HIV Prevention Trials Network

Letter of Amendment # 1 to:

HPTN 094

INTEGRA: A Vanguard Study of Health Service Delivery in a Mobile Health Delivery Unit to Link Persons who Inject Drugs to Integrated Care and Prevention for Addiction, HIV, HCV and Primary Care

DAIDS Study ID: 38715

Version 1.0, dated 15 July 2020

Date of Letter of Amendment: 25 March 2021

LETTER OF AMENDMENT SIGNATURE PAGE

I will conduct the study in accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable US Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., US National Institutes of Health, Division of AIDS) and institutional policies.

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."

Signature of Investigator of Record

Date

Name of Investigator of Record
(printed)

HIV Prevention Trials Network

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The following information impacts the HPTN 094 study and must be forwarded to all responsible Institutional Review Boards/Ethics Committees (IRBs/ECs) as soon as possible for their information and review. This Letter of Amendment (LoA) must be approved by all responsible IRBs/ECs before implementation.

The information contained in this LoA does impact the informed consent forms (ICFs).

Upon receiving final IRB/EC approval for this LoA, sites should implement the LoA immediately. Sites are required to submit an LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). As part of the registration package, sites must submit the Letter of Amendment Investigatory Signature Page, signed and dated by the Investigator of Record. Sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. A LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with the LoA and any IRB correspondence should be retained in the site's regulatory files.

If the full HPTN 094 protocol is amended in the future, the changes in this LoA will be incorporated into the next version.

Summary of Revisions and Rationale

1. The DAIDS pharmacist and representatives from Gilead pharmaceuticals and the HPTN 094 Community Working Group were added to the protocol team roster. The acronym DSMB was removed and the acronym TAM added to the List of Abbreviations and Acronyms.
2. A small edit was made to Section 5.3.1 to clarify that intervention arm participants will be transitioned to community-based services by 26 weeks after enrollment. Text was added to Section 5 to provide/revise details regarding the study product. Restriction on offering PrEP only per CDC guidelines and requiring local DEA approval for study dispensation of buprenorphine was removed. Text was revised to reflect that MOUD medications will be acquired at the site level rather than centrally for the study. Table 1 was updated to reflect that not all urine testing will be performed by dipstick. Table 2 was updated to remove provision of long-acting naloxone for MOUD treatment and to alter language about PrEP regimens. Section 6.3 was modified to remove language about expecting to provide long-acting injectable product to participants. Some additional small changes were made to Section 9.5 regarding the description of study product
3. It was determined that there were adequate data sources for implementation evaluation without conducting ethnographic observations, so these were removed from Section 6.6. The time-and-motion studies were previously described under ethnographic observations but are more accurately a component of the cost effectiveness analysis, so the relevant text was moved and revised.
4. SUSAR reporting is a requirement of the clinical trials agreement between the sponsor and the manufacturer donating pharmaceutical product for this study. Therefore, Section 7 was revised to accommodate SUSAR reporting.
5. Language was added to Section 9.1 to as requested by DAIDS in conjunction with the cessation of Critical Event reporting.
6. The study team agreed that there were questions included in the study instruments that could make participants uncomfortable that had not been identified as such. The study team also felt it was important to specifically mention the risks to confidentiality that could arise if participants and peer navigators choose to communicate through messaging apps. These risks were added to protocol in Section 9.3 and the informed consent form. The informed consent form was also revised to more accurately describe procedures a participant should expect at study visits.
7. Small revisions to the laboratory collection procedures were made in Section 10.1 and to the schedules of visits and procedures in Appendices IA & IB. Appendices 1A and 1B were also revised to reflect a change in the specification of the tool for determining diagnosis of OUD, the schedule for assessing for OUD, and the components of the physical exam.
8. Language was removed from sections 5.3, 6.3 and the informed consent regarding provision of cell phone minutes to participants.
9. It was determined that a properly constituted SMC would be a more appropriate independent oversight body for this study than a DSMB. Therefore, language was updated in sections 7.1, 7.4, 8.7, and 9.1 to reflect the change from having a DSMB to an SMC.

Deletions to the protocol text are indicated by ~~strikethrough~~; additions are indicated in **bold**.

Revision 1: PROTOCOL TEAM ROSTER

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Revision 1: LIST OF ABBREVIATIONS AND ACRONYMS

~~DSMB Data and Safety Monitoring Board~~

[…]

TAM Time and Motion

Revision 2: Section 5.2.1 Medical Services – Intervention Arm

[…]

For those identified as HIV positive during Screening and Enrollment (and not already established in ART elsewhere), and for those who acquire HIV infection during the intervention period, ART will be provided in the mobile unit. Those identified as HIV negative at Enrollment

will be provided risk reduction counseling~~.~~**, assessed for PrEP** and offered PrEP according to ~~current CDC recommendations;~~**assessment.;** these participants will be tested for HIV infection during the intervention period. Clinical care including applicable laboratory test monitoring for HIV-positive participants and those on PrEP will be provided per national clinical guidelines. Over time, these participants will be linked to appropriate long-term ART or PrEP service settings.

[…]

Revision 2: Section 5.3.1 Medical Services – Intervention Arm

Peer navigators in the intervention arm will assist their participants to access medical services provided from the mobile unit. They will also assist their participants to obtain care from community-based services for those tests or services that cannot be addressed in the mobile unit. Initial visits between the participant and their navigator are expected to occur in person, beginning with introductions at the Enrollment Visit in the mobile unit. As the participant-navigator relationship becomes more established, interactions can be expected to take place at locations other than the mobile unit and may occur by phone or by messaging app/text. The peer navigator will also be responsible for working with the participant during the intervention period to prepare them to transition to community-based services ~~as the 26 weeks of study-provided care in the mobile unit comes to an end.~~**by 26 weeks.**

Revision 2: Section 5.4 Drug Supply

5.4 ~~Drug Supply~~ **Study Medication Considerations**

All of the drugs that will be provided as part of services in the mobile unit will be US Food and Drug Administration (FDA)-approved medications in common use for these ~~indications~~**conditions**; this study does not involve any investigational study products. ~~Drug supply and management will be an important issue for this study since a core component of the intervention is provision of drugs for MOUD, ART and PrEP. It is anticipated that it will be possible to obtain these drugs through manufacturer donation to the study, and that manufacturers' donations will be received and distributed to the sites by a qualified contractor. Once the contractor has been selected, policies and procedures for management, storage, distribution, dispensation and accountability will be established for the study and documented in the SSP Manual and site SOPs. Donated product will be received by the research pharmacies at the CRS, who will be responsible for local storage, dispensation and accountability.~~ Because the MOUD medication expected to be used in this study will be buprenorphine, ~~a~~**or combination buprenorphine/naloxone, both** schedule III controlled ~~substances~~**substances**, the study team will work with the US Drug Enforcement Administration **at the national and local level** to ~~obtain approval~~**comply with policies** for dispensation of buprenorphine ~~from the site pharmacy~~**or buprenorphine/naloxone** to participants ~~on the mobile unit.~~**.** Study sites are responsible for procuring antibiotics locally for STI treatment ~~for~~**and for procuring buprenorphine-containing regimens for MOUD.**

5.4.1 Study Supplied Medications for HIV

The following are medications that will be centrally supplied by the study to the sites, and that that will be offered to participants in the intervention arm, as appropriate, for HIV treatment or prevention (ART or PrEP). Study medications must be stored in the original bottles and in accordance with the manufacturer's recommendations.

Study-supplied PrEP

- **Emtricitabine/tenofovir disoproxil fumarate 200mg/300mg (FTC/TDF, Truvada®)**
- **Emtricitabine/tenofovir alafenamide 200mg/25mg (FTC/TAF, Descovy®)**

Study-supplied ART

- **Bictegravir/emtricitabine/tenofovir alafenamide 50mg/200mg/25mg (BIC/F/TAF, Biktarvy®)**

5.4.2 Study-Supplied Medication Acquisition and Accountability

FTC/TDF 200 mg/300 mg tablets (Truvada®), FTC/TAF 200 mg /25 mg tablets (Descovy®), and BIC/F/TAF 50mg/200mg/25mg tablets (Biktarvy®) are manufactured and provided by Gilead Sciences, Inc. and will be supplied by the National Institute of Allergy and Infectious Diseases (NIAID) Clinical Research Products Management Center (CRPMC). The study site pharmacist can obtain the study-supplied medications through the CRPMC by following the instructions in the ~~mobile units.~~***Pharmacy Guidelines and Instructions for DAIDS Clinical Trial Networks*****, and instructions in the SSP Manual.**

The site pharmacist is required to maintain complete records of all study-supplied medications received from the CRPMC and subsequently dispensed to study participants. All study-supplied medications must be stored in the pharmacy. All unused supplied medications must be returned to the CRPMC after the study is completed or terminated or otherwise instructed by the study sponsor. The procedures to be followed are provided in the Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks.

Revision 2: Table 1- Summary of Services Provided to the Intervention and Active Control Arms

Diagnostic Testing	**Screening/ Enrollment**	Screening and Enrollment will occur on the mobile unit for all participants. **Screening Visit:** • HIV rapid testing • Urine ~~dip stick~~ testing for substances of abuse and MOUD.
	After Enrollment	**At week 26 and 52 Visits** **In both arms,** • HIV rapid testing (for those not previously confirmed to be HIV positive) • Rapid pregnancy testing (as appropriate)

		• Urine ~~dip stick~~ testing performed for substances of abuse and MOUD. • Collection of blood and swabs for laboratory testing for HIV, STIs and (week 52 only) incident HCV infection in those who were anti-HCV negative at study entry. Those with chronic HCV will receive HCV RNA testing at week 52. Laboratory results will not be available until after the visit; clinically-relevant results will be conveyed by navigator, clinician or trained staff member, as appropriate, in person or by phone, medical app, or letter.

Revision 2: Table 2- Overview of Medical Care Provided in the Mobile Unit for Intervention Arm Participants

Condition	Notes
OUD	MOUD will be managed on the mobile unit. Will include dispensation of drugs ~~(pending donation)~~, to include: • Buprenorphine-based medicine (sublingual and **possibly** injectable regimens) • ~~Long-acting naltrexone~~ Participants who prefer methadone will be referred to community-based services if available
Stimulant Use	Participants who also use stimulants (methamphetamine, cocaine) will be referred to 12-step meetings such as crystal meth anonymous, narcotics anonymous and alcoholics anonymous, and evidence-based behavioral treatment, where available.
HIV-ART	ART will be managed from the mobile unit for those not already in HIV care, including: • Dispensation of one first-line, single-pill regimen to participants for whom this is indicated (pending donation) • Prescription provided for fulfillment at a pharmacy if a different regimen is indicated
HIV-PrEP	PrEP will be managed from the mobile unit including: • Dispensation of ~~one,~~ single pill regimen**s for PrEP** (pending donation) • Prescription provided for fulfillment at a pharmacy if a different regimen is indicated

Revision 2: Section 6.3 Clinical Care and Navigation Visits Between Enrollment and Week 26

[…]
It is anticipated that the COVID-19 pandemic will require accommodations to how participant visits with peer navigators or on the mobile unit can be conducted. Enhanced infection control procedures such as wearing of personal protective equipment (PPE), reduced density of persons allowed in and around the unit, and thorough disinfection of the unit between participants will be undertaken. Participants will be assessed for COVID-19 before beginning a visit and deferred from continuing if COVID-19 is suspected. Guidelines for resumption of in-person visits will be per CDC and/or local guidelines for discontinuation

of isolation. CDC and local guidelines will be followed regarding quarantine of staff with potential exposure to persons with suspected COVID-19. If the intensification of the COVID-19 pandemic prevents routine in-person clinical care or navigation visits between staff and participants, the study team will use available tools and approaches to continue to provide services to participants, as possible. As of the time of the writing of this protocol, DEA regulations allow participants to be prescribed buprenorphine over the telephone with home induction. If participants have mobile phones, the study will provide airtime minutes to allow participants to continue to receive peer navigation and clinical care via telemedicine, with appropriate training of peer navigators and clinicians in these approaches. Uninterrupted provision of medications for MOUD, ART and PrEP may be instituted through in-person delivery that maintains social distancing while insuring delivery to the prescribed recipient. Measures will be taken to ensure that participants taking ART or PrEP are receiving appropriate clinical follow-up, including periodic laboratory testing. ~~The expectation that donated, long-acting buprenorphine injection will be the preferred offering for MOUD in this study will enable participants to maintain adherence with once-monthly dosing, eliminating the need to remember to take a daily dose during times of heightened disruption to daily routines.~~

Revision 2: Section 9.5 Population-Specific Considerations

[…]
In considering the risks and benefits presented by the participation of pregnant women in this study, the intervention being investigated is the *combination* of ~~*standard of care*~~ *therapies* ***commonly prescribed*** for people with OUD and people with (or at risk for) HIV, in a mobile health delivery unit, with peer navigation. The medications that will be prescribed and provided are not investigational but will be US FDA-approved medicines ~~used for their approved indication.~~**commonly used to treat or prevent these conditions.** Providing these standard therapies, in a manner that we expect will improve their uptake and adherence (i.e., in an accessible mobile health delivery unit, with supportive navigation), will not increase risks to either a pregnant woman or to her fetus greater than would be encountered if she were to obtain them in a standard clinic setting.
[…]

Revision 3: Section 6.6 Implementation Evaluation and Cost-Effectiveness Data Collection Procedures

3. Ethnographic observations of the surrounding environment and delivery of integrated healthcare and peer navigation at each study site. These data will be captured by experienced ~~research assistance~~**staff** trained in the conduct of ~~ethnographic observations~~**qualitative methods**.

- ~~—~~Landscape analysis conducted in the pre-implementation phase of the study will document the availability of MOUD, HIV, harm reduction, and primary care services regularly availble at local clinics at each study site, how these services were impacted by COVID-19, as well as structural determinants of existing service delivery (e.g. policy regulating the distribution of clean needles, public health infrastructure~~).~~
- ~~Ecological assessment check lists and field notes of "hot spots" in the community will be collected during the pre-implementation phase of the study and used to determine where integrated services should be delivered via mobile unit at each site. These assessments will be routinely conducted throughout the implemenation phase~~**)** to ensure participant recuitment and intervention delivery occur in the local areas with the greatest need.

- ~~Qualitative ethnographic observations (3-5 per site) will be conducted at each study site during the implemenation phase at two timepoints. First, at each study site within six months of the intervention implementation, and second at each site at least six months after Week 26, when the initial participants transiton from integrated health care delivered on the mobile unit to community-based services. Field notes and check lists will document contextual factors that: (i) affect protocol implementation and the process through which MOUD, ART, and PrEP services are delivered in the community and in the mobile unit; and (ii) document the patient-provider workflow and the contextual variables (environment, interpersonal) that may affect the process of initiating services in a mobile unit and transitioning to community-based services.~~
- ~~Time-and-Motion Studies will be implemented during the ethnographic field observations. They will be conducted over a two-week period at each site during study initiation and again when the intervention is running at full capacity. An experienced research assistant will collect data on the time required to complete each step of the intervention. This work may be completed as part of QA/QC activities, i.e., routine periodic observation of intervention staff to ensure they are implementing the intervention correctly. QA/QC checklists created for this staff evaluation will be used to guide the time-and-motion studies.~~ **Ecological assessments will document** ~~community- and care-environmental~~ **factors that may affect recruitment, retention and delivery of services in both arms. These brief assessments will be routinely conducted throughout the implementation phase to guide real-time improvements and refinements in the conduct of the study and to document process-oriented factors that may affect primary and secondary outcomes.**
- ~~—~~

Cost-Effectiveness Procedures

No participant-oriented procedures are required to complete the planned cost-effectiveness analyses (CEA). Data sources for ~~cost-effectiveness~~**CEA** will include estimates of effectiveness from modeling, and estimates of costs to include (1) costs of all commodities used in the intervention; (2) labor costs for intervention workers; (3) intervention startup costs; (4) average time participants spent with intervention including transportation / staff time / time for referrals; (6) local wages of target population; (5) rent; (6) maintenance; (7) volunteer activities; (8) user fees; (9) value of donated goods and services; and (10) other relevant costs, including training of providers and mobile unit fuel costs.

Cost estimates will ~~also~~ incorporate data from time-and-motion **(TAM)** studies ~~as described above in this section, which~~**. These studies** will be ~~collected~~**conducted at each study site** during **the implemenation phase at two timepoints: soon after study initiation and again when the participants have begun to transition from integrated health care delivered on the mobile unit to community-based services. These data will document the number of staff and number of staff hours involved in delivering the intervention to participants receiving (i) integrated healthcare on the mobile unit, and (ii) transitioning PWID from the mobile unit to community-based care via peer navigation. TAM studies will collect data during staff** interactions with ~~staff~~**participants**, but ~~which~~ will not entail collection of participant-specific data.

Revision 4: Section 7.1 Adverse Event Definition and Reporting

In this study, the only drugs that will be dispensed or prescribed will be US FDA-approved medications for treatment or prevention of OUD, HIV, and STIs and prescriptions for contraceptives, primary care concerns, and chronic conditions, if indicated. There are no investigational products in this protocol. Therefore, ~~there will be no~~ monitoring ~~or~~**and** reporting of unanticipated treatment-related risks ~~with~~**will be limited to** the following~~ exception; site investigators will report to the FDA any serious adverse events that are "unexpected" per the current version of the package insert for~~ **: Suspected Unexpected Serious Adverse Reactions (SUSARs) to** drugs provided **centrally by the study** for ~~MOUD,~~ ART or PrEP ~~via the FDA's MedWatch form, copying the RSC Safety Office.~~ **will be collected and reported in an expedited manner to the DAIDS Adverse Event Reporting System (DAERS) (https://rsc.niaid.nih.gov/clinical-research-sites/manual-expedited-reporting-adverse-events-daids)**...

… All SAEs will be entered into the study data base, with appropriate levels of documentation and notification of the IRB and sponsors. **SAEs will be assessed for relatedness to centrally supplied medication(s) (ART or PrEP) by the site study clinician.** ~~For this trial, the intervention is the provision of peer navigation and the approach of providing medical care in a mobile health delivery unit. Investigators will therefore need to assess whether the SAE is related to the participant's receipt of peer navigation services or receipt of medical care in the mobile health delivery unit as opposed to a conventional health care clinic.~~ SAEs are included in reports to the Data and Safety Monitoring Board (DSMB) for review.

~~There will be no~~ **In addition to** expedited reporting of ~~adverse events~~**SUSARs** to DAIDS~~. However~~, it will be important that site teams routinely review clinical events that occur among their participants and alert study leadership if any individual incidents or trends raise concern about conduct of the study at that site or raise the possibility of serious or unanticipated risks to study participants posed by the trial. If such a risk is identified, by either site staff or other study team members, it will be reported and responded to as described below in Section 7.~~6~~**4**.

7.1.1 Grading Severity of Events

The Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Corrected Version 2.1, July 2017, will be used for determining and reporting the severity of adverse events. The DAIDS grading table is available on the DAIDS Regulatory Support Center (RSC) website at ~~https://rsc.niaid.nih.gov/clinical-research-sites/daids-adverse-event-grading-tables.~~**https://rsc.niaid.nih.gov/clinical-research-sites/daids-adverse-event-grading-tables.**

7.1.2 Reporting Timeframe

The reporting period for all participants is from the time of enrollment through when a participant exits the study. However, any SAEs that come to the attention of the investigator after a participant has exited the study, but before the database has been locked, will also be reported in the same manner as when the participant was on study.

7.1.3 SUSAR Assessment

An SAE with onset after exposure to centrally supplied medication(s) (ART or PrEP) will be reported as a SUSAR if the SAE is deemed both related and unexpected. ~~These A~~assessments for relatedness and unexpectedness shall be made by a site study clinician. SUSAR assessment will be as specified in Version 2.0, January 2010 (or most current version) of the Manual for Expedited Reporting of Adverse Events (EAE) Reporting to DAIDS.

7.1.4 AE Reporting to DAIDS

For all SUSARs as defined above, DAERS, an internet-based reporting system, must be used for EAE reporting to DAIDS. In the event of system outages or technical difficulties, EAEs may be submitted via the DAIDS EAE form. This form is available on the RSC website: https://rsc.niaid.nih.gov/clinical-research-sites/paper-eae-reporting. For questions about DAERS, please contact DAIDS-ES at DAIDS-ESSupport@niaid.nih.gov. Site queries may also be sent with the DAERS application itself. For questions about EAE reporting, please contact the RSC at DAIDSRSCSafetyOffice@tech-res.com.

7.3 Other Unanticipated Problems

In addition to SAEs ~~related to the study intervention,~~ **SUSARs and** social impacts ~~and unanticipated medication-related SAEs~~, other unanticipated problems may arise in the conduct of this research. An unanticipated problem is any incident, experience, or outcome that meets all of the following criteria:

[...]

Revision 5: Section 9.1 Ethical Review

[...]
Subsequent to initial review and approval, the IRB will review the protocol at least annually. The investigators will make safety and progress reports to the IRB 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 **must comply with the requirements of 45 CFR 46.108(a)(4) and 21 CFR 56.108b for promptly reporting the following:** all unanticipated problems involving risks to human subjects or others**; serious or continuing noncompliance with applicable regulations or the requirements or determinations of their IRBs/ECs; and any suspension or termination of IRB approval**. In addition, all open ~~DSMB~~ **SMC** reports will be provided to the IRB. Study sites will submit documentation of continuing review to the DAIDS Protocol Registration Office, in accordance with the current DAIDS Protocol Registration Policy and Procedure Manual.

Revision 6: Section 9.3 Risks

[…]

We will make every effort to protect participants' confidentiality during the study, however, it is possible that others may learn of a person's participation in this study and may think that the participant is living with HIV or at high risk for acquiring HIV or may make assumptions about the participant's use of drugs. **If participants communicate with a peer navigator using texting or messaging apps and others are able to access their phone, this could be a confidentiality risk. This will be highlighted in the consent process.** The participant could face stigma related to HIV or drug use. Participants may be nervous while waiting for HIV or other test results. If the tests show that a participant has HIV or another infection, they may worry about their health and future. The questions we will ask participants about sexual behavior ~~or~~ **, medical history,** drug use **and drug treatment history, history of being incarcerated, and experiences of depression, anxiety or trauma** may make them feel uneasy.

[…]

Revision 6: APPENDIX II: SAMPLE INFORMED CONSENT FORM- MAIN STUDY

7. We will confirm if you qualify for the study.

[…]

At the Enrollment Visit**, before you're enrolled in the study,** we will:

- Ask you questions to assess for COVID-19 infection and take your temperature. If you are suspected to have COVID-19, you will need to wait until it is safe for you to be seen by study staff before continuing with the visit.
- Confirm where you live and how to contact you.
- Collect urine to test for drug use and drug treatment, STIs ~~(if you are male)~~**,** and, if you are enrolled, to check for pregnancy (if you are someone who can become pregnant)
- Collect ~*XX* mL (about *x* teaspoons) [*sites to complete*] of blood for HIV testing and STIs. If you are enrolled, we will then also test your blood for hepatitis (a liver disease) and to assess the health of your blood and liver.
- Provide you with HIV test results and HIV counseling.
- Ask you about your **sexual practices and medical history, about your history of** drug use and **drug** treatment ~~history and sexual practices.~~**.** We will also ask you about other research studies you are participating in.
- **We will ask you to show us the places on your body where you've most recently injected drugs.**

8. If you qualify, you will enter the study

If you are eligible to participate in the study, you will be enrolled during the Enrollment Visit. You will then be placed by random chance into either the group that will receive medical care in the mobile health delivery unit, or the group that will not. After that, the Enrollment Visit will continue and we will:

- Ask you questions about your medical history **including MOUD treatment, HIV risk behaviors,** and ~~how~~**participation in other research studies. We will also ask** you ~~feel~~ about ~~how~~ your ~~life is going.~~**history of being in jail or prison, and about experiences of depression, anxiety or trauma, and your use of tobacco, alcohol and other drugs.**

- Collect swabs from you to test for STIs. These swabs may be taken from the throat, rectum and vagina.
- ~~Obtain your medical history, including MOUD treatment, HIV risk behaviors, participation in other research studies~~
- Give you a physical exam, that includes measuring your height, weight, heart rate, temperature and blood pressure; looking into your ~~ears,~~ mouth and throat; listening to your heart and lungs, feeling your **neck and** abdomen, looking at your skin, arms and legs, ~~checking~~**additional procedures if indicated for** your ~~reflexes and strength~~**care** and asking you about any medicines you are taking.

[…]

9. You will have two study visits over a year. In addition to this you will work with your peer navigator several times over the first six months of the study. If you are in the group that will receive medical care in the mobile unit, you will also have medical visits in the mobile unit at various times over the first six months of the study.

Study Visits
If you join the study you will have at least two additional study visits after your Enrollment Visit. These visits will be approximately six months (26 weeks) and 12 months (52 weeks) after the Enrollment Visit.

During the week 26 and 52 study visits, we will:

- Ask you questions to assess for COVID-19 infection and take your temperature. If you are suspected to have COVID-19, you will need to wait until it is safe for you to be seen by study staff before continuing with the visit.
- Confirm where you live and how to contact you.
- Ask you questions about your sexual practices~~,~~ **and** medical history, **about your history of** drug use and drug treatment ~~history and how you feel about how your life is going~~**, about your history of being in jail or prison, and about experiences of depression, anxiety or trauma**.

[…]

Medical Care Visits in the Mobile Unit

[…]

- Give you a physical exam that may include measuring your weight, temperature, blood pressure, looking into your mouth and throat, listening to your heart and lungs, feeling your abdomen (stomach and liver), **additional procedures if indicated for your care** and asking you about any medicines you are taking.

[…]

14. There may be risks to being in this study.

[…]

DISCLOSURE OF PERSONAL INFORMATION

We will make every effort to protect your confidentiality during the study. However, it is possible that others may learn that you are part of this study and they may think that you are living with HIV or are at high risk for acquiring HIV. They could make assumptions about your use of drugs. Because of this, you could face stigma related to HIV or drug use. This could cause you trouble finding or keeping a job. You could also have problems with your family, friends and community. **If you work with a peer navigator, you may choose to communicate with your navigator by text or messaging apps. If others have access to your phone, they may be able to see these communications. You should consider carefully what kind of information you want to share in this way.** We can tell you more about how we will protect your information.

SENSITIVE QUESTIONS

The questions we will ask you, **like** about your sexual ~~behavior or~~ **practices, medical history,** drug use ~~may~~**, history of being in jail or prison, experiences of depression, anxiety or trauma may** make you feel uneasy. However, you do not have to answer any question that you do not want to and you can stop answering the questions at any time.

[…]

Revision 7: Section 10.1 Local Laboratory Specimens

As described in Section 6.0, the following types of specimens will be collected:

- Blood
- Urine
- Swabs (~~oral~~**oropharyngeal** , rectal, vaginal)

As described in Section 6.0, the following types of testing will be performed in the mobile unit or at the local laboratory:

- HIV testing – see SSP Manual
- CD4 cell count and HIV viral load testing (if HIV positive)
- Hepatitis testing, including HBsAg, HBsAb, HBcAb, HCV Ab, HAV IgG, HCV RNA (if HCV positive), and HBV DNA (if needed for clinical management
- Syphilis testing and GC/CT by NAAT: ~~oral~~**oropharyngeal** swab and rectal swab (all), vaginal swab (women only), urine (men ~~only~~**and women as a less prefered alternative to vaginal swab**).
- ~~Substance~~**The schedule of GC/CT testing by NAAT may be adjusted or prioritized at the discretion of the site investigator if there is a potential for shortage of supplies for collection and/or testing. Please see CDC recommendation September 8, 2020. https://www.cdc.gov/std/general/DCL-Diagnostic-Test-Shortage.pdf**
- **Urine substance** use testing ~~by urine dip stick~~ (must include opioid, cocaine, amphetamines, benzodiazepines)
- **Urine** MOUD testing ~~by urine dip stick~~ (must include buprenorphine and methadone)
- Urine pregnancy testing

- Chemistry testing for creatinine, ALT, AST, total bilirubin
- Hemoglobin
- HIV drug resistance testing, if needed for clinical management

[…]

Revision 7: Appendix IA

Clinical Evaluations/Procedures					
Assessment for COVID-19[2]	X	X	X	X	X
Assessment for OUD[3], recent injection drug use (track marks)		X	~~(X)~~	~~X~~	~~X~~

[…]

Laboratory Evaluations/Procedures					
MOUD testing (urine ~~dip stick~~)[13]	X	X		X	X
Substance use testing (urine~~ dip stick~~)[14]	X	X	(X)	X	X

[…]

[3] Assessment for OUD will be **performed** ~~by a validated screening a tool to be a specified~~ **using a tool provided** in the SSP Manual. All sites will use the same tool.

[…]

[5] Physical exam at enrollment to include vital signs, height, weight, general appearance, ~~head, ear, nose~~**mouth** and throat, neck, chest, abdomen, extremities~~,~~ **and** skin ~~and a brief neurologic exam~~. Additional elements at clinician's discretion for patient care.

[…]

[11] The types of samples collected (~~oral~~**oropharyngeal**, rectal, vaginal) are specified in the SSP Manual.

[…]

[17] Perform HCV viral load testing at enrollment, 26 weeks, and 52 weeks for participants who have a positive HCV Ab test. **HCV RNA viral load testing may be performed on a date after HCV Ab results are available.**

Revision 7: Appendix IB

Clinical Evaluations/Procedures					
Assessment for COVID-19[2]	X	X	X	X	X
Assessment for OUD[3], recent injection drug use (track marks)		X	~~(X)~~	~~X~~	~~X~~

[…]

Laboratory Evaluations/Procedures					
MOUD testing (urine ~~dip stick~~)[11]	X	X		X	X
Substance use testing (urine~~ dip stick~~)[12]	X	X	(X)	X	X

[…]

[3] Assessment for OUD will be ~~by a validated screening tool to be specified~~**performed using a tool provided** in the SSP Manual. All sites will use the same tool.

[…]

[5] Physical exam at enrollment to include vital signs, height, weight, ~~general appearance, head, ear, nose~~**mouth** and throat, neck, chest, abdomen, extremities~~,~~ **and** skin ~~and a brief neurologic exam~~. Additional elements at clinician's discretion for patient care.

[…]

[10] The types of samples collected (~~oral~~**oropharyngeal**~~.~~, rectal, vaginal) are specified in the SSP Manual.

[…]

[15] Perform HCV viral load testing at enrollment, 26 weeks, and 52 weeks for participants who have a positive HCV Ab test. **HCV RNA viral load testing may be performed on a date after HCV Ab results are available.**

Revision 8: Section 5.3 Provision of Peer Navigation Services

[…]

For participants with a phone, it is expected that the peer navigator will use messaging apps/texts to maintain regular contact with participant, confirm appointments, locate those who have missed scheduled visits, etc. throughout the 26 weeks of navigation ~~(cell phone minutes will be provided)~~.
[…]

Revision 8: Section 6.3 Clinical Care and Navigation Visits Between Enrollment and Week 26

[…]

As of the time of the writing of this protocol, DEA regulations allow participants to be prescribed buprenorphine over the telephone with home induction. If participants have mobile phones, ~~the study will~~ **sites may** provide ~~airtime minutes to allow participants to continue to receive~~ peer navigation and clinical care via telemedicine, with appropriate training of peer navigators and clinicians in these approaches.
[…]

Revision 8: APPENDIX II: SAMPLE INFORMED CONSENT FORM- MAIN STUDY

9. You will have two study visits over a year. In addition to this you will work with your peer navigator several times over the first six months of the study. If you are in the group that will receive medical care in the mobile unit, you will also have medical visits in the mobile unit at various times over the first six months of the study.

[…]

You will mostly work with your navigator in-person at the start of the six months. Over time you may work together more over the phone/through messaging apps. ~~The study will provide airtime minutes to allow participants who have phones to continue to receive peer navigation.~~

[…]

Revision 9: List of Abbreviations and Acronyms

[…]

~~DSMB Data and Safety Monitoring Board~~

Revision 9: Section 7.1 Adverse Event Definition and Reporting

[…]

SAEs are included in reports to the ~~Data and Safety Monitoring Board~~**Study Monitoring Committee** (**SMC**~~DSMB~~) for review.

Revision 9: Section 7.3 Safety Monitoring and Clinical Data Review

[…]

This study also will be monitored by a~~n~~ **HPTN** ~~NIAID~~ **SMC** ~~DSMB~~, which will meet at least annually to review safety and efficacy data. More frequent or *ad hoc* reviews of safety data may be conducted by the **SMC** ~~DSMB~~ as needed. The **SMC** ~~DSMB~~ may make recommendations based on review of safety and efficacy data.

Revision 9: Section 8.7 Data and Safety Monitoring Oversight

[…]

HPTN ~~NIAID DSMB~~ **SMC** oversight is planned for this study. The **SMC** ~~DSMB~~ will conduct interim reviews of study progress, including rates of participant accrual, visit retention, completion of primary and secondary endpoint collection, and, in a closed report, safety data by arm. The frequency and content of ~~DSMB~~ **SMC** reviews will be determined prior to the start of the study and outlined in the SSP Manual.

Revision 9: Section 9.1 Ethical Review

[…]

In addition, all open ~~DSMB~~ **SMC** reports will be provided to the IRB. Study sites will submit documentation of continuing review to the DAIDS Protocol Registration Office, in accordance with the current DAIDS Protocol Registration Policy and Procedure Manual.