Hepatitis C Pharmacy-based Strategy for Injectors: Phase 2 Pilot Study (HepPSI Study Phase 2)

IRB Protocol Number: STUDY00010476

National Clinical Trial (NCT) Identified Number: NCT04698629

Principal Investigator: Judith Tsui, MD, MPH

Funded by: NIDA 1R34DA047660

Version Number: v2.7

10 May 2022

This is the Protocol for "A Prospective Study to Pilot a Community-pharmacy Program for Medications to Treat HCV, and Prevent Overdose and HIV, Among PWID With HCV," also known as Hepatitis C Pharmacy-based Strategy for Injectors: Phase 2 (HepPSI Study Phase 2)

Table of Contents

STATEMENT OF COMPLIANCE

The HepPSI Study will be carried out in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812)

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

A protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any major amendments to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

STUDY TEAM MEMBERS AND OTHER CONTACTS

UW Research Group

Judith Tsui, PI
Email: *tsuij@uw.edu*
Office number: 206-744-1835

Alex Gojic, Research Coordinator
Email: *agojic@uw.edu*
Office number: 206-744-1801

Ellie Pickering, Research Assistant
Email: *eipicke@uw.edu*
Office number: 206-744-1838

Sarah Glick, PhD
Email: *snglick@uw.edu*

Emily Williams
Email: *emily.williams3@va.gov*

Elizabeth Austin, MPH
Email: *austie@uw.edu*

Michael Ninburg
Email: *mhninburg@hepeducation.org*

John Scott
Email: *jdscott@uw.edu*

Joanne D. Stekler
Email: *jstekler@uw.edu*

Other Contacts

Elyse Tung
Email: *etung@kelley-ross.com*

Kathleen Pierce
Email: *kpierce@kelley-ross.com*

Madison McPadden
Email: *madison@hepeducation.org*

Sarah Deutsch
Email:*sarah@hepeducation.org*

Angelica Bedrosian
Email:*angelica@hepeducation.org*

Sarah Villafuerte
Email:*srv@hepeducation.org*

1 INTRODUCTION

1.1 OVERVIEW

This is the protocol for a single-arm, prospective observational study concerned with the feasibility and acceptability of a newly implemented community pharmacy model to treat HCV for persons who inject drugs who historically have faced many barriers to care within conventional healthcare systems.

1.2 BACKGROUND

Opioid use disorder (OUD) and related health problems have emerged as a national health crisis. In 2017, an estimated 1.7 million American adults had a pharmaceutical opioid use disorder (OUD), and 0.7 million had a heroin-involved OUD.(1) The increase in opioid abuse and injection drug use (IDU) has led to a rise in overdose deaths(2) and new cases of HIV and hepatitis C virus infection (HCV).(3, 4) Injection drug use is the primary mode of transmission for HCV infection in the U.S.(5-7) After more than a decade of decline, the incidence of HCV is again on the rise, particularly among young adults, (8, 9) and in rural areas.(10) The recent outbreak in rural Indiana is also a stark reminder of the ever-present risk for HIV associated with IDU. (4)

We are at a unique historical moment, as we possess effective medications that can improve and sustain the lives of people who inject drugs (PWID). Currently there are medications that can be prescribed to 1) cure HCV (directly-acting antivirals), 2) prevent HIV infection (Pre-exposure Prophylaxis [PrEP]) and treat/prevent overdose (naloxone and medications to treat OUD). Furthermore, there is an unprecedented opportunity to eliminate HCV, a disease that affects the majority of PWID and causes substantial morbidity and mortality.(11) With the introduction of new directly-acting antiviral (DAA) medications, nearly all patients with HCV can be cured with 2–3 months of oral medications with minimal side effects. Expanding HCV treatment to populations at risk can reduce incidence and prevalence over time(12) (a concept known as “treatment as prevention”) and as such, the World Health Organization has proposed an ambitious goal to eliminate HCV by 2030.(13) Unfortunately, there is a translational gap in the delivery of these medications to PWID. Prior studies, including our own, show that <10% of PWID have been successfully treated.(14-16) While models of HCV care integrated in addiction treatment have been successful,(17, 18) many PWID lack access. Moreover, there are still major gaps in access to naloxone and PrEP among PWID.(19-22)

A community-pharmacy model has the potential to expand health services delivery and provide comprehensive, patient-centered care to PWID. For decades, pharmacists have been utilized in clinic and hospital settings to assist with management of acute and chronic diseases.(23, 24) Many successful specialty clinics that treat HCV currently depend heavily on the services of pharmacists. Pharmacists have extensive clinical training and highly developed expertise in pharmacotherapy, which makes them ideally suited for the management of HCV. Through the mechanism of Collaborative Drug Therapy Agreements (CDTAs), pharmacists are granted the authority to autonomously perform tasks related to medication management in collaboration with the practitioner through detailed protocols.(25) Restrictions on these designated services vary from state to state but can include all aspects of

medication management from testing and counseling to prescribing and dispensing medication.(26) Kelley-Ross, our community-pharmacy partner, in 2012 successfully implemented a take-home naloxone program for persons at risk for opioid overdose(68) and more recently started a program for providing PrEP ("One-Step PrEP"),(27) which enables persons to receive all services (screening, counseling, prescribing, dispensing, and follow-up) at their pharmacy site.

The HepPSI Study builds upon the existing Kelley-Ross PrEP clinic platform to offer a comprehensive package for HCV treatment that would also include access to naloxone and PrEP on-site, as well as linkages to low-threshold opioid treatment programs that provide buprenorphine or methadone. During Phase 1 of this research, we conducted qualitative interviews with people who inject drugs living with hepatitis C regarding motivators, barriers, and preferences for HCV treatment. Phase 1 findings have since been used to inform the development of the community-pharmacy program (One-Step Hep C Free) that will be piloted in this Phase 2 research.

2 STUDY OBJECTIVE

Single-arm, prospective observational study of 40 adult persons who inject drugs (PWID) who screen positive for hepatitis C virus (HCV) with a reactive antibody test at community sites who are offered facilitated linkage to community-pharmacy program through patient navigators. Individuals who are eligible and enroll will complete a baseline survey to assess sociodemographics, substance use, HIV risk behaviors, and awareness of and interest in HCV treatment. After the survey, the participants will be linked to the community-pharmacy program, via the patient navigator, where treatment for HCV and opioid use disorder (OUD), as well as pre-exposure prophylaxis (PrEP), Naloxone and vaccinations, will be offered to participants.

After 6 months, participants will complete a follow-up survey, which will include questions on: whether an evaluation for HCV occurred at the community pharmacy or elsewhere, whether HCV treatment was initiated since baseline visit and whether cure was achieved, substance use, HIV risk behaviors, receipt of medications for opioid use disorder, Naloxone and PrEP receipt, medication adherence, and information on injecting networks.

3 STUDY DESIGN

3.1 OVERALL DESIGN

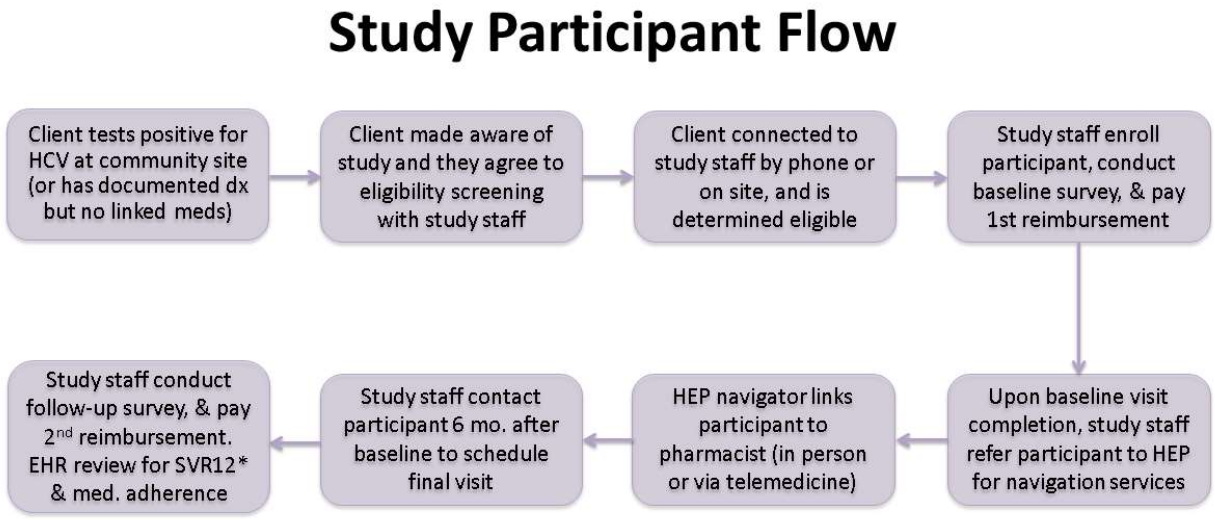
Forty participants will complete two study visits during this time. After screening and enrollment at a community site, participants will complete a Baseline Survey. Upon completion of the Baseline Visit, participants will either be connected to a patient navigator responsible for linking the participants to the community-pharmacist OR referred directly to the community-pharmacist if on site. Six months after the initial Baseline Visit, participants will be contacted to complete a final Follow-up Survey.

3.1.1 COMPENSATION

Participants will be compensated for their time and may receive up to $80. Payment for visits will differ as follows:

- $30 reimbursement for the completion of Baseline Survey
- $50 reimbursement for the completion of Follow-up Survey

3.1.2 STUDY SCHEMA



*For individuals who have SVR12 data missing at 6-month visit, additional chart reviews will occur up to 3 months after SVR12.

3.2 ELIGIBILITY

3.2.1 INCLUSION CRITERIA

1. ≥18 years old
2. Reports injecting drugs with 90 days of screening
3. Positive HCV test documented (screening antibody test or viral load test)
4. Not currently taking medications to treat HCV, and never previously treated with direct-acting antivirals (DAAs) for HCV
5. Willing to undergo evaluation for HCV through a community pharmacy program and work with Patient Navigators
6. Provides release of information ("ROI") to access community pharmacy program records and/or other HCV treatment providers

3.2.2 EXCLUSION CRITERIA

1. People who plan to leave the Seattle area within 6 months
2. Who do not wish to be treated for their HCV infection
3. Who are known to be pregnant
4. Who report impending incarceration that would disrupt clinical care
5. Who are not comfortable reading and speaking English

At researcher's discretion, participants may be excluded if their behavior poses safety concerns for research staff or other participants.

3.3 RECRUITMENT AND RETENTION STRATEGIES

3.3.1 RECRUITMENT STRATEGY

Subjects will be recruited though (1) syringe services programs (including the Downtown Needle Exchange at Robert Clewis Center) (2) opioid treatment and behavioral health programs (including Evergreen Treatment Services) (3) community-based agencies that serve persons who inject drugs living with HCV (including the Hepatitis Education Project), and (4) low-income housing sites/homeless shelters. We will also recruit participants from the Phase 1 qualitative study who gave permission to be contacted in the future to participate in this new study.

The uncertainty of the COVID-19 response's impact has led us to develop multiple recruitment plans:

1. Research staff may receive referrals to the study from personnel who interact with potential subjects at these sites.
2. Potential participants may self-refer to the study by contacting Research staff directly using information on public recruitment materials.
3. If research staff are able to go to sites listed above for recruitment, they will approach potential subjects directly.

We will primarily rely on staff at the community sites listed above to make referrals to study staff members and will keep signage and flyers on-site at these locations with our recruitment times at a given site. When appropriate, we may directly approach potential participants at these sites. Prior to conducting eligibility screening visits in person at these agencies, staff will identify a physical space at a given agency that will allow staff to maintain confidentiality.

3.3.2 RETENTION STRATEGY

During the consent process, study staff will collect the participant's contact information (HepPSI Participant Locator Form, Appendix 8.1). Participants consent to providing additional contacts in case a

study staff person is unable to reach the study participant. Forms have space for up to four additional contacts. The study staff person collecting this information will inform the participant, again, that these individuals will only be contacted if they themselves cannot be reached. This form will be stored in a locked filing cabinet with the research team and should never be stored with participant study data. This information will be entered into the HepPSI Phase 2 Participant Tracking Database project on REDCap under the form "Participant Contact Information".

Research staff will contact participants every 2 months to ensure contact information is up to date and to check-in. Staff will utilize Patient Navigator to stay connected with participants when possible. Each time contact with a participant is made, that instance will be documented in the HepPSI Phase 2 Participant Tracking Database project on REDCap under the form "Contact Log".

For further information regarding HepPSI Phase 2 Participant Tracking via REDCap, refer to the **HepPSI Phase 2 REDCap Manual of Procedures.**

3.3.3 PATIENT NAVIGATOR RESPONSIBILITIES

Primary

1. Facilitated linkage to community-pharmacy program
2. Outreach at syringe exchange programs, addiction treatment programs, homeless shelters, and advocacy groups for individuals who may be eligible for the community-pharmacy program

Secondary

1. Maintain contact with participants throughout treatment; facilitated by medical case management intake (see section 8.4)
2. Refer interested participants to other resources (including linkages to existing "low-threshold" programs that offer OUD medications in close proximity)

3.4 STUDY SITES

3.4.1 HEPATITIS EDUCATION PROJECT

The Hepatitis Education Project (HEP) is an advocacy group that provides numerous services for persons with HCV, including medical case management, Hepatitis B and C screening, a syringe access program, and more. Participants will be recruited from the various community sites where the Hepatitis Education Project currently offers HCV screening. This includes local syringe exchange programs, opioid treatment programs, homeless and urban drop-in shelters, low income housing units, and the main HEP office near downtown Seattle*.

Community Pharmacists will be onsite at the main HEP office during their syringe service program hours (Thursdays 1-5pm, as of 11/05/2020).

*11/05/2020 – as a result of the COVID-19 Pandemic, HEP has limited their outreach services and general operations. Their syringe service program will be located outdoors in a lot adjacent to the main HEP office.

3.4.2 EVERGREEN TREATMENT SERVICES/ DOWNTOWN EMERGENCY SERVICE CENTER

Evergreen Treatment Services (ETS) is an opioid treatment program organization with three locations in the Puget Sound region. Study recruitment will be focused at the Seattle Clinic site where ETS patient attend medical provider appointments, counseling services, and receive their medications for opioid use disorder (MOUD). ETS medical providers and counselors can refer their patients for HCV treatment to the Community Pharmacists and Patient Navigator when both are located at the ETS Seattle Clinic one morning a week, or directly to the Kelley-Ross pharmacy/HEP locations. Community Pharmacists and Patient Navigator will be onsite at the Seattle Clinic on Thursdays mornings 9am-12pm, as of 03/04/2021.

Downtown Emergency Service Center (DESC) provides supportive housing, case management, substance use disorder treatment, and medical services at 12 locations throughout Seattle and several other adjacent cities. DESC providers at several locations are able to refer clients interested to HCV care to the Community Pharmacists for treatment. However, given the limited space available at DESC locations, DESC clients who are interested in participating in the study would need to travel to HEP so that research staff could screen for eligibility and complete consent procedures.

4 STUDY ASSESSMENTS AND PROCEDURES

4.1 SCREENING

Staff at community sites will be educated about the study and asked to refer interested individuals who may be eligible. If research staff are onsite, community site staff will “hand off” potential participants to speak with research staff directly. Otherwise, interested individuals will be referred or self-refer to research staff via phone or email. Once connected to interested individuals, the trained research staff will explain the study and screen them in a private space on site or over the phone (See IRB-approved Screening Script, Appendix 8.2). Each screened subject will receive a unique screening ID (YXXX) that will be documented in a protected spreadsheet, along with the results of the screening encounter.

4.1.1 DETERMINING ELIGIBILITY

A REDCap Screener assessment has been designed to notify the assessor when a subject meets all inclusion criteria and is considered eligible. If an eligible subject is uninterested in participating, the

assessor should document the reason on REDCap. Please refer to the **HepPSI Phase 2 REDCap Manual of Procedures** for further information and procedures when eligibility has been determined.

If time allows, consenting, enrollment, and the baseline visit will follow the screening visit on the same day.

4.1.2 DATA COLLECTED DURING SCREENING

Data collected during screening will be captured in REDCap. This data includes the subject's date of birth, basic demographic information, any major comorbidities that would preclude treatment through the community-pharmacy program, and other items related to determining whether the subject meets inclusion criteria. The screener form is coded in REDCap to automatically notify the assessor on whether the subject is eligible or ineligible to participate in the study.

No personal identifying information will be entered into the REDCap Phase 2 Screener Project.

4.2 ENROLLMENT PROCEDURES

Once deemed eligible to participate in the study, study staff will facilitate enrollment procedures, beginning with informed consent after which subjects will confirm their intent to continue the enrollment process. During the enrollment process, participants will also consent to provide contact and alternate contact information for tracking purposes (See Retention Strategies). At the end of the enrollment process, participants will be assigned a unique Study ID (40XX).

4.2.1 INFORMED CONSENT

Consent will be obtained by trained research staff from patients who meet all inclusion criteria. The PI will not consent patients. The process of consenting participants will occur in a private space. The study will be described and the potential subject will be asked if they have any questions about the study procedures. If the individual agrees to participate after consideration of all options, they will provide written consent.

The research staff will give the subjects adequate time to look at and read the informed consent form, summarize each section and ask the subjects if they understand and if they have any questions about the study procedure. As part of the informed consent, the research staff may assess the subjects' understanding of the information presented during the consent process. This may include having the subject articulate their understanding of the study purpose, procedures, risks, etc.

After reading through informed the consent form, subjects who agree to participate will sign two copies. One copy will be sent home with the participant and the other will be stored in a locked cabinet with the research study team. This form should never be stored with participant study data.

4.2.1.1 HIPAA AUTHORIZATION AND RELEASE OF INFORMATION FORMS

4.2.1.1.1 HIPAA AUTHORIZATION FORM

The University of Washington IRB office has been contacted to obtain an organization specific HIPAA Authorization template, and study staff made necessary changes to the template to meet study needs. Study staff must have the study participant complete and sign two HIPAA Authorization Forms. One form will be given to the participant and the other will be stored in a locked filing cabinet with the research team. This form should never be stored with participant study data.

4.2.1.1.2 RELEASE OF INFORMATION FORMS

Participants will be asked to sign Release of Information (ROI) forms that allow study staff to disclose medical information relevant to the study. Medical information may include sexually transmitted disease, acquired immunodeficiency syndrome (AIDS), or human immunodeficiency virus (HIV). Participant's health records may also include sensitive information about behavioral or mental health services and treatment for alcohol and drug abuse

Upon enrolling in the study, participants will sign two ROI forms permitting disclosure of medical information: one for Hepatitis Education Project, and one for Kelley-Ross Pharmacy.

4.3 STUDY VISITS

Participants will be enrolled and complete the baseline assessment at study start. Over the course of the study, two total assessments will be conducted: one at baseline visit (study start) and one at final visit (six months post-study start date). Study visits will take place in-person at Hepatitis Education Project or other community sites hosting HEP services. Due to the COVID-19 pandemic, study staff are prepared to transition to remote visits if need be. After the baseline study visit, participants will receive a $30 reimbursement, and then they will be linked to a HEP Patient Navigator who will facilitate their connection to the community pharmacy program. After the final study visit, participants will receive a $50 reimbursement.

Assessment data will be collected primarily on REDCap, but research staff completing research visits should have, at all times, IRB approved paper assessment copies in case of any technical difficulties with study laptop.

Besides having paper copies of all assessments, research staff will carry a small binder of Assessment Cards. These Assessment cards are response options to all assessment items in large printed font to assist participants during the assessments.

4.3.1 ASSESSMENTS OVERVIEW

The baseline survey will assess socio-demographics, substance use*, HIV risk behaviors*, and awareness of and interest in HCV treatment. After 6 months, participants will complete a follow-up (final) survey which will include information on:

a) Whether an evaluation for HCV occurred at the community pharmacy or another site since the baseline visit

b) Whether HCV treatment was initiated since baseline visit— assessed by self-report and pharmacy/medical records for confirmation.

c) For patients who report that they have not been treated for HCV, reasons why (co-morbid conditions interfering, competing priorities, lack of interest, spontaneous clearance, etc.).

d) Substance use*—measured by the modified Addiction Severity Index (ASI)(28)

e) HIV Risk Behaviors*—measured by the modified HIV Risk Behaviors Survey (RBS)(29, 30)

f) Receipt of naloxone, PrEP, and medications for OUD: self-report, confirmed with review of pharmacy record of dispensation/refills.

g) Medication satisfaction, tailored to direct-acting antiviral treatment

h) Medication adherence— assessed by record of medication pick-ups and also through self-report

i) Injecting network (number of partners they have shared injected drugs with and, of those, how many they would be willing to refer to the site where they were treated)

j) Completion of HCV Treatment – self-report and medical record chart review to assess if HCV treatment was fully completed.

k) Sustain Virologic Response (SVR12) – Medical record review to assess obtainment of SVR12 results among participants who complete HCV treatment. For patients missing SVR12 results at the time of 6 month follow-up (either due to not yet having reached 12 post-treatment date or simply missing data), chart reviews will be conducted again up to 3 months after the 6 month follow-up.

4.3.1.1 DATA VARIABLE TABLE

	Baseline Visit	Final Visit	Medical Record Review
Social History (age, sex, gender, housing/employment status, healthcare insurance coverage)	X	X	
Treatment history (methadone, buprenorphine, direct-acting antivirals, interferon, pre-exposure prophylaxis)	X	X	
Lifetime (ASI- drug of concern + injection drug use) 30 days (ASI)	X X	 X	
HIV Risk Behaviors (RBS)	X	X	
Depression (PHQ-9)	X	X	
Anxiety (GAD-7)	X	X	
Value of Health (EQ-5D-5L)	X	X	
HCV Treatment experience/satisfaction		X	
Pharmacist care satisfaction		X	
Patient Navigator satisfaction		X	
Injection Network/Community Pharmacy Recommendation		X	
HCV Treatment Completion		X	X

Sustain Virologic Response (SVR12)			X

4.3.2 DATA COLLECTION TOOLS

The primary method of collecting data will be completed electronically through REDCap. REDCap is a web-based HIPAA compliant platform that will be used to collect and export participant data. Each participant will have a unique Study ID (40XX) that will be used to distinguish their REDCap records. Identifiable participant information will be kept separately from participant data. In instances where paper assessments are used, those documents will be stored in a locked cabinet at Harborview Medical Center, separated from any identifiable patient information as well. Study ID assignments and participant names will be tracked through a password-protected Excel spreadsheet that will be stored on a secure drive accessible to only study staff. This Excel spreadsheet will also document information regarding study visits, including start date, the projected final visit date, and actual final visit date, as well as any study withdrawal details.

Further information about REDCap can be found in the **HepPSI REDCap Manual of Procedures**.

4.4 PAYMENT TRACKING

After completing a research visit, research staff administering assessments will provide the participant their monetary reimbursement for the information they provided and their time. The reimbursements should be kept in an envelope when given to the participant. It is important that research staff track participant payments and document that the participant did in fact receive their payment. Research staff should carry paper copies of the Participant Payment Tracking Form and have the participant sign and date that they received their incentive. These forms should then be kept and locked in designated study file folders, away from any participant data. Additionally, at the bottom of the verification form is a HepPSI Payment Reference number. This number will be entered into the REDCap HepPSI Participant Tracking Database project in the “Participant Visit and Payment Log” form within each participant’s record.

Study staff should work with their office’s designated finance officer to determine the set-up and maintenance of field advances. Money and ATM card will be kept in a secure lock-box. Along with the money and ATM, the study staff should have a log of when the lock-box is accessed for proper tracking purposes. Research staff should also keep every ATM receipt as their office’s finance officer will need this to reconcile the budget and field advances later at the end of the budget year and end of project.

5 PARTICIPANT SAFETY

5.1 POTENTIAL RISKS

5.1.1 PSYCHOLOGICAL STRESS

There are no anticipated risks to participants' physical health during this study. However, there are other risks to be considered. Talking about sensitive topics may cause participants to feel uncomfortable or distressed. This will be minimized by training the research staff to look for signs of distress and provide reassurance. Participants will be reminded that they have the option to refuse answering assessment questions that cause undue distress. They will also be offered regular breaks during the assessment session.

5.1.2 LOSS OF CONFIDENTIALITY

Breach of security of data collected is a potential risk for study participants. To reduce this risk, all data analysis will be conducted on data identified by study ID only and will not include any direct identifiers. Only a unique ID will be used to identify individual data collection forms; no subject names will be recorded on data collection forms. A crosswalk file linking subject identifiers and unique ID will be stored in a separate location from the data. All data will be stored on secure server and access to the data will be restricted by means of unique login names and passwords. All study files with identifiable information will be kept in locked file cabinets in a private office space, and only research staff will have access.

5.2 PRIVACY AND CONFIDENTIALITY

Study staff will safeguard the confidentiality of personal data collected from study participants through the use of Study ID codes instead of names on all research materials. The link referencing code number to name will be kept in a password-protected file accessible by computers that are password protected, as will all files related to the study.

Any printed study materials will be marked with participant's code and kept in a locked file cabinet in a private office. No one other than study staff will have access to these materials. The list relating names to number codes will be destroyed at the end of the investigation.

Only trained and approved study staff (research assistants, coordinators or PI) will interview subjects. We will work to arrange assessments with participants at a time and location so they can have privacy.

Participants will be covered by the Certificate of Confidentiality. This will help protect participant privacy by allowing study team members to refuse to provide identifying information about participants even if asked to by a court of law. We will use the Certificate to resist any demands for identifying information.

This does not prevent participants from sharing information about themselves or a part of the research if they choose to do so.

5.2.1 REDCAP

Study staff will enter data captured in visits from all participants into REDCap. The system is password protected and restricted to study staff. Participant assessment data, screening data, and tracking/payment information are each stored in separate REDCap projects with different record IDs. Research staff will have paper copies of all assessments in case REDCap is not accessible to collect participant's information.

5.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

5.3.1 DEFINITION OF ADVERSE EVENTS (AE)

Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure.

5.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

An adverse event (AE) or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect.

5.3.3 CLASSIFICATION OF AN ADVERSE EVENT

Adequate review, assessment, and monitoring of adverse events require that they be classified as to severity, expectedness, and potential relatedness to the study intervention. Study protocols will include a description of how adverse events will be classified in these terms and the appropriate course of action.

5.3.3.1 SEVERITY OF EVENT

Classifications include the following:

Mild: Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.

Moderate: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning

Severe: Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating

Severity is not synonymous with seriousness. A severe rash is not likely to be an SAE.
Likewise, a severe headache is not necessarily an SAE. However, mild chest pain may result in a day's hospitalization and thus is an SAE.

5.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

The site investigator assesses the potential event relationship to the study intervention and/or participation. A comprehensive scale in common use to categorize an event is:

- Definitely Related: The adverse event is clearly related to the investigational agent/procedure – i.e. an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject's clinical state.
- Possibly Related: An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.
- Not Related: The adverse event is clearly not related to the investigational agent/procedure. – i.e. another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

5.3.3.3 EXPECTEDNESS

AEs must be assessed as to whether they were expected to occur or unexpected, meaning not anticipated based on current knowledge found in the protocol, investigator brochure, product insert, or label. Categories are:

Unexpected - nature or severity of the event is not consistent with information about the condition under study or intervention in the protocol, consent form, product brochure, or investigator brochure.

Expected - event is known to be associated with the intervention or condition under study.

5.3.4 ADVERSE EVENT (AND SAE) REPORTING

Adverse Events (AEs) and Serious Adverse Events (SAEs) have specific reporting procedures. AEs will be collected via REDCap. If REDCap is down, research staff should use the paper form **Adverse Event Reporting Form (See Appendix 8.3)**.

All AEs are collected on an Adverse Event Form that includes the date of the event, what occurred, actions taken by project staff, planned follow up (if any) , whether the event appears to be related to the intervention, the seriousness of the event, and whether participant will continue in the study (see appendix). All AEs experienced by the participant during the time frame specified in the protocol (e.g., from the time of study drug administration through the end of the study intervention period) are to be reported.

Please note that the AE form contains a column to indicate whether the event is serious. Thus, SAEs are a subset of the reported AEs.

All SAEs, unless otherwise specified in the protocol and approved by the IRB or DSMP (as applicable), require expedited reporting by the Principal Investigator to the study's safety monitoring bodies. Serious adverse events will be reported to the site PI within 24 hours of research staff becoming aware of the event. SAEs that are unanticipated problems will be reported to the NIDA PO within 24 hours by email and a written follow up will be submitted within 2 days of the event.

Any IRB action response will be reported to NIDA PO within 3 days of the receipt of notice of the action.

5.4 DATA SAFETY MONITORING PLAN

5.4.1 SAFETY OVERSIGHT

Principal Investigator (PI) will be responsible for ensuring participants' safety on a daily basis. The Independent Safety Monitor will act in an advisory capacity to monitor participant safety, to evaluate the progress of the study, and to review procedures for maintaining the data confidentiality, collection quality, management, and analyses.

5.4.1.1 INDEPENDENT SAFETY MONITOR

Jeanette Tetrault, MD – Professor at Yale University School of Medicine

The Independent Safety Monitor will oversee the safety of the participants and the validity and integrity of the data. Responsibilities will include:

• Evaluating the research protocols and plans for safety and data monitoring

• Evaluating the progress of the study, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, performance of the trial sites, and other factors that can affect study outcome

• Considering factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics or practicality of the trial

• Reviewing study site performance, making recommendations and assisting in the resolution of problems reported by study team

• Ensuring the confidentiality of the trial data and the results of monitoring

5.4.1.2 INDEPENDENT SAFETY MONITOR MEETINGS

The PI will meet annually with the ISM by teleconference. At each meeting the ISM will review individual SAEs and cumulative AE reports. Following each meeting, the monitor will make recommendations on continuation, modification, or termination of the study.

5.5 COVID-19 REGULATIONS

Study staff will follow UW Human Subjects Division protocols regarding COVID-19 safety. Staff members will wear recommended face coverings in accordance with UW guidelines to prevent possible SARS-CoV-2 transmission, and will ask participants to do the same. When possible to do so while maintaining confidentiality, visits will be conducted in well-ventilated spaces, rooms with open windows, contained spaces outdoors, etc. As is expected at the time of writing, staff members will complete the COVID-19 Symptoms Self-Attestation for On-Site Personnel and Visitors on Workday prior to conducting in-person visits. As recommendations and protocols for COVID-19 safety are subject to change, we will adjust our procedures to match the most up-to-date recommendations and protocols available.

Kelley-Ross Pharmacy Program and HEP staff will operate under the COVID-19 safety protocols of their respective home agencies.

6 STATISTICAL ANALYSES

This study will provide estimates of what proportion of HCV-infected PWID successfully link to and utilize the community-pharmacy model.

The primary feasibility/acceptability outcome will be the proportion (and 95% confidence intervals) of participants who are evaluated for HCV treatment in the community-pharmacy program. Secondarily, we will evaluate HCV treatment outcomes (initiation, completion, and SVR12/cure), medication adherence, substance use, HIV risk

behaviors, and receipt of other medications (naloxone, PrEP, and medications for OUD). Finally, we will assess treatment satisfaction and willingness to refer an injecting partner to the community pharmacy for treatment.

Given our estimated sample size of 40 we can provide a range of estimates and 95% confidence intervals (CIs) for the following hypothetical scenarios: Using binomial "exact" calculation to estimate CIs, if we assume 0.5 of the sample (i.e., 20/40 participants) achieves the outcome, the estimated 95% CI is 0.34 to 0.66. If 10/40 achieves the outcome (0.25), the estimated 95% CI is 0.13-0.41; if 30/40 achieves the outcome (0.75) the estimated 95% CI is 0.59-0.87.

7 REFERENCES

1. Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health. Rockville, MD2018 [Available from: *https://www.samhsa.gov/data/report/2017-nsduh-annual-national-report*.

2. Prevention CfDCa. Drug Overdose Death Data 2017 [updated December 19, 2017. Available from: *https://www.cdc.gov/drugoverdose/data/statedeaths.html*.

3. Zibbell JE, Asher AK, Patel RC, Kupronis B, Iqbal K, Ward JW, et al. Increases in Acute Hepatitis C Virus Infection Related to a Growing Opioid Epidemic and Associated Injection Drug Use, United States, 2004 to 2014. Am J Public Health. 2018;108(2):175-81.

4. Peters PJ, Pontones P, Hoover KW, Patel MR, Galang RR, Shields J, et al. HIV Infection Linked to Injection Use of Oxymorphone in Indiana, 2014-2015. N Engl J Med. 2016;375(3):229-39.

5. Klevens RM, Hu DJ, Jiles R, Holmberg SD. Evolving epidemiology of hepatitis C virus in the United States. Clin Infect Dis. 2012;55 Suppl 1:S3-9.

6. Edlin BR, Carden MR. Injection drug users: the overlooked core of the hepatitis C epidemic. Clin Infect Dis. 2006;42(5):673-6.

7. Williams IT, Bell BP, Kuhnert W, Alter MJ. Incidence and transmission patterns of acute hepatitis C in the United States, 1982-2006. Arch Intern Med. 2011;171(3):242-8.

8. Centers for Disease Control and Prevention. Notes from the field: risk factors for hepatitis C virus infections among young adults--Massachusetts, 2010. MMWR Morb Mortal Wkly Rep. 2011;60(42):1457-8.

9. Suryaprasad AG, White JZ, Xu F, Eichler BA, Hamilton J, Patel A, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. Clin Infect Dis. 2014;59(10):1411-9.

10. Zibbell JE, Iqbal K, Patel RC, Suryaprasad A, Sanders KJ, Moore-Moravian L, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged </=30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. MMWR Morb Mortal Wkly Rep. 2015;64(17):453-8.

11. Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising Mortality Associated With Hepatitis C Virus in the United States, 2003-2013. Clin Infect Dis. 2016;62(10):1287-8.

12. Martin NK, Vickerman P, Grebely J, Hellard M, Hutchinson SJ, Lima VD, et al. Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. Hepatology. 2013;58(5):1598-609.

13. World Health Organization. Combating hepatitis B and C to reach elimination by 2030. Switzerland2016.

14. Carey KJ, Huang W, Linas BP, Tsui JI. Hepatitis C Virus Testing and Treatment Among Persons Receiving Buprenorphine in an Office-Based Program for Opioid Use Disorders. J Subst Abuse Treat. 2016;66:54-9.

15. Mehta SH, Genberg BL, Astemborski J, Kavasery R, Kirk GD, Vlahov D, et al. Limited uptake of hepatitis C treatment among injection drug users. J Community Health. 2008;33(3):126-33.

16. Tsui JI, Miller CM, Scott JD, Corcorran MA, Dombrowski JC, Glick SN. Hepatitis C Continuum of Care and Utilization of Healthcare and Harm Reduction Services among Persons who Inject Drugs in Seattle. Drug Alcohol Depend. 2018.

17. Litwin AH, Soloway IJ, Cockerham-Colas L, Reynoso S, Heo M, Tenore C, et al. Successful treatment of chronic hepatitis C with triple therapy in an opioid agonist treatment program. The International journal on drug policy. 2015;26(10):1014-9.

18. Litwin AH, Harris KA, Jr., Nahvi S, Zamor PJ, Soloway IJ, Tenore PL, et al. Successful treatment of chronic hepatitis C with pegylated interferon in combination with ribavirin in a methadone maintenance treatment program. J Subst Abuse Treat. 2009;37(1):32-40.

19. Glick SN, Tsui J, Hanrahan M, Banta-Green CJ, Thiede H. Naloxone uptake and use among people who inject drugs in the Seattle area, 2009–2015. Drug Alcohol Depend. 2017;171.

20. Freeman PR, Hankosky ER, Lofwall MR, Talbert JC. The changing landscape of naloxone availability in the United States, 2011 - 2017. Drug Alcohol Depend. 2018;191:361-4.

21. Edelman EJ, Moore BA, Calabrese SK, Berkenblit G, Cunningham C, Patel V, et al. Primary Care Physicians' Willingness to Prescribe HIV Pre-exposure Prophylaxis for People who Inject Drugs. AIDS Behav. 2017;21(4):1025-33.

22. Adams LM, Balderson BH. HIV providers' likelihood to prescribe pre-exposure prophylaxis (PrEP) for HIV prevention differs by patient type: a short report. AIDS Care. 2016;28(9):1154-8.

23. Santschi V, Chiolero A, Burnand B, Colosimo AL, Paradis G. Impact of pharmacist care in the management of cardiovascular disease risk factors: a systematic review and meta-analysis of randomized trials. Arch Intern Med. 2011;171(16):1441-53.

24. Bond CA, Raehl CL. Pharmacist-provided anticoagulation management in United States hospitals: death rates, length of stay, Medicare charges, bleeding complications, and transfusions. Pharmacotherapy. 2004;24(8):953-63.

25. Snyder ME, Earl TR, Gilchrist S, Greenberg M, Heisler H, Revels M, et al. Collaborative drug therapy management: case studies of three community-based models of care. Prev Chronic Dis. 2015;12:E39.

26. Association; AP. Consortium recommendations for advancing pharmacists' patient care services and collaborative practice agreements. J Am Pharm Assoc. 2013;53(2):e132-41.

27. Tung E, Thomas A, Eichner A, Shalit P, editors. Feasibility of a pharmacist-run HIV PrEP clinic in a community pharmacy setting. Conference on Retroviruses and Opportunistic Infections; 2017.

28. McLellan AT, Luborsky L, Woody GE, O'Brien CP. An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. J Nerv Ment Dis. 1980;168(1):26-33.

29. Weatherby NL, Needle R, Cesari H, Booth R, McCoy CB, Watters JK, et al. Validity of self-reported drug use among injection drug users and crack cocaine users recruited through street outreach. Eval Prog Plann. 1994;17(4):347-55.

30. Needle R, Fisher DG, Weatherby N, Chitwood D, Brown B, Cesari H, et al. Reliability of self-reported HIV risk behaviors of drug users. Psychol Addict Behav. 1995;9(4):9.

8 APPENDICES

8.1 PARTICIPANT LOCATOR FORM

HepPSI Phase II Participant Contact Document

Do not list the participant's Study ID Number on this document.

Participant's personal contact information

Name on medical records - legal (Last, First)	
Name you go by, if different	**Pronouns you use** ☐ She/her ☐ They/them ☐ He/him ☐ Something else: _____
DOB (MM/DD/YYYY)	**SSN** (if none, use 999-99-9999)
Mailing address 1:	**Do you receive mail at this address?** ☐ Yes ☐ No
Mailing address 2:	**Do you receive mail at this address?** ☐ Yes ☐ No
Best way(s) to contact you: ☐ Cell phone ☐ Landline phone ☐ Text ☐ Email ☐ Facebook message ☐ Other social media: _____ ☐ Through someone else – who?*	[Still collect even if not the preferred method of contact] **Primary phone #:** _____ ☐ Cell ☐ Landline ☐ Work ☐ Shared phone **Alternate phone #:** _____ ☐ Cell ☐ Landline ☐ Work ☐ Shared phone **Alternate phone #:** _____ ☐ Cell ☐ Landline ☐ Work ☐ Shared phone **Primary Email address:** _____ **Email address:** _____ **Social media handle/link:** _____ **Social media handle/link:** _____

*Should be alternate contact 1

If we attempt to contact you through one of the alternate contacts you provide, we will not disclose your involvement in this research study or any health information about you. We will announce our name, that we work with the University of Washington, and that we are trying to reach you. We will ask whomever we contact to put you in touch with us if possible. If you would like us to take care regarding any other information, please let us know.

Please provide us with as many alternative contacts as you can (up to 4). This could include family members or friends who know how to get ahold of you. This can also include case managers, social workers, or organizations you go to frequently (such as Bailey-Boushay House or the Seattle Indian Health Board).

Alternate contact 1

Name	**Relation to you** □ Friend □ Family member (specify): _____ □ Case manager □ Other:
Best way(s) to contact them: □ Cell phone □ Landline phone □ Text □ Email □ Facebook message □ Other social media: _____	**Cell phone#:** _____ **Landline#:** _____ **Email address:** _____ **Social media handle/link:** _____

Alternate contact 2

Name	**Relation to you** □ Friend □ Family member (specify): _____ □ Case manager □ Other:
Best way(s) to contact them: □ Cell phone □ Landline phone □ Text □ Email □ Facebook message □ Other social media: _____	**Cell phone#:** _____ **Landline#:** _____ **Email address:** _____ **Social media handle/link:** _____

8.2 IRB-APPROVED SCREENING SCRIPT

My name is _____, and I am part of a UW research team. I am talking with individuals to see if they qualify for a study we are doing, and if they are interested in participating. Participants in this study will receive HEP patient navigation services and will be linked to a community pharmacy program, where they may be offered several medications, including those that treat HCV. I am interested in asking you some questions to see if you may be eligible for this study. Would you like to be screened?

- ☐ Yes → *Continue with screening.*
- ☐ No → *Thank individual for their time, end screening.*

Before we start, I want to provide you with more information about this eligibility survey. You will not be compensated for the answers you provide for this eligibility survey. Participation in the study is not required; it is entirely your choice to participate and saying yes right now does not mean you have to be in the study. This survey will take just a few minutes. The answers you provide will be assigned a unique ID and stored in our password protected computer. If you are eligible to participate in the study, I can explain more about the study. Is this okay with you?

- ☐ Yes → *Continue with screening.*
- ☐ No → *Thank individual for their time, end screening.*

8.2.1 ELIGIBILITY SCRIPT

Eligible – *Thank you for your time. I'd like to briefly explain more about the study you are eligible for. Participants in this study will be linked to a community pharmacy program where they will be offered medications that (1) treat hepatitis C, (2) treat opioid use disorder, (3) prevent overdose, and (4) prevent HIV infection. You may get other medications that you need through the pharmacy program, too. We are interested in whether this new method of offering hepatitis C medications through a community pharmacy program that is convenient and accessible for people who inject drugs, who are living with hepatitis C, in Seattle. We will have two study visits over six months. Upon completing the first visit, you will receive a $30 cash or gift card honorarium, and for the second you will receive a $50 cash or gift card honorarium.*

We will also review your medical records related to receiving medications that treat hepatitis C, treat opioid use disorder, prevent overdose, and prevent HIV. We will complete a release of information together that gives the study staff access to this information. Your enrollment in the study is contingent upon completing this paperwork. If you are interested in learning more and participating, we can review the consent process and discuss more details of the study.

Are you interested in participating?

- ☐ Yes
- ☐ No → Why are you uninterested in participating? *(Select all that apply)*
  - ☐ Too busy
  - ☐ No interest in participating in research
  - ☐ Transportation difficulties
  - ☐ Other – Please specify: _____

Ineligible – *It looks like you are not eligible for this research study. We are looking for people with a different combination of characteristics. Thank you for your time today.*

8.3 ADVERSE EVENT FORM

HepPSI Phase II Adverse Event Report Form

Adverse event- Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure.

This form is to be completed by HepPSI Phase II Research staff upon notice of an adverse event and updated until event is resolved and all necessary parties are notified of the specific singular event.	
Adverse Event Record ID:	__ __ __
Date of Report:	Date report was written.
Name of staff completing report:	First and Last Name of Research Staff Person
Research Role of staff completing initial report	☐Research Assistant ☐Research Coordinator ☐Co-Investigator ☐Primary Investigator
Date Research Staff became aware of event:	Date Staff became aware of event
How did Research Staff become aware of event:	☐Electronic Medical Record ☐Informant: Who was the informant? ☐Other: How did you become privy to the event?

Date of Event:	When did the event occur?
Participant's Study ID:	__ __ __ __
Description of Event:	Describe the event – what happened, how did it happen, how upset does the participant seem, etc.

1. Was the event serious? ☐ YES (please indicate reason) ☐ NO	☐ Death ☐ Life-Threatening ☐ Hospitalization ☐ Persistent or significant disability/incapacity ☐ Result in birth defect ☐ Breach of Confidentiality ☐ Other – Specify the other serious outcome	
2. Was the event related to study participation? ☐ YES (please indicate degree of relatedness) ☐ NO	☐Possibly Related ☐Definitely Related	**Justification for degree of Relatedness** Refer to DSMP to explain reasoning for selected degree of relatedness.
3. Was the event expected?	☐ YES	☐ NO
4. Which organ system(s) were affected?	☐ Blood and Lymphatic System Disorders ☐ Cardiac Disorders ☐ Congenital, Familial and Genetic Disorders ☐ Ear and Labyrinth Disorders ☐ Endocrine Disorders ☐ Eye Disorders ☐ Gastrointestinal Disorders ☐ Hepatobiliary Disorders ☐ Immune System Disorders ☐ Infections and Infestations ☐ Injury, Poisoning and Procedural Complications ☐ Investigations ☐ Metabolism and Nutrition Disorders ☐ Musculoskeletal and Connective Tissue Disorders ☐ Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) ☐ Nervous System Disorders ☐ Pregnancy, Puerperium and Perinatal Conditions ☐ Product Issues ☐ Psychiatric Disorders ☐ Renal and Urinary Disorders ☐ Reproductive System and Breast Disorders ☐ Respiratory, Thoracic and Mediastinal Disorders ☐ Skin and Subcutaneous Tissue Disorders ☐ Social Circumstances ☐ Surgical and Medical Procedures ☐ Vascular Disorders	

What is the severity of the event? ☐ Mild ☐ Moderate ☐ Severe	**Justification for degree of Severity** Refer to DSMP to explain reasoning for selected degree of severity

If the answer to Q1 and Q2 above are "YES" and Q3 is "NO", then:

- Research staff should notify and report to Site PI within 24 hours of becoming aware of the event
- Research Team should then notify the NIDA PO within 24 hours of the event by email and then submit a written follow-up plan to the PO within 2 days of the event.
- Research Team should also plan to report the event to their Site IRB

Action taken by research staff following notice of event:	**Describe action taken** Describe any actions staff took once they became aware of the event.
Is a planned follow-up need? ☐ YES (please indicate follow-up plan) ☐ NO	**Description of Follow-up Plan:** What is the Follow-up plan to resolve any issues?
Date of Follow-up plan implemented	What date was the follow-up plan implemented?

To be completed by PI upon notice of an event

Has the Site PI been notified of the event? ☐ YES (Please provide dates of notification and reviewed) ☐ NO (notify Site PI immediately)	Notified: Click here to enter a date. Reviewed: Click here to enter a date. (Completed by Site PI)

Does the Site PI believe that the event put greater than minimal risk than was previously known or recognized?	☐Yes ☐No
If the event is determined to be a Serious Adverse Event that is an unanticipated problem, then the NIDA PO needs to be notified.	
NIDA PO Notified? ☐ YES (please note dates of contact) ☐ NO	Initial Email Date: Click here to enter a date. Follow-up plan Email: Click here to enter a date.
Has the site IRB been notified of the event?	☐Yes ☐No
Date of Site IRB notified:	Click here to enter a date.
Action Requested by IRB: ☐ YES (please describe IRB action) ☐ NO	**IRB Requested Action** Describe the requested IRB action.
Date of IRB Action Request:	Click here to enter a date.
Date of NIDA PO notified of IRB Action Request	Click here to enter a date.
Outcome of Event:	☐Unresolved – yet to be reviewed by PI ☐Ongoing – PI reviewed, waiting for responses from necessary parties ☐Unknown (lost to f/u) ☐Resolved – No more further action required (Resolved Date: Click here to enter a date.) ☐Death (Date: Click here to enter a date.)
Will the participant continue study involvement?	☐ YES ☐ NO

Additional Notes

Actions to be taken by HepPSI Phase II Research Staff for Events

Unanticipated Problems

If the event is 1) **serious**, resulting in at least one of the 5 listed outcomes and/or causes greater risk of harm than was previously known or recognized (i.e. "Other"); 2) either possibly or definitely **related to the participant's study involvement**; and 3) **unexpected**, then research staff must do the following for this unanticipated problem:

- Report to Site PI, Dr. Judith Tsui within 24 hours of becoming aware of the event (*tsuij@uw.edu*)
- Report to NIDA PO within 24 hours by email and submit a written follow-up within 2 days of the event *[NIDA PO – Minnjuan Flournoy (minnjuan.flournoyfloyd@nih.gov)]*
- Report to IRB
    - UW – (*link to UW HSD IRB Reporting Guidelines*)
        - If the event is a breach (risk or loss) of confidentiality – report event to IRB within 24 hours.
        - If the event did not result in breach of confidentiality but still an unanticipated event UW Research Team must report to IRB within 10 business days of the event

Events that are not unanticipated problems

If the event is not considered to be an unanticipated problem, then the event is considered an AE/SAE and will need to be reviewed by research team at the following weekly meeting. In addition, research staff then must do the following:

- Report to Site IRB
    - UW – Report recommendations made by the ISM at yearly meetings as Reportable New Information.
- Report all AE/SAEs to NIDA PO at annual continuing review/progress reports (i.e. RPPR and 6-month review)
- Report all AE/SAEs to ISM during annual Data Safety Monitoring Meeting

ISM Reviews and Reports

All individual SAEs and cumulative AEs are to be reviewed by the project's designated Independent Safety Monitor, Dr. Jeanette Tetrault , annually. Research staff will be notified a month prior to the meeting to begin preparing all reports for review. Following the annual ISM AE/SAE Review, reports and, if needed, plans of action to modify study design to improve participant safety will be submitted to the IRBs. Reports are to be shared with the NIDA PO within a month of being written.

UW – must send in Data Safety Monitoring reports and audit reports, regardless if changes are requested or not, within 10 days following the review

8.4 Medical Case Manager "Step by Step" Document: (Integration of HepPSI PN roles)

1. **Meeting Client** (referral, community, phone call)
    a. Introduce self, discuss MCM program and inquire if client is interested in enrolling into MCM program
    b. Take down client's name, DOB, and contact information
        i. *ask if it is okay to leave a voicemail/text message in order to provide a reminder for the scheduled appointment
    c. Schedule an appointment to conduct MCM intake
    d. Schedule a "future appointment" on the database to remind client of intake appointment
    e. Input client intake information on work calendar
        i. *invite Conference Room calendar to event to reserve the space
2. **Intake Appointment**
    a. Introduce self, offer refreshments, build rapport, discuss Hepatitis Education Project as a non-profit agency, and discuss different programs (ex. MCM, DOC, POP, SSP, Advocacy)
    b. Ask how client heard about HEP
    c. Explain what Medical Case Management is/expectations of being in the program
    d. State that today's appointment will be to fill out paperwork to be enrolled in MCM program
    e. Inquire if the client has insurance and a PCP in order to see an overview of what the rest of the intake appointment will look like
    f. Provide hepatitis C education
        i. Inquire what the client already knows about hepatitis C
        ii. Discuss hepatitis C basics (ex. what is hep C, transmission, treatment)
    g. Go over MCM Intake documents
        i. Client's Rights and Responsibilities
        ii. Client Consent for Services
        iii. Demographic Form
            1. After client has completed filling out demographic form, scan the form for answers that may prompt more discussion (ex. hep A/B vaccines, alcohol use, SSP needs, etc.)
3. **Insurance**
    a. If client does not have insurance, help client sign up for insurance on Washington Health Plan Finder or refer client to a clinic that has Insurance Navigators on staff
        i. Seattle Indian Health Board
        ii. NeighborCare 45th St. Clinic
        iii. *when scheduling an appointment at any of these clinics, ask to schedule an appointment on day where the insurance navigator will be there
4. **Linkage to Care**
    a. Discuss whether the client would be interested in receiving treatment at a community pharmacy
        i. **If no**, discuss where client would like to be seen
            1. Offer suggestions/referral to PCP's that are treating for hepatitis C
            2. Fill out HEP's Release of Information with chosen Clinic's information
            3. Fill out chosen Clinic's Release of Information with HEP's information
            4. Call clinic to schedule an appointment

a. When calling to schedule an appointment at a PCP, request an appointment as a new patient and report that you have hepatitis C.

5. Provide client with HEP's fold over business card with appointment information in order to request appropriate lab work.

ii. **If yes**, please ask the client the following questions to assess if their medical care would be appropriate for treatment from a pharmacist.

1. Do you have HIV?
2. Do you have active hepatitis B?
3. Have you ever been diagnosed with liver cirrhosis, had a liver transplant, or had liver cancer?
4. Have you ever been diagnosed with kidney disease or had a kidney transplant?
5. Are you currently pregnant?
6. Have you ever been treated for Hep C before?

iii. If the client reports yes to any of the above conditions, please refer to section 4i above. If the client reports no to all of the above conditions, please move to next section (4iv)

iv. fill out HEP's Release of Information with Kelley-Ross' information

1. Fill out Kelley-Ross' Release of Information with HEP's information
2. Inform client they can seen by the pharmacist on [days/hours TBD] at HEP for HCV treatment if they'd like
3. Provide client with HEP's fold over business card with appointment information in order to request appropriate lab work.

b. ***** If client might be a candidate for HepPSI study and HCV treatment at Kelley-Ross***** (HCV+, potential interest in receiving HCV treatment, likely recent IVDU)

i. Ask if client would be interested in participating in a paid research study. Remind client that their answer will not affect whether they can be treated or where they would like to seek treatment.

1. **If yes**, refer client to Ellie and Alex for study screening
   a. Study cell number: (206) 659-6181
   b. Onsite at HEP: Days/hours TBD
   c. Onsite at ETS: Mondays 8am-1pm

5. Database

a. Input all demographic information into MCM/Testing database
b. Write case note of intake with important information that was discussed
c. Schedule a future appointment to remind client about appointment
d. Schedule a follow-up appointment on when to check-in with client about doctor or pharmacy visit

6. Follow-up on Initial Appointment

a. Follow-up with client after initial doctor or pharmacy visit and inquire how the visit went
b. Ask when upcoming appointment will be either for further hepatitis C testing or discussion of results
c. Input client appointment date in the MCM database as a reminder that the client will be having an appointment to prompt a reminder call/text and follow-up

7. Reminders & Follow-ups on Appointments

a. When a client has an any type appointment, ask if the client would like a reminder call/text message about the appointment

i. Appointments include: further hepatitis C related testing, liver ultrasound, liver biopsy, and pharmacy appointment

b. Always follow-up with a client after their appointment to gather more information about their hepatitis C (ex. genotype, viral load, fibrosis score, etc.)

8. Client started treatment!

a. Once the client has started treatment inquire on treatment information (ex. Medication prescription, start date, and # of weeks on treatment)
b. Inquire when/what time the client will be taking the medication.
c. Discuss the importance of taking medication the same time everyday

9. Check-ins on treatment

a. Discuss adherence support with client
b. Check-in with clients to see if they are experiencing any side effects.
c. Inquire if there are any other upcoming appointments they may have

10. 4 week/8 week/End of Treatment Blood Draws

a. Provide appointment reminders and post appointment follow-up to inquire on lab results
b. Input lab result information on MCM database

11. After Treatment

a. Congratulate client for finishing up treatment!
b. SVR-12
    i. Discuss with client if they can get hepatitis C again, after they have been cured.
    ii. State that an "undetectable" hepatitis C viral load does not mean that the client is cured. Discuss the importance of getting SVR-12 (sustained virological response) is what determines if a client is cured. If the client's results come back "undetectable" it means the client is cured
c. Discuss Re-infection
    i. Tell clients that there is no hepatitis C vaccine = no immunity to hepatitis C
    ii. Inform clients that they can get re-infected from their own old blood before they cured. Advise clients to throw away any hygiene equipment (ex. Razors, clippers, toothbrushes, ect.) or anything that may have their old blood on it.
    iii. Provide information on syringe exchange programs in order to pick up new clean sterile supplies.
    iv. Avoid other people's blood AT ALL COST! Discuss the importance of not sharing any injection supplies or personal care items that may be an exposure risk.
    v. Encourage client to stay engaged with doctor to keep track of overall health.
d. State that you will continue to follow-up with client until their SVR-12 appointment and results. Report that you will check-in on a monthly basis instead of normal check-in occurrences while client was on treatment

12. Monthly post treatment check-ins

a. Schedule (3) future appointments for "monthly check-ins" with clients to ensure that you do not lose client contact while they are waiting for SVR-12
b. Check-in with client about how they are feeling post treatment, if they need any additional services, extend invite to MMU and SSP, and discuss re-infection as often as possible
c. Inquire when client's SVR-12 appointment is

13. SVR-12

a. When client has reached SVR-12, inquire on date and results.
b. If client's test results come back "undetectable" that means the client is cured!

c. If client does not need any other support post SVR-12, close client case.