To help study staff keep your personal information confidential, we have obtained a Certificate of Confidentiality from the US Federal Government. This certificate protects researchers from being forced to tell people who are not connected with this study, such as the court system, about your participation.

People who may review your records include the ***(insert name of site)*** IRB, National Institutes of Health (NIH), government and regulatory agencies, study staff and study monitors. Also, the Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study. The certificate cannot keep the United States Government from auditing or evaluating federally funded projects such as this one.

Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, we will tell the proper authorities.

Your participation in this focus group is voluntary. You are not required to participate in the focus group in order to remain in the rest of the HPTN 061 study. You may refuse to answer any of the questions, or leave the focus group, at any time.

What are Some Reasons Why You May Be Withdrawn From This Activity without Your Consent?
You may be withdrawn from the focus group activity without your consent for the following reasons:

- The research study, or the focus group activity, is stopped or canceled before you participate.
- The study staff feels that completing the study or focus group would be harmful to you or others.

What Happens If You Are Injured by This Research?
Because this activity only involves participating in a focus group discussion, it is very unlikely that you could be injured. However, if you are injured as a result of being in this study, you will be given immediate treatment for your injuries. However, you may have to pay for this care. There is no program for compensation either through this institution or the US National Institutes of Health (NIH). You will not be giving up any of your legal rights by signing this consent form.

Persons to Contact for Problems or Questions
For questions about this study or a research-related injury, contact:

- ***(site insert name of the investigator or other study staff)***
- ***(site insert telephone number and physical address of above)***

For questions about your rights as a research participant, contact:

- ***(site insert name or title of person on the Institutional Review Board (IRB) or other organization appropriate for the site)***
- ***(site insert telephone number and physical address of above)***

SIGNATURE PAGE

If you have either read or have heard the information in this consent form, if all of your questions have been answered and if you agree to take part in the focus group, please sign your name on the line below.

_____	_____
Participant's Name (print)	Participant's Signature and Date
_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature and Date
_____	_____
Witness' Name (print) (As appropriate)	Witness's Signature and Date