I. STUDY IDENTIFICATION INFORMATION

TITLE OF PROTOCOL: Emergency Department Longitudinal Integrated Care 2.0 (ED-LINC 2.0)

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FUNDER OF PROTOCOL: National Institute of Drug Abuse (NIDA)

CLINICALTRIALS.GOV: A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. ***NCT03699085***

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II. STUDY OVERVIEW

A. Background and Rationale

The overarching goal of this investigation is to develop and determine the feasibility of a multi-component intervention adapted from a collaborative care framework initiated in the ED for patients at risk for opioid use disorder. According to the 2015 national survey on drug use and health, an estimated 3.8 million individuals over 12 years of age were currently misusing opioid pain relievers. An additional 329,000 people use heroin. The Emergency Department (ED) is currently at the forefront of this public health emergency and often a place where patients come for treatment of overdose and for treatment of medical problems related to illicit opioid use or prescription opioid misuse (POM). Additionally, patients with substance use disorders use the ED more than patients without substance use disorders and the ED can often be a place where patients with opioid use disorder (OUD) can present for any type of medical care and may be a place where patients with OUD seek treatment. There is a growing body of evidence that patients with OUD who are started on treatment in the ED with buprenorphine are more likely to be engaged in substance use treatment at 30 days.[1] Additionally, other ED-based interventions such as take-home naloxone[2] and brief intervention utilizing principles of motivational interviewing[3,4] have a growing body of evidence. Additionally previous work has been done evaluating care coordination programs from the ED showing decreases in ED utilization and opioid prescriptions[5,6]. However, to date, there has been no study which has aimed to **combine these elements into a single intervention**.

Collaborative care is a comprehensive patient-centered model of healthcare delivery targeting behavioral health or substance use that stems from the chronic disease management framework. While collaborative care interventions have been tested in primary care, substance use treatment centers and inpatient settings, the feasibility of a collaborative care intervention aimed at patients in the ED at-risk for OUD has not been established. This investigation aims to establish the feasibility of the 'Emergency Department Longitudinal Integrated Care 2.0' intervention or ED-LINC for patients at risk for OUD from the ED. Elements of ED-LINC are based on evidence based treatments and are central components of collaborative care. ED-LINC will be supported by a novel Emergency Department Information Exchange (EDIE) technology platform that allows for the creation of ED care plans and electronic alerts and will assist in care coordination of this complex population. Overall, this study will provide important feasibility information for future studies of ED-LINC.

B. Method and Design

Patients in the ED ≥ 18 years of age will undergo pre-screening via the electronic medical record (EMR) screening for increased risk for opioid use disorder. Patients who are at risk based on the EMR pre-screen will be approached for additional screening procedures. After verbal consent is obtained, patients will be asked questions regarding risk behaviors including questions about lifetime heroin use and prescription opioid misuse. Patients who endorse lifetime heroin use will be administered the NIDA mASSIST for heroin or illicit opioids. Patients who endorse lifetime prescription opioid misuse will be administered the NIDA mASSIST for misuse of prescription opioids. Patients who endorse chronic opioid therapy prescribed by a provider for a pain condition that is chronic will be excluded. If patients receive a NIDA m-ASSIST score of four or higher for heroin or illicit opioids or for prescription opioids will be assessed

further for eligibility using the participant eligibility summary (PES). Eligible participants will undergo informed consent procedures and a total of 60 participants will be randomized to the collaborative care intervention (n = 30) or care as usual (n =30) condition. Intervention activity will continue for three months after the ED visit, while follow-up continues for six months after the ED visit. Primary outcomes include feasibility. Secondary outcomes include substance use measured by days of use of opioids as well as utilization of healthcare services including ED visits, primary care visits, mental health visits and substance use treatment visits.

1. Aims and Hypotheses

1) The primary aim of the investigation is to determine the feasibility of the collaborative care intervention initiated from the ED and delivered longitudinally. Taken together, all elements of the intervention are referred to as ED-LINC. Feasibility measures include enrollment rates, retention rates at each outcome and follow-up assessment, intervention completion rates and number and types of contacts made by the interventionist. Feasibility of implementation will also be assessed. Guided by Proctor's taxonomy of implementation outcomes[7], acceptability, feasibility and fidelity to ED-LINC will be measured.

2) The secondary aims of the study are to determine differences in substance use and health care utilization between the two arms. While the study is not powered to detect a difference as this is a feasibility pilot study, substance use and health care utilization will be measured. Specifically, substance use will be measured utilizing a time-line follow back calendar administered by the research assistant to determine days of heroin or illicit opioid use and days of prescription opioid misuse. Additionally, EDIE will be utilized to determine ED utilization and inpatient admissions across Washington, Oregon, Alaska and other areas that EDIE is active. Participants will provide self-report information on primary care visits, mental health and substance use treatment visits. Engagement in substance use treatment will be confirmed via phone by study staff at all periods of assessment.

2. Participants

a. Inclusion Criteria:

- Aged 18-65
- Patients with at least one risk factor for opioid use disorder via the EMR pre-screen
- Patients with score of ≥ 4 on the NIDA modified ASSIST for illicit opioids (e.g. heroin) OR a score of ≥ 4 on the NIDA modified ASSIST for prescription opioids
- Currently have a phone
- Able to provide a phone number and one additional piece of contact information

b. Exclusion Criteria:

- They are incarcerated or under arrest
- Non-English speaking
- Live beyond a 50 mile radius of HMC
- Require active resuscitation in the ED or other clinical area at the time of RA approach
- Are receiving palliative care services or hospice care for a chronic illness such as metastatic cancer
- Are in the ED or hospital for a primary psychiatric emergency such as suicidal ideation or attempt

- Receiving chronic opioid therapy (COT) defined as prescription opioids for most days out of the last 90 days for a chronic pain condition
- In the ED for sexual assault

3. Recruitment and Retention Estimates

Estimates for the recruitment plan are based on literature related to feasibility studies. Specifically, the sample size of this pilot is related to the pragmatics of recruitment and a sample of n=30 for each group is related to the necessity for examining feasibility including rates of refusal for each group as well as retention in both arms.[8] Previous work by the research team delivering collaborative care from the ED for patients with injury and prescription drug misuse (ED-LINC 1.0) described excellent recruitment and retention rates of > 80% over six months for subjects getting the intervention.[9] Therefore the study intends to recruit at least 30 participants per arm with retention rates at each assessment and/or follow-up time point of 80%.

III. STUDY PROCEDURES

A. EMR pre-screen OR staff referral

The study team will be accessing and obtaining PHI from the HMC electronic medical record (EMR) to determine if patients have risk for opioid problems or opioid use disorder. Specifically, each morning a member of the study team will review the current census of patients in the ED and first determine if they are eligible based on criteria listed above easily obtainable (e.g. age, chief complaint) by looking at the track shell using FirstNet. Next, the study team member will look at the EMR for possible eligible participants to see if one of the following items exists in the EMR which are associated with an increased risk of opioid use disorder based on literature:

- Previous overdose
- Diagnosis of OUD in the problem list
- Previous healthcare visit related to substance use
- Chief complaint for the current ED visit suggestive of injection drug use
    - Skin/soft tissue complaint
    - Request for detox or concern for withdrawal
    - Overdose
- Any EDIE criteria which includes:
    - 5 ED visits in 12 months
    - PMP criteria
        - More than three (3) prescribers within 12 months
        - More than 4 controlled substance II-V prescriptions within 12 months
        - More than 2 controlled substance II-V prescriptions within last 40 days
        - Any prescription for Methadone, Suboxone, fentanyl transdermal, LA morphine, and LA oxycodone within last 6 months
        - Any overlapping prescriptions for narcotics (controlled substance II-V) and benzodiazepines within last 6 months
        - More than 100 average MED/day prescribed within last 40 days
    - Care Plan
        - From HMC
        - From other hospital

- Patient Requiring Coordination (PRC) program

In addition to using the EMR pre-screen, the study team will take referrals from staff working with patients in the ED. Specifically, structured assessments are often provided to patients while in the ED and if a patient is known to be at-risk for OUD, the study team can be notified to perform further self-report screening (see below).

If the study team has approached all possible eligible patients in the ED based on EMR pre-screen criteria and have exhausted staff referrals for the time being, they can continue to approach possible eligible participants based on eligibility criteria listed in Section 2 with the self-report screening questions (e.g. universal screening).

B. Approach and verbal consent for verbal screen and additional eligibility criteria

After reviewing eligibility criteria as described above, a study team member will go to the Emergency Department (ED) at HMC. First, appropriateness of the study for the participant will be determined by discussing with a member of the care team if possible (e.g. physician or nurse) and determining if the patient has an appropriate mental status for screening. The study team member will then introduce themselves to the patient and gauge interest in hearing more about the screen. Specifically, the study team member will let the patient know that they are here with 'ED-LINC, a project being conducted out of the Emergency Department at Harborview and can I ask you a few questions to see if you are a good fit for our project'. Once verbal consent is obtained, the study team member will proceed with self-report screening which includes the NIDA m-ASSIST for illicit opioids and prescription opioid misuse.[10] Participants who endorse any use of illicit opioids and/or misuse of prescription opioids in the past 3 months AND have a score of ≥ 4 on the ASSIST are eligible for enrollment.

A member of the research team will then complete the patient eligibility summary (PES) that includes the following:

- NIDA modified-ASSIST for illicit opioids or prescription opioid misuse is ≥ 4 (**yes**/no)
- Between 18-65 years old (**yes**/no)
- English speaking (**yes**/no)
- Medical or injury complaint (e.g. not psych) (**yes**/no)
- Current address is within 50 miles of HMC and valid for six months (**yes**/no)
- Has a cell phone or phone number (**yes**/no)
- Can provide one additional contact (**yes**/no)
- Not currently receiving hospice or palliative care (**yes**/no)
- Currently receiving prescribed opioids from a physician for most days out of 90 (yes/**no**).

If all answers in the PES confirm eligibility, the potential participant will be offered the opportunity to hear more about the study. If the patient has a NIDA m-ASSIST score for illicit opioids or prescription opioid misuse ≥ 4 but is otherwise ineligible, they will be provided a resources list (see Resources Hand Out). More information on informed consent can be found in Section IV Human Subjects Protocol.

C. Obtaining written Informed Consent for those with positive OUD screen and confirmed eligibility on the PES

The study team member will provide an overview of the study and provide an unsigned copy of the informed consent to the potential participant, allowing ample time to read. If the patient is interested in participating, the study team member will review the informed consent verbally with the participant, answer any questions and obtain a signature on the consent form located in RedCap. If a patient does not want to consent to the study, the study team member will politely inquire rationale behind the refusal and this will be tracked as part of the main outcome related to feasibility. In previous studies, reasons for refusal at this point have included 'too much pain', 'not interested', 'do not want to do follow-up surveys and/or other study procedures' and 'discharged and don't want to wait'.

D. Randomization

After participants have undergone informed consent, the randomization procedure will take place. The investigation will employ a blocked randomization strategy with random assignment of block size of either 4 or 6 participants. Randomization will also be stratified by inclusion for prescription opioid misuse based on a NIDA m-ASSIST score of ≥ 4 for prescription opioid misuse. It is hypothesized that the majority of participants will screen in for illicit opioid use and stratified randomization will be used to ensure balance of participants with prescription opioid misuse given this is an important but likely small population of participants. Participants will be randomized to the following conditions:

a. Usual Care control condition
b. ED-LINC 2.0

Study condition will be assigned using the RedCap randomization module which will be programmed prior to study start by a data analyst. After the study team member obtains informed consent, randomization of condition will be performed using RedCap and the participant will be notified of their random assignment.

E. Baseline Interview

The study team member will next administer the baseline assessment. The additional survey items will be administered via RedCap by the study team member and is anticipated to take an additional 20-30 minutes. Specifically, the study team member administering the survey will enter the responses directly into RedCap or assist the participant with direct data entry. The RedCap application is sponsored by the University of Washington ITHS and is encrypted. The application will be run on an encrypted I-pad using the University of Washington wi-fi network. Participants can complete the baseline survey in the ED during their clinical evaluation or in any inpatient area. The study team members will not delay or interrupt clinical care and the baseline assessment can be stopped and restarted to allow for continuity of clinical care. If the participant is discharged before the assessment is complete, the participant will be offered the chance to continue after discharge outside of clinical space. Importantly, if there are issues with data entry for RedCap (e.g. wi-fi connection, application malfunction) the study team member will be ready to administer the survey using paper and pen and this hard copy of the survey response will be kept as a source file in a locked file cabinet in a locked office per confidentiality procedures. These responses will later be entered into RedCap.

F. Usual Care Condition

Previous investigations at HMC suggest that patients with substance use comorbidity may receive a spectrum of consulting services visits including social work services, psychiatric consultation, inpatient psychiatry consult, rehabilitation psychology consultation, addiction intervention services, pain team consultation services that include MD psychiatric and PhD psychologist providers, spiritual care or other consulting services. Some of these services social work routinely visit patients with substance use concerns. Other services must be generated by a consult request from the clinical team, such as psychiatry consultation. The services provided to participants in the Usual Care condition will be abstracted form the EMR and tracked in RedCap. There is no cost to patients for interacting with the study team members. However, services received from other hospital staff may incur cost to patients as these services will be billed to patients and their insurance per usual billing procedures.

G. ED-LINC Intervention Condition

Participants randomized to the Intervention Condition will receive 'ED-LINC' which is a multi-component intervention based on the collaborative care framework It is hypothesized that patients with risk for OUD have fragmented healthcare, might receive opioids from many sources and use the ED for episodic acute healthcare needs and often as an entry point for seeking treatment for OUD. The intervention is built on the hypothesis that patients with risk for opioid use disorder (OUD) from illicit opioid use or prescription opioid use will benefit from coordinated care. There is no cost to patients for interacting with the study team members. However, services received from other hospital staff may incur cost to patients as these services will be billed to patients and their insurance per usual billing procedures. Therefore all components of ED-LINC aim to improve coordination of care and decrease care fragmentation. Consistent with other ED-based interventions, there is an emphasis on initiating services and then linking to outpatient service providers. ED-LINC will include **1)** A brief negotiated interview at the bedside with an emphasis on motivation to link to services **2)** Pharmacotherapy including a discussion of opioid safety, take-home naloxone and initiation of buprenorphine from the ED for participants that are interested and eligible; **3)** Longitudinal care management which will proceed for 3-months; and **4)** Care plan in the Emergency Department Information Exchange (EDIE) system. Linking all these elements will be weekly supervision and case conferences attended by the research assistant, study PI and study psychiatrist along with other relevant team members as required in addition to a study cell phone which will be used by study team members to provide care management. The study cell phone will be answered as soon as possible by study team members with messages/texts returned within 1-2 hours during 9-5 M-F and messages/tetxs returned within 12-24 hours overnight and on weekends. All elements of ED-LINC will be discussed in further detail below.

<u>Brief Negotiated Interview</u>

The study research coordinator (RC) will be trained in delivering evidence-based Motivational Interviewing (MI). There is a large body of evidence that supports the use effectiveness of motivational interviewing from the ED for patients with substance use [3,11-14] using the Screening Brief Intervention and Referral to Treatment (SBIRT) framework. However, SBIRT is not effective in decreasing problematic drug use when used alone.[15] During ED-LINC, the research coordinator will perform a brief negotiated interview (BNI) with a goal of increasing motivation to link to outpatient services including

primary care and/or outpatient substance use services. It is expected that the BNI will last 10-15 minutes and the RC will record the length in minutes of each session in RedCap. Important steps to the BNI include; 1) raising the subject 2) providing information and feedback 3) enhancing motivation 4) development of an action plan. The RC will build rapport through non-judgmental active listening and affirming patient strengths and values through complex reflections.

1) Raising the subject/Building Rapport
    - Establish rapport through non-judgmental active listening
    - Ask permission to discuss substance use

2) Providing feedback
    - Ask about the patient's frequency and pattern of drug use
    - Review screening results
    - Ask about connection between substance use and health (if applicable)
    - Provide information about substance use treatments and referrals

3) Enhancing motivation
    - Evoke change talk with MI techniques such: the readiness ruler, assessing pros and cons
    - Use opened ended questions, affirmations, reflections, and summaries (OARS).
    - Emphasize personal autonomy and responsibility

4) Negotiate a plan
    - Negotiate a goal for use and/or treatment engagement
    - Provide thoughts with permission
    - Discuss details for a follow up meeting

A procedural checklist will be used by the RC to document process fidelity to the BNI. (See Appendix A).

<u>Pharmacotherapy</u>

Medications and pharmacotherapy is an important part of collaborative care. It is hypothesized that many patients will not have primary care and might be experiencing fragmented health care delivery. The pharmacotherapy element will be guided by the principle of ultimately linking to care. First, the RC will address the need for coordinated care. After conducting the BNI (above) The RC will step away from the patient and have a conference with one of the supervisory physicians of the study team. In-line with published HMC protocols, the RC will have a conversation with the participant about <u>take-home naloxone</u>. This conversation will be tailored to participant risk for overdose based on their use of illicit opioids, misuse of prescription opioids or both. Naloxone is distributed in many locations around Seattle without a prescription based on pharmacy collaborative agreements. If the participant desires a prescription, the RC will talk with the treating clinical team or the study physicians.

Next, for participants with prescription opioids, the RC will discuss <u>safely storing prescription opioids and safe disposal of prescription opioids</u>. This conversation will be

guided by resources published on stopoverdose.org and med-project.org which are publically available materials.

Lastly, the study physicians in coordination with the RC will discuss medication assisted treatment for participants with risk for opioid use disorder secondary to illicit opioids. It is recognized that opioid agonist treatment improves outcomes for patients with opioid use disorder (OUD)[16] and patients with OUD that initiated buprenorphine in the ED had improved engagement in treatment at 30 days compared to those that received only BNI or standard care.[1] Therefore study participants will be assessed for willingness for opioid agonist treatment. If participants are interested in opioid agonist treatment, the RC will discuss this with both the treating clinical team and study physicians. Based on the patients clinical course, this can be managed by the treating clinical team (e.g. patient is getting care inpatient, patient is in the ED) or the study physicians (e.g. patient is already discharged) or the study physician will offer to coordinate with the treating clinical team (e.g. patient is in the ED). Initiating buprenorphine from the ED for patients with opioid use disorder is an evidence-based treatment[1] with recently published guidelines.[17] Specifically, participants will be screened for opioid withdrawal using the clinical opioid withdrawal scale (COWS)[18] and if they are in moderate or severe opioid withdrawal the RC and study physicians will communicate this with the treating clinical team and the treating clinical team can offer one dose of buprenorphine dispensed from the ED to treat withdrawal if this is clinically appropriate. If the participant is not in moderate or severe withdrawal, or if the participant has already discharged from the ED, the study physician can determine appropriateness for a home induction of buprenorphine with appropriate transition to an outpatient based opioid treatment (OBOT) clinic. We anticipate that many patients that do not have a PCP will be appropriate for the HMC After Care clinic or the Adult Medicine Clinic although there are several community clinics around Seattle which will offer continued buprenorphine and there are several local places that will dispense buprenorphine or initiate buprenorphine with low barrier or same-day service. A list of clinics offering buprenorphine for OUD has been compiled. While all efforts will be made to link to an outpatient buprenorphine provider as described above, it is a known risk of initiating any medication including buprenorphine from the ED that some patients will fail to link to care. This risk is part of the standard of care of initiating treatment from the ED for any condition. Specifically, failing to link to care after initiation of buprenorphine could result in opioid withdrawal. Some participants will be interested in other types of opioid agonist treatment such as methadone or naltrexone and the RC will discuss this request with the treating clinical team if appropriate (e.g. inpatient) and provide coordination to a opioid treatment provider that can provide this service after the ED visit as part of the 'longitudinal care management' element. Participants in the ED-LINC condition that are already linked to opioid agonist treatment will work with the RC to strengthen these connections. It is anticipated that eligible participants that report engagement in opioid agonist treatment will require strengthened linkages and potential dose adjustments. These dose adjustments will likely occur by the prescribing provider.

Longitudinal Care Management

Participants will be followed by the study team for care management for three months. During the initial recruitment interview, the RC will ask the participant about preferences and schedule ongoing times to communicate based on participant preferences. All participants will be contacted by the RC within 3-4 days of enrollment by the preferred method of contact (e.g. text, call) to check-in. Participants who received buprenorphine will receive a phone call within 24 hours by a member of the study team. The RC will

work with the study participant to establish with a new primary care provider, or schedule and attend a follow-up appointment with their existing primary care provider. Additionally, tailored to each participant, the RC will work to actively connect participants to substance use treatment and community mental health providers. Previously care management tasks included coordinating care with existing providers, providing referral and information for housing, managing care for substance use, meeting participants during subsequent HMC ED or outpatient visits to check-in and accompany participants to HMC appointments as needed.[9] Care management tasks will be logged and tracked in RedCap by the RC and other members of the study team.

Care Plan

During the initial recruitment, participants will be notified that a Care Plan will be placed in the Emergency Department Information Exchange (EDIE). The Emergency Department Information Exchange (EDIE) system allows team members to implement electronic health care record innovations, such as the creation of care plan notifications that provide the care team contact information for the study team which can be viewed across emergency department sites utilizing the system. EDIE also provides real-time work-flow integrated electronic alerts that allow collaborative team providers to be notified when patients make recurrent visits to an emergency department in the state of Washington and Oregon. Care Plans in EDIE are used as standard of care at HMC and the care plan for ED-LINC was adapted from exiting projects (See Appendix B)

Weekly Supervision and Case Conference

Consistent with the guidelines of collaborative care, the RC will receive supervision from the study physicians. The study PI, Dr. Lauren Whiteside and study psychiatrist, Dr. Doug Zatzick will be available to discuss all new ED-LINC participants at the time of enrollment and regularly scheduled supervisory meetings will be held with all study team members weekly to every-other week depending on case load and availability. During these meetings, the RC will lead a discussion of all newly enrolled participants as well as any active participants. A discussion of relevant assessments will take place for all discussed participants to tailor further care management and linkage to services. Content of these discussions will be documented in RedCap. All members of the team attending the supervision and case conference meetings will have obtained human subjects training prior to participating.

Cell Phone

The study cell phone number (206-636-8372) will be provided to all participants in the ED-LINC intervention. Specifically, after the baseline interview participants randomized to ED-LINC will be provided with the cell phone number and notified that they can call or text this number with any concerns during the course of their intervention time. The cell phone will be covered by the study RA/RC or study PI from 9a-5p M-F and by one of the study physicians on evenings, nights and all day weekends and holidays. All efforts will be made to answer the call during business hours and response to calls and text during business hours will be within 1-2 hours. Efforts will be made to be timely after hours as well. Participants will be notified that calls and texts that occur after hours, on weekends and on holidays can be anticipated to be answered within 24 hours. All interactions with participants on the study cell will be tracked in research logs and notes captured in RedCap.

H. Intervention Training and Supervision

1. Training

The study research assistant will receive training in Motivational Interviewing in order to perform the Brief Negotiated Interview (BNI) with fidelity. Specifically the RA will attend a 1-day workshop specific to Motivational Interviewing techniques in substance use and will complete practice sessions (e.g. standardized patients) and receive feedback on the core principles of BNI. The RA will receive at least 16 hours of training which is consistent with other studies conducting similar interventions.

2. Supervision
The study research assistant will receive direct supervision daily by the study PI (Dr. Lauren Whiteside). As part of the mentorship process for the grant, Dr. Whiteside will receive at least weekly supervision from Dr. Doug Zatzick. As part of the ED-LINC Collaborative Care intervention, the study RA will receive supervision during a weekly case conference. This regular caseload supervision will be facilitated by the study intervention data management tool (e.g., REDCap). This computerized data management system will be password protected and accessible only to study team members. Access will be available 24 hours a day 7 days a week. As information is available in real time, the system can be used by intervention team supervisors to monitor and support RA and ED-LINC.

I. Patient Tracking and Scheduling

At the time of recruitment, the study team will ask subjects for at least two pieces of contact information (the absence of sufficient contact information is exclusion criteria). One piece will need to be a phone number, while the second piece of contact information could include the patient's address, email address, social media (e.g., Facebook page) or any of the aforementioned pieces of contact information for a relative or friend (referred to as alternate contacts). In the event that the subject's contact information changes (a common event in this population); the follow-up team may reach out to these alternate contacts in an effort to get back in touch with the subject. Over the 6 months after the ED visit, the follow-up team may perform scheduling or check-in phone calls with subjects to ensure that the contact information on file is up to date. During these check-in calls or while scheduling upcoming interviews, study staff will confirm all contact information on file and ask for any new information relevant to the subject.

Previous studies have demonstrated instability of phone numbers and phones in general in this population. Therefore, in addition to contacting patient subjects through the information they initially provide at the baseline interview, the follow-up team may utilize several other approaches to try and stay in touch with subjects throughout the duration of the study. These approaches are:

1. **Harborview Medical Center EHR or EDIE Records**
If the follow-up team is unable to reach a patient subject after repeatedly trying to contact them through the information provided, the study team may utilize the Harborview EHR or EDIE records for any updated contact or appointment information that may help to reach the subject.

2. **Public Records Search**
The follow-up team may also conduct a public records search to find new contact information. Examples of public records searches the study team may utilize include Google, the White Pages, public jail records, or other paid public record searches.

The follow-up team will search for records or information on forums that are open to the public either for free or at a cost.

3. **Social Media**
   If the follow-up team is given or finds a URL or a social media website (e.g., Myspace, Facebook, Google+, etc.) for the subject, they may view the profile information and status updates posted publicly. They may also attempt to contact a subject through these websites via private message from TSOS. They will only send this message if they are able to match at least two identifiers with information from public records or provided by the subject or their alternate contacts. This information may include: name, date of birth, email, phone number, links to other personal social media sites with two pieces of information (e.g., GoFundMe), injury event, or picture. Given that this is a local trial, there will likely be too much overlap to utilize information such as location or friends as one of the two required identifiers, so this would be considered supplemental information to ascertain a subject's social media page. Any messages will be sent to the subject's private inbox and will not be viewable to the public. The study team will not browse subjects' social media posts except to confirm the patient's identity to be able to send a private message to the subject.

A. Follow-up Interviews

Patient-reported outcomes will be assessed at 1, 3 and 6 months after the ED visit. Length of the follow-up interviews varies and is estimated that the shortest interview may take about 15 minutes to complete and up to 60 minutes to complete the longest follow-up assessment depending on subject answers. Subjects will be remunerated for their time. The study team will be flexible with regard to completion method of the follow-up interviews. The study team intends to complete follow-up interviews with subjects primarily in-person at Harborview Medical Center or other convenient public location or over the phone. Responses will entered into REDCap. If scheduling time with an interviewer is difficult, a subject may also have the option of completing the follow-up assessment through the encrypted REDCap app or web-based platform, or by another preferred method (e.g., faxed interview, hardcopy mailed to their residence). If a subject is completing the assessment on their own, the interview form (e.g., PDF, hardcopy, REDCap) would not include their name or any directly identifying information. Subjects will be given explicit instructions on certain assessments such as the timeline follow back (TLFB) in order to complete this with accuracy and without RA/RC assistance. Subjects will be reminded they should complete the interview in a private space where no one else can have access or see the interview.

Some subjects will have difficulty completing the entire interview, such as due to fatigue. The study team will allow for patients who are unable to tolerate a full-length interview the option of completing an interview over multiple sessions

Prior observations from the study team's effectiveness implementation spectrum investigations suggest flexibility is also required with regards to the timing of outcome assessments. Biostatistical considerations related to power encourage obtaining follow-up assessments, even if the actual assessment date deviates from the planned outcome assessment point. The study team will attempt follow-up on the appropriate date (e.g., within 30 days for the one month follow-up interview) but understand that flexibility on timing of followup interviews are needed.

Additionally, the study team anticipates about 20% attrition for follow-up interviews in this population. Missing or being unable to complete a follow-up interview is a common event and will not be counted and/or reported as a protocol deviation. This information will be documented and reported. If a subject misses a particular assessment, they are still able to complete subsequent assessments. This may occur if a subject is unreachable for several months or becomes incarcerated during the follow-up portion of the study.

At baseline, being a prisoner (i.e., incarcerated or taken in to custody immediately after discharge) falls under the exclusionary criteria for study participation. However, a subject may become incidentally incarcerated during the follow-up period. Study team members may become aware of a subject's change in incarceration status via public records search or from alternate contacts. The study team does not directly contact or collect any information from subjects while they are incarcerated. However, in accordance with the UW Prisoner SOP, section 8.3.2.4, the study may resume follow-up (and intervention, if applicable) activities with subjects who have incidentally become prisoners during the course of their trial participation once they have been released. The study team intends to search public jail records to track if patients have become incarcerated and when they are released in order to facilitate contacting them for subsequent study interviews.

B. End of Study Participation

While final UC and intervention patient subject follow-up interviews take place approximately 6 months post-consent, intervention activities with intervention patients are anticipated to conclude approximately 3 months after subjects consent into the trial. The team may need to exercise flexibility in the duration of the intervention as specific situations may arise where intervention activities extend beyond the 3-month planned intervention period (e.g., crisis intervention needed at two months). The ED-LINC intervention will attempt to have a final intervention contact with all intervention patients. The objective of the final ED-LINC intervention contact is to negotiate a specific plan for ongoing care beyond the study. The study team will discuss strategies for maintaining treatment gains with each intervention patient. This means proper handoff of medication prescription management to a subject's preferred primary care or other medical provider, linkage to community resources, and any referrals. Treatment maintenance may also include ongoing relationships with the subject's social support (e.g., family, friends, and other community support groups). UC activities are expected to conclude when a patient leaves the ED or hospital.

IV. HUMAN SUBJECTS PROTECTIONS

A. Informed Consent Procedures

After potential patients have been deemed eligible using the eligibility criteria and self-report screen a study team member will introduce the study and continue to assess the patient's level of consciousness and cognition. Prior to engaging in the informed consent process, the recruiting study team member will review the Glasgow Coma Scale (GCS) which provides best response to 'eye opening', 'verbal' and 'motor' and is on a scale from 3-15. Patients with a score of 8 or less often require emergent procedures and resuscitation and will not be eligible. Patients with a score of 9-13 will be monitored for improvement of mental status. Patients with a score of 14 or 15 will be eligible for approach. The GCS is often calculated as part of routine care by the bedside RN in the ED and will be reviewed prior to approach by the research team. At approach, the first two questions of the Mini Mental Status Exam (MMSE) which include 'what is the year'

and ‘where are we now’ will be asked. These are standard questions within emergency medicine to determine if a patient has capacity for decision making. Patients who are disoriented or delirious will not be able to undergo informed consent procedures. The study team member will return at a later time to check if the patient is ready and able to participate in research related activities including informed consent procedures. If the patient is appropriate and cognizant, a study team member will provide the patient with an unsigned consent form to review. The study team member will provide ample time for patients to read the consent form; however, once the patient indicates that they are willing and able to proceed, the team member will verbally go through the written consent form item by item with each participant and will emphasize the following points:

- Participants may choose not to answer any question at any point during the study. They may also choose to drop out of the study at any time.
- Information told to the study team will be kept confidential and will not be shared in identifiable form in study team publications or at public conferences, with exception only for maintaining the safety of the patient or others (e.g., suicidality; child abuse).
- The data will be kept in locked offices and drawers or electronically on a secure server and only the study team members will have keys or access to the server via password and designated login.
- The link between identifiers and the research data will be destroyed after the records retention period required by state and/or federal law, in this case 7/1/2024.

Once everything has been explained and all questions have been answered, the participant will sign and date an ***electronic version*** of the consent form utilizing RedCap. Specifically, the research team member will have accessed RedCap utilizing a secure log-in. If RedCap is not available (e.g. wi-fi not available in the hospital, problem with the RedCap application) at the time the research assistant is ready to obtain a signature on the e-consent form, a standard paper copy of the consent form can be used. The participant will be able to view the consent form and sign the form using features standard in RedCap as provided by the University of Washington ITHS. At the bottom of the page they will need to select “I certify that all the information in the document above is correct, and I understand that signing this form electronically is the equivalent of signing a physical document.” The participant will provide a signature which will be witnessed by study staff. The participant will be given a paper copy of the electronic consent form for themselves. This e-consent will be stored in RedCap as a PDF in the file repository accessible only to study staff.

Participants will be informed during the consent process that they may choose not to answer any question, to stop and take a break, or to drop out of the study at any time. They will be reminded of this before beginning each interview.

If a patient is unable to read and/or sign the consent form due to physical limitations (e.g., injured hand or eyes), the study team member will provide the patient and/or a 3rd party witness who is not affiliated with the study team (e.g., nurse, family member) with an unsigned version of the consent form that the study team member will read to the patient in the presence of the witness. The study team member will allot enough time for questions/answers to ensure full comprehension of the consent information by the patient. If the patient decides they do want to participate, the subject will mark the e-

consent form with an “X", the witness and study staff obtaining consent will sign and date, and a signed copy will be given to the patient while one is maintained by the study team. If a subject is unable to mark the consent form with an “X,” the same procedure described above will be used and the witness and study staff obtaining consent will sign and date the consent form. If a witness is used, per the UW IRB SOP for informed consent documentation, the communication method (e.g., oral) with the subject and the means used by the subject to provide consent (e.g., oral consent) will be documented on the consent form.

B. Potential Benefits Associated with Study Participation
Subjects in the intervention group may directly experience the greatest benefits from the proposed investigation. Intervention subjects will receive brief intervention and care management using the collaborative care framework. Also, results of the investigation may be disseminated beyond the ED settings to other intervention contexts, such as in outpatient settings. Previous research suggests that participation in a brief intervention for substance use will benefit the average patient. needs post-injury.

C. Potential Risks Associated with Study Participation

1. **Emotional discomfort:** The survey and subsequent interview asks sensitive questions related to health status, and substance use and other emotionally laden topics may produce emotional discomfort such as anxiety, shame, or guilt. Participants in the intervention group may experience emotional stress during the brief intervention.

2. **Testing burden:** Patients may experience inconvenience and an invasion in privacy during an approach. Patients may feel burdened when completing the initial survey as well as during follow up interviews.

3. **Confidentiality:** Patients will contribute personal and protected health information to the study both through self-reports during research interviews, as well as through the EMR and EDIE. Patients will be initially approached in public clinical locations, including the Emergency Department, and asked to answer potentially sensitive questions about depression, suicide, and substance use. The follow-up interviews which may be conducted in a variety of means including over the phone or in person, will also include these and other sensitive questions. There is a risk of breach of confidentiality if private information about participants was overheard, taken by, or seen by someone who should not have access to it.

4. **Coercion:** Participants may feel obligated to participate in study protocols especially if they present with opioid related complaints. There is a risk that patients perceive their clinical care is contingent on participation in the study.

5. **Medication side effects:** The main risks associated with the study include the initiation of medications such as those used for the treatment of opioid overdose such as naloxone or buprenorphine. Other medications that may be prescribed for those in the patient population target depression, and anxiety. In general, these medications are widely used and are well-tolerated in adults. Known side effects of these mediations at doses used in this study and for approved indications include, headache, upset stomach, nervousness, sleep disturbance, and dizziness.

D. Mitigation of Potential Risks Associated with Study Participation

1. **Emotional discomfort:** Patients will be informed during the approach that not all questions during the survey or interview need to answer and may be skipped at their digression. Patients will be told that the interview can stopped at any point to take breaks to be completed at a later time. These options will be discussed with each participant during initial recruitment and at every follow-up assessment. Study steam staff will be trained in motivational interviewing, empathic listening, and certified in mental health first aid.

2. **Testing burden:** Patients will be informed that they may stop the interview at any time to resume at a later point. All efforts will be made to schedule follow-up interviews at a time and method that is convenient for the participants. Patients will be told that they can withdraw at any point in the study.

3. **Confidentiality:** All study team members will complete human subjects training (e.g., Good Clinical Practice, Collaborative Institutional Training Initiative, HIPAA) prior to accessing PHI and engaging with potential participants. The study team will make every effort necessary to safe guard data and protect participant privacy. Exceptions include the need to notify relevant authorities in the event that a participant is suicidal or homicidal or the research staff becomes aware of child or elder abuse through working with the participant (e.g., scheduling, interviews, social media, etc.). All information regarding participant information will be stored in a secure password protected databases with the majority of information de-identified. Data will be coded and any paper files will be stored in a locked office in a locked filing cabinet. Participants will not be personally identified in public conferences or in publications. Study interview responses will not be entered into patients' medical charts or EDIE. Managing risks associated with participant confidentiality and security of research data is of the utmost importance in the study. A variety of data transmission and storage procedures, as described in relevant Data Quality and Data Security sections, will be used to ensure that patient data is not inadvertently observed or obtained by persons other than the study team members or regulatory bodies who may need to view data to ensure the proper conduct of the study.

   All participants will be assigned a study ID number, which will be associated with patient names and identifiers as well as patient-reported outcomes and intervention process data in the REDCap data collection system. To protect patient privacy and limit potential intercept by a non-study team member of any identified data, any data collected on hard copies will utilize the patient study ID number only until entered into the REDCap system. Information regarding the security of REDCap and related systems can be found in the Data Security section. To practicably conduct the research, the study data will remain in identified format in REDCap until the end of the record retention period (July 1, 2024), at which point all data will be de-identified and the research data only associated with patient study ID.

4. **Coercion:** As described in the informed consent form procedures, patients will be informed that the research is voluntary and non-participation will have no impact on their receipt of routine clinical care. Research team members who have clinical roles at Harborview Medical Center may come in to contact with patients who may be eligible for study participation during the course of their hospital clinical work. However, the

informed consent procedures will only be conducted by research team members who are not actively seeing patients on clinical services in order to avoid potential coercion.

5. **Medication side effects:** Patients may experience study-related psychotropic medication side effects. Although patients may tell a variety of study team members about potential medication side effects (e.g., care manager, follow-up interviewers), only licensed medical doctors will follow-up with psychotropic medication symptom assessments and recommendations. All administrations of medications associated with this study will be provided by licensed medical doctors who evaluate the benefits of the medication greater than the potential risks. The clinical team will assess any medical side effects and document any side effects that they become aware of.

V. DATA AND SAFETY MONITORING PLAN

This Human Subjects Research meets the definition of a clinical trial

To address the NIH policy for data and safety monitoring, Dr. Whiteside and her mentorship team have developed a system for oversight of the study and its participants. Dr.'s Whiteside, and Zatzick will be responsible for monitoring the data quality and safety. All research projects that involve human subjects at the Harborview Medical Center Emergency Department require approval from the University of Washington (UW) Institutional Review Board (IRB). The UW IRB will review and approve the protocol before any data is collected for the project. Dr. Whiteside and her mentorship team will adhere to UW IRB procedures. Specifically, all participants in the trial will: 1) understand, agree to and sign written consent forms prior to participation; 2) participant right to withdraw or refuse to answer questions will be maintained; 3) consent forms and identifying information will be kept separate from participant data; 4) all identifying information will be kept locked at all times and computer files will be saved with passwords on secure servers; and 5) participants will be informed in writing how to contact the PI and the IRB office at UW with any questions or concerns. This protocol was presented to the University of Washington Emergency Medicine Research Interdisciplinary Research Committee (EMIRC) which reviews all study proposals that aim to recruit patients in the Harborview Medical Center ED. In general, this committee provides comments on study design, subject recruitment in the ED related to operations and patient flow and will voice human subjects concerns. This protocol (ED-LINC) received review and approval by EMIRC in July, 2018. Many senior faculty members from a variety of disciplines (e.g. surgery, neurology, emergency medicine) with extramural funding sit on this committee.

The Principal Investigator (PI), Dr. Lauren Whiteside, provides day-to-day oversight of the trial along with members of the mentorship team. Dr. Doug Zatzick is a practicing Psychiatrist that has clinical duties at Harborview Medical Center. Dr. Whiteside will train research staff and ensure that informed consent is appropriately obtained prior to performing research procedures, that all subjects meet eligibility criteria, that all subjects receive information for how to contact the study PI and how to contact the UW IRB office for questions or concerns. Dr. Whiteside will ensure the study is conducted according to the IRB-approved research plan. Quality control and reliability of all self-assessments at screening, baseline and follow-up will be monitored by Dr. Whiteside via regular meetings and direct observation of the research assistant. Dr. Whiteside will also monitor the quality of the data files by directly supervising research staff involved with data management.

A. Data and Safety Monitoring

The study team and IRB will provide oversight of patient safety throughout the trial. The PI will meet weekly with the study mentorship team including study Psychiatrist, Dr. Zatzick and review reports of patient safety data, and make reports of patient safety concerns to the IRB as outlined in below. Common research patient safety concerns include adverse events, serious adverse events, and unanticipated problems, as defined by OHRP below.

1. Reporting of Adverse Events (AE) and Serious Adverse Events (SAE)

   Office of Human Research Protection (OHRP) Definitions:

   Adverse Event (AE). An adverse event (AE) is any untoward medical occurrence in a subject temporally associated with participation in the clinical study or with use of the experimental agent being studied. An adverse finding can include a sign, symptom, abnormal assessment (laboratory test value, vital signs, electrocardiogram finding, etc.), or any combination of these.

   Serious Adverse Event (SAE). A serious adverse event (SAE) is any adverse event that results in one or more of the following outcomes:
   - Death
   - A life-threatening event
   - Inpatient hospitalization or prolongation of existing hospitalization
   - A persistent or significant disability/incapacity
   - A congenital anomaly or birth defect
   - An important medical event that may jeopardize the subject's health and may require medical intervention to prevent one of the other events listed above (based upon appropriate medical judgment)
   -

   Unanticipated Problems. In general, unanticipated problems include any incident, experience, or outcome that meets **all** of the following criteria:
   1) ***unexpected*** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
   2) ***related or possibly related*** to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
   3) suggest that the research ***places subjects or others at a greater risk of harm*** (including physical, psychological, economic, or social harm) than was previously known or recognized.

   AE and SAE Identification
   The study population is known to experience a number of AEs and SAEs, as defined by OHRP that are not expected to be study-related. For instance, prior investigation by the research group with this population suggests that as many as 50% of subjects report "thoughts that they would be better off dead or of harming themselves in some way" over the course of the six months after their ED visit (See Appendix C for Participant Suicidality Safety Protocol). Overdose is also common in a population of

patients with risk for opioid use disorder and in previous work by Dr. Whiteside and others approximately 25% of patients in the HMC ED at high risk for opioid overdose had an overdose event (e.g. non-fatal or fatal) within 3 years. The study population often suffers from comorbid medical conditions pre-dating and possibly exacerbated by the ED visit and thus is likely to experience recurrent hospitalizations. Additionally, the study population is known to experience a high rate of incarceration.

Given the high frequency of AE/SAE events in the study population, and having identified those SAEs/AEs that we anticipate to be study-related in the patient consent form, the study team has opted not to systematically assess for AEs or SAEs at each patient contact. However, the study team may become aware of AEs/SAEs through routine interactions with study subjects. Examples include while scheduling interviews or other patient contact, during baseline or follow-up interviews, intervention related activities, within the EMR, through a public records search (e.g., WA state death records), from public posts or private messages sent through the subject's social media (e.g., Facebook), or relayed by an alternate point of contact for the subject. Study team members will ensure that the PI and other relevant team members (e.g., research coordinator) are made aware of any relevant problems or SAEs via email, phone, or in-person within 24 hours.

SAEs/AEs that the study team becomes aware of through the course of conducting study procedures will be reviewed by the PI and study team to assess relatedness and expectedness will be classified by attribution, or an assessment of the relatedness to participation in the study protocol, with particular regard to the intervention. Specifically, they will be classified as one of the following:

1) ***Not Related***
2) ***Probably Related***
3) ***Related***

AE/SAE and Unanticipated Problems Reporting

Study team members will report unanticipated problems on the Reportable New Information (RNI) form to the IRB, consistent with the UW IRB requirements. The UW IRB definition of Unanticipated Problem includes *a problem or event that meets all of the following criteria: unexpected, probably related to study, and places subjects at greater risk of harm*. Events meeting these criteria must be reported on a Reportable New Information (RNI) form to UW IRB within 10 business days. AEs/SAE's that are not unanticipated problems will not be reported. Additionally, Dr. Whiteside will notify the NIDA Project Officer of any unanticipated problems or significant human subject protection issues within 24 hours of discovery.

Anticipated AE/SAE

Anticipated AEs/SAEs will be tracked systematically and will be reviewed within 24 hours of discovery by the study PI to determine if it is an unanticipated problem. The following AEs/SAEs are anticipated in this study population and will be tracked systematically:

- Suicidality including fatal suicide and non-fatal suicide attempt
- Overdose (fatal and non-fatal)
- Hospitalization
- Medication side effects

As mentioned above, the study team may become aware of one of these anticipated AEs/SAEs through a variety of means, which may include self-report by the subject while completing baseline or follow-up interviews, intervention related activities, relayed by an alternate point of contact for the subject, within their EMR or EDIE, through a public records search (e.g., WA state death records), or public posts or private messages sent through the subject's social media (e.g., Facebook). Any clinical questions about medications and possible/probably side effects will be triaged to the study PI (Dr. Whiteside) and her mentor, Dr. Zatzick (psychiatrist) to determine if it is related to the study and to make a determination about medication recommendations, reporting, and next steps. Anticipated AEs/SAEs will be systematically tracked using an Excel document to track the event and any comments related to this event. Specific actions around the event will also be documented if necessary. After the study PI is notified a decision will be made to determine if it is an unanticipated problem and this will be documented in the Anticipated AEs/SAEs log. See the Subject Suicidality Safety Protocol (see Appendix C) for details regarding how the study team will address subject suicidality during the conduct of the trial.

Other Patient Safety Reporting
Any other unanticipated problems, compliance issues, or safety concerns identified by the study team will be addressed within the study team including Dr. Whiteside and/or Dr. Zatzick, and/or other study team members as appropriate, to assess severity and what steps, if any, are appropriate to take.

Protocol Deviations
The study team may determine the need to deviate from the approved study protocol. The team will make every effort to anticipate the need for protocol deviations and have these approved by the UW IRB prior to engaging in a change to procedures; however, the study team may be required to make deviations to eliminate hazards to patient safety without prior IRB approval.

The study team will document any known instances of non-compliance and report to the IRB per UW Human Subject Division policies per specifications in Table A.

Table A. Protocol Deviation or other Problems Reporting Requirements

Event Type	**UW IRB Reporting**
Loss or breach of subject confidentiality or privacy	Submit completed RNI form to UW IRB within 24 hours
Inappropriate use or access of PHI	Submit completed RNI form to UW IRB within 24 hours
Other protocol non-compliance	Submit completed RNI form to UW IRB within 10 business days

VI. **DATA SECURITY**

The secure collection, transmission, and storage of data to protect patient privacy as well as the integrity of the data is detailed below for each data type and source. Any breaches of data security that may compromise patient confidentiality will be reported within 24 hours to the DSMB and UW IRB

A. Data Management, Collection, Transmission and Storage

1. REDCap and iPad Data Collection

The University of Washington (UW) Institute of Translational Health Sciences (ITHS) REDCap instance will be utilized for collection and storage of patient enrollment data, patient-reported outcomes, intervention and enhanced usual care delivery documentation, and the tracking of patients for follow-up assessments. The ITHS REDCap installation is configured to be completely HIPAA compliant. REDCap is safe-guarded and hosted in a secure data center to maintain physical security. The installation is housed in the secure UW data center underneath the 4545 Building in Seattle, Washington. The installation currently runs on two virtualized environments, one for the webserver and one for the database itself. Both environments are run on servers with data encrypted at rest. All web traffic to and from the REDCap installation is encrypted with the most current protocols available.

All connections to the server are automatically encrypted by a 128 bit Secure Sockets Layer (SSL) encryption and the Operating System of each server is consistently patched and firewalled in accordance with UW Medicine Information Security Policy SEC05.04.

The REDCap support team strives to update the REDCap installation as often as possible with minimal interruption to service. Security fixes take priority over normal updates with new functionality. The entire REDCap installation is backed up daily to a secondary location. REDCap natively tracks any and all user activity and these logs are available to project owners and related roles on a project by project basis. IP logging happens on a server and network level, but these logs are not made public without a compelling reason. The UW Medicine IT security office regularly scans the REDCap installation for vulnerabilities and audits the REDCap support team on a yearly basis. Additionally, REDCap conducts comprehensive auditing to record and track access to the database and any data changes therein.

Project users must have a valid and current user ID to access the installation. Study team members will not share their usernames or passwords with any other team member or person outside of the study team, in accordance with UW policy. The individual REDCap user passwords will be different than the passwords used to log on to study iPads or computers; thus making this data entry system double-encrypted. Users can only gain access to a project in REDCap after they have been authenticated, added, and appropriate user rights have been assigned to them by the owner/administrator of the project. Project owners, generally, are responsible for who has access as well as the level of access to their project through the user rights mechanism.

2. UW Medicine Computers and Servers

In addition to the use of REDCap to collect data, the study team utilizes UW Medicine secure servers for the storage and transmission of electronic or digital files. Access to these servers is available only through password-protected UW Medicine computers connected to the UW Medicine secure network in accordance with UW Administrative Policy Statement (APS) 2.6 Information Security controls and Operational Practices, and UW Medicine Compliance Policy COMP.102 Safeguarding the Privacy and Security of Protected Health Information (PHI). Data will be hosted on a MS SQL Server database, exchanged via a webserver, and stored on a secure UW server in accordance with UW Information Security Policy SP-01 Electronic Data Policy and SP-02 Computing Device and Systems Security Policy. Data transmitted through the server utilizes the Transport Layer Security (TLS) protocol, a cryptographic protocol that provides transmission security, derived from the SSL protocol. TLS and SSL encrypt the segments of network connections above the Transport Layer, using asymmetric cryptography for key exchange,

symmetric encryption for privacy, and message authentication codes for message integrity.

UW security analysts have the ability to drill down into detailed activity logs that are tracked, logged, and stored to see what data on the server was accessed by whom and when. These activity log files and audits will be able to track any IP traffic that reaches the UW server. Backups will be captured and stored in redundant copies in separate data centers which all share the same security controls of the main database.

3. UW Department of Emergency Medicine Harborview Medical Center Research Offices

The study team has offices in the 3 East Clinic area on the Harborview campus. These offices are on a secure part of the 3rd floor, requiring code access to the door entering the office space. The study team has access to locked offices and file cabinets in this secure space for the storage of hard copies of documents and electronic equipment.

B. Data Types

1. Electronic Medical Record (EMR)

For daily study activities, a study team member will manually abstract EMR data into RedCap to determine eligibility. Later, to obtain clinical outcome data, the study will utilize a UW Medicine EMR data warehouse (Amalga) query to facilitate automated abstraction of information. The study team will work with the Department of Emergency Medicine clinical analyst to support this query who has undergone extensive GCP training and signed the confidentiality waiver for this study. The clinical analyst will conduct an Amalga query and data abstraction may occur through one of three delivery methods:

- A SQL Server Reporting Services (SSRS) Report hosted on a UW Medicine server
- An upload to a custom built REDCap project hosted by the UW ITHS
- A flat file delivered to the study team on a secured shared drive

Data from the automated Amalga query or manual chart review will be imported or entered into the enrollment log housed within REDCap or equivalent data capture method (e.g., Excel).

2. Patient Enrollment Log

The study team will document all patients that screen in or out of the study in an electronic log housed within REDCap or equivalent data capture method on a secure UW Medicine server (e.g., Excel). The enrollment log will contain a single form with variables abstracted from the EHR and PHI will only be obtained for patients that screen-in and provide informed consent. At the conclusion of the record retention period the form containing identifiers will be deleted from the enrollment log database, thus severing the link between participant identifying information and de-identified study data.

The enrollment log will also be used to track patient approach date and status (e.g., consented, refused, excluded); if the patient was excluded, the reason for exclusion (e.g., active psychosis); overall study status (e.g., active, completed, withdrawn); and randomization assignment (for those patients that screen in to the study and provide informed consent). This data will be obtained from the Harborview EMR, from interviewers' contact with patients, or from patient self-report and entered directly entered in to REDCap via secure login and password by a member of the

study team. The team is aware that at times, due to technical issues or lack of Wi-Fi access, the enrollment logging procedures may require the team to take alternative measures (e.g., computer/iPad or paper logging) for subsequent entry into REDCap.

3. **Patient-Reported Outcomes (PRO)**
The baseline and follow-up study assessments for collecting patient-reported outcomes (PRO) may be completed using various methods. PRO data will typically be obtained from the patient during in person or telephone interviews with a study team member (e.g., research coordinator or research assistant). The study team member will log in via user name and password to the REDCap web-based platform on a computer on the secure UW Medicine server or log in via user name and password to the REDCap application on an encrypted iPad. Participants will also have the option of receiving an email link to the survey questions to complete follow-up interviews on their own directly in to the encrypted REDCap web-based platform. If a participant has received the email link from the study team they do not need a REDCap user name or login in order to access and complete the survey.

The study team could also use a hard copy paper version of the assessment to be completed by an interviewer in the hospital or convenient location, or the hard copy interview could be mailed or faxed directly to participants for them to fill in own their own and return in a pre-paid, self-addressed envelope.

After receiving the hard copy interview back in the a member of the study team would then enter the responses from the hard copy or PDF into REDCap. Data collected in a hard format (e.g., on paper) will be stored in a locked cabinet in locked study office space. Regardless of the data collection method, interview responses will not be labeled with directly identifying information; instead, they will be labeled with the participant's study ID number to maintain confidentiality. As mentioned above, all data stored in REDCap is encrypted and safe-guarded behind firewalls.

4. **ED-LINC Intervention and Usual Care (UC) Delivery Documentation**
Data collected about the process of care, including ED-LINC intervention care management notes and UC documentation will be obtained from encounters with the patient or their providers, or from the EMR or EDIE, and entered directly into REDCap. Due to the nature of these encounters, the data related to the intervention may contain identifying information or may have identifying information piped in or linked from the patient contact form (e.g., patient name, birthdate, address) and the provider contact form (e.g., provider name, position, phone number) within the project. Intervention specific logging will be accessible only to members of the intervention team granted permission by the PI in order to maintain the blinding of the follow-up interview team.

If limited by technological constraints, intervention study team members may need to take hard copy notes from encounters for subsequent entry into REDCap. As these hard copy intervention notes may contain identifiable information, they would be stored in a locked office or filing cabinet, separate from participant's de-identified study data.

5. **Emergency Department Information Exchange (EDIE)**
Collective Medical Technologies (CMT) owns and manages EDIE, which collects health care utilization data including emergency department utilization data for patients across WA and OR state. The CMT servers, networks, and databases that house and transmit EDIE data are co-located in certified Data Centers with fully redundant systems and 24/7/365 security monitoring. CMT Data Centers are certified

in, or have been audited against the following: SOC I, SOC II Type II and SOC III reporting; ISO/IEC 27000 Series; NIST 800-53; ITIL 3.0; HIPAA Privacy and Security & HITECH Rules; and Gramm-Leach-Bliley Act (GLBA) Interagency Guidelines.

CMT maintains a HITRUST Common Security Framework (CSF) certification to ensure they are compliant with HIPAA and all state and federal patient privacy protection laws. HITRUST CSF is a healthcare oriented security framework required to safeguard PHI which harmonizes the requirements of existing standards and regulations including HIPAA, HITECH, Peripheral Component Interconnect (PCI), and Control Objectives for Information and Related Technologies (COBIT). CMT undergoes a HITRUST CSF recertification process every two-years to ensure they continually meet stringent health care industry standards in protecting PHI and managing risk. These safeguards include: intrusion prevention and detection; PHI transmission protection, external breach protection, malware protection, restricted physical and logical access; strong encryption, password and user account controls; and strict change management, software code, network security topologies and monitoring system review and approval.

VII. DATA QUALITY AND INTEGRITY MONITORING

The study team will internally monitor data quality for electronic health record screening procedures, enrollment, and process (i.e., intervention and UC documentation) and outcome variables. Data quality is a method of measuring data properties from different perspectives to assess a data's fitness to serve its intended purpose. Data quality can be affected by how the data is entered, handled, or maintained. Effective data quality assurance procedures involve periodic data monitoring and cleaning with regard to the following characteristics: completeness, accuracy, credibility, timeliness, consistency, and integrity. With this in mind, data collection, documentation, and quality monitoring procedures for the study will be consistent with Good Clinical Practice guidelines.

A. Frequency of Review

Study data will be reviewed internally by the study data team on a weekly-to-monthly basis. The study team will prepare reports for weekly study meetings, which will include reports on recruitment and refusal rates. Major recruitment, follow-up, or data quality concerns will also be reviewed with the study PI and mentorship team on an as-needed basis.

B. Data Collection Procedures and Quality Metrics

1. Patient Enrollment and Follow-up Assessment Completion (i.e., CONSORT) Data

The enrollment log will track participant status from the pre-screen; approach status (e.g., consented, refused); self-report screen; randomization; and overall study status (e.g., active, completed, withdrawn, deceased). Some of this data may be automatically imported into REDCap from the Amalga query or entered directly into REDCap by a member of the study team. Follow-up assessment completion rates will also be tracked by condition in REDCap. This data will be checked against signed e-consent forms and patient-reported outcome data received.

The team is aware that at times, due to computer outage or lack of Wi-Fi access, the enrollment logging procedures may require the team to take alternative measures (e.g., computer/iPad or paper logging). If a study team member logs enrollment information or obtains written informed consent on a hard copy because

of technological issues, then the data is subsequently entered into the enrollment log in REDCap. In these instances, someone on the team other than the person who entered the data into REDCap will compare the accuracy of the entry into REDCap against the original data source (hard copy). Any hard copy data sources will be kept in locked file cabinets and any data with identifying information will be stored separately from de-identified study data.

2. Patient-Reported Outcomes

Patient-reported outcomes are collected using a variety of potential methods, such as REDCap, hard copy, emailed PDF and may be completed either by telephone, in person, or by the participant independently. Regardless of how they are collected, all patient-reported outcomes will ultimately be entered into REDCap, and then downloaded into computer software (e.g., SPSS, STATA) at the end of the study for data analysis. Data entered into REDCap from a hard copy will be checked by a second data enterer to ensure data entry accuracy from the hard copy version.

REDCap data quality will be monitored periodically by the study PI and/or data analyst. In the event that any changes need to be made to the data, these changes will be made directly in REDCap. There is a data logging tool in REDCap that allows administrators to track changes to the project. This tool provides access to an audit trail created by REDCap. For each entry that changes data in the database, REDCap records the date, time, username of the person logged in at that time, the type of event and the changes that were made. This audit trail in the data logging tool stores every entry/change throughout the life of the database. Specific checks for completion and accuracy are outlined below for the primary and secondary outcomes and for intervention and usual care activity. Certain patient-reported outcomes (PRO) will be used in the 'Anticipated AE/SAE' log as well. Specifically, PRO's on suicide and overdose will be reviewed as described above.

- **Feasibility**

  Feasibility measures include enrollment rates, retention rates at each outcome and followup assessment, intervention completion rates and number and types of contacts made by the interventionist. At team meetings, the CONSORT diagram will indicate enrollment and retention rates. At least monthly, the study RA/RC and PI will review the ED-LINC contact log in RedCap for completeness, accuracy and content. Feasibility of implementation will also be assessed using specific assessments of ED-LINC participants at the 6-month follow-up visit. The rates of completion of these assessments will be assessed.

- **Substance Use and TLFB**

  Past 30-day substance use will be obtained at baseline and every follow-up assessment and calendar will be used to track substance use on specific days. Prior to performing this assessment, members of the study team will receive training on TLFB methods including a webinar published by NIDA, review of the methods with current NIDA CTN project coordinators that have performed these assessments for a variety of substances in a variety of settings including the ED and will practice obtaining this data with practice participant encounters. This training will be completed prior to study start to ensure accuracy of obtaining this data. Episodic shadowing by study PI will be done to ensure there isn't drift of accuracy in data collection. TLFB data will be captured on a hard copy calendar and transferred to RedCap by study staff. The hard copy will not contain any PHI and be labeled with a study ID and will be kept in a locked cabinet in a locked

office. At least 25% of these forms will be double-entered into RedCap to ensure accuracy of data entry.

- **Health Care Utilization**
  Emergency department (ED) utilization will be assessed throughout the duration of the trial using either the UW EMR system (e.g., the UW Amalga data repository) or the Emergency Department Information Exchange (EDIE) web-based platform on an approximately monthly basis. Additionally, EDIE data will be pulled for all consented patients to capture all ED visits, inpatient visits and any available outpatient visits from five years before enrollment up to five years after enrollment in the trial.
- **ED-LINC Intervention and Usual Care**
  The study team will document ED-LINC intervention activities in REDCap. These notes are not static and are modifiable over the course of the trial. For instance, information may be added or modified as a consequence of supervision discussion. The study team will review documentation during team meetings and case conference supervisions and update notes as needed to provide the most complete and accurate picture of what transpired. The data logging tool in REDCap allows administrators to track these types of historical changes. REDCap records the date, time, username of the person logged in at that time, the type of event and the changes that were made. This audit trail in the data logging tool stores every entry/change throughout the life of the database which will help the study team check completeness of intervention data.
  The study team will document how many and what type of consults each patient in the usual care (UC) condition receives. This consultation information will be obtained primarily from the EMR and entered in to REDCap. The team will rely on information from the EMR to ensure completeness and accuracy of all UC documented in REDCap

VIII. INTERIM ANALYSIS PLANS

Interim analysis is not relevant as this is a pilot study and effect sizes are not being measured.

IX. CONTENT AND FREQUENCY OF DSM REPORTS TO NIDA

Annually, the PI (Dr. Whiteside) will submit a grant report (RPPR) to NIDA. The grant report is due in June every year and will include details on:

- Study progress which will include details on feasibility measures, secondary outcomes including substance use and health care utilization and any problems reported to the IRB. An enrollment table will be completed per NIH guidelines
- Responsible conduct of research training received

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Appendix A
BI Evaluation Sheet

Did the provider				What did the provider do?	How did the client respond
Raise Subject	• Establish rapport?	Yes	No		
	• Respectfully ask permission to discuss substance use	Yes	No		
	• Ask for description of substance use patterns?	Yes	No		
Provide Feedback	• Ask about connection between substance use & health issues (if any)?	Yes	No		
	• Review screening results?	Yes	No		
	• Compare results to national norms?	Yes	No		
	• Review low risk guidelines?	Yes	No		
	• Express professional concern?	Yes	No		
Enhance Motivation	• Review pros and cons of use?	Yes	No		
	• Use a scaling question (ruler) to elicit arguments for positive change?	Yes	No		
	• Emphasize personal responsibility?	Yes	No		

Negotiate Plan	• Elicit change plan by asking about next steps? • Summarize? • Re-state professional recommendation?	Yes Yes Yes	No No No		
To what degree did the clinician use a Motivational Interviewing style?					
Self-evaluation of the BI session focusing on strong points, skills to work on, and observations about the entire SBIRT process.					

Appendix B. Sample Care Plan

This patient is part of the ED-LINC (Emergency Department Longitudinal Integration and Coordination) Pilot Program at Harborview Medical Center. *If you have any questions or if we can be of any help, please call or text the 24/7 program cell phone at 206-636-8372*

1. Please provide patient with clinic phone number, provider name and instruct them to contact their provider's office for follow-up visit as needed

- Provider Name:
- Clinic Name:
- Clinic Phone Number:

Updated xx/xx/xxxx (insert date)

Appendix C. ED-LINC PATIENT SAFETY SUICIDALITY PROTOCOL

This protocol addresses potential subject suicidal risk given that suicidal ideation is common among the patient population. Suicidal risk is indicated by subject self-report of suicidality or suicidal behavior. The following procedure addresses positive responses to the PHQ-9 or other reports of suicidality by study patients. Importantly, patients with a primary chief complaint of suicidal ideation or in the ED for treatment after a suicide attempt are not eligible for participation.

The study team collects patient-reported outcomes at baseline, prior to randomization, and at a series of post-randomization follow-up assessments according to a pre-determined schedule (1, 3, 6 months after the baseline assessment). These assessments include questions about patient psychological and emotional distress. Each assessment includes a question about having thoughts of self-harm or being better off dead on the Patient Health Questionnaire 9 item (PHQ-9) depression measure. The PHQ-9 question #9 asks patients "how often have you been bothered by thoughts that you would be better off dead or of hurting yourself in some way?" The response choices are: 0 = Not at all, 1 = A little of the time, 2 = More than half the time, 3 = Nearly all the time.

Work by Gregory Simon et al. (2013) in a general medical setting documented a low risk of completed and attempted suicide by subjects that endorsed a "1" on the PHQ-9 item #9 question; of those that responded with a "1", approximately 1% attempted suicide and 0.08% completed suicide. The rates of attempts and completed suicide did increase with higher scores on the PHQ-9 item #9; however, the absolute risk remained relatively low; of those that endorsed a "3" on the PHQ-9 item #9, 4% attempted suicide over the course of a year The low risk of suicide completion associated with a positive PHQ-9 led the study team to include a follow-up question to directly assess whether patients are currently having thoughts of suicide.

Suicidality or suicidal behavior discovered at baseline

If a patient indicates anything greater than 0, "Not at all," on PHQ-9 item #9, the interviewer will ask a Yes/No follow-up question, labeled #9a "*Over the past two weeks, have you had any plans to harm yourself or take your own life*? (or "in the past month" for follow-up interviews" If the patient endorsed a "Yes" to item 9a, following completion of the assessment (or earlier if needed), the interviewer will provide the patient with a suicide crisis line and call the study's 24/7 cell phone after the assessment to inform the study clinical team about the patient. A member of the clinical team will assess the patient either in person at the hospital or via phone to assess risk and safety plan. If there is imminent danger of self-harm the interviewer or member of the study team will inform the participant of the need to inform hospital staff. Of note, if during the baseline interview or during the initial follow-up by the study team to baseline interview responses the study team learns that the subject's initial injury was due to a suicide attempt, the subject will be withdrawn by the study team per the exclusion criteria. If the study team learns that the initial injury was due to a suicide attempt at any other point during the subject's trial participation, the subject will be eligible to continue study participation.

If the patient reports a "No" to item 9a, but is otherwise positive on PHQ-9 item #9, the interviewer will provide the patient with a suicide crisis line (see below). A member of the clinical team will visit the patient in the hospital to assess risk and discuss suitable safety planning.

Should the patient inform the interviewer that they have current suicidal ideation and intent outside of the interview questions; the interviewer will inform hospital staff. If the patient

indicates they are having suicidal thoughts at any other time during the baseline assessment, even if the response to the PHQ-9 item 9 is 0, the recruiter will inform the clinical team following completion of the baseline assessment who will, in turn, follow the aforementioned procedures according to randomization assignment.

Suicidality or suicidal behavior discovered at follow-up
The following protocol is initiated if a subject indicates anything greater than 0, "Not at all," on PHQ-9 item #9.

If the participate indicates a response > 0 on the PHQ-9 item #9, the subject will be asked the follow-up question, item #9a: "Do you currently have thoughts of killing yourself or ending your life?"

If 9a = Yes
If the subject responds "yes" to item #9a, ("*Over the past two weeks (or "month" at follow ups), have you had any plants to harm yourself or take your own life*?") the study team member will conduct a warm hand-off with the subject to a member of the study clinical team (e.g., physician or MSW). The subject will also be provided with a crisis line number.

*If subject endorses a "Yes" on item #9a and he/she refuses a warm hand-off to the clinical team, the follow-up interviewer will let the subject know they will be contacted by our clinical team to follow-up. The interviewer will provide the subject with a crisis line number and immediately notify the clinical team at the 24/7 study cell.

- A clinical team member will attempt to call the subject within 24 hours and assess the patient's suicide risk and determine the appropriate action (e.g., develop a safety plan; help patient obtain emergency services).
- If the subject is in the intervention, the subject's suicidality will be addressed ongoing as part of the ED-LINC intervention.

If 9a = No, 9 = 3
If the subject responds "no" to item #9a and responded as a "3" to item #9, the study team member will provide the subject with a crisis line number and inform the subject that the clinical team will follow up with the subject over the phone in the coming weeks. The study team will add the subject to a list for the clinical team to call and assess risk and discuss suitable safety planning. The clinical team will regularly set aside time (e.g., weekly) to call subjects from the list. It may take the team more than one week to reach any given subject.

If 9a = No, 9 = 2 or 1
If the subject responds "no" to item #9a and endorses a "1" or "2" to item #9, the study team member will provide the subject a crisis line number.

For all subjects that endorse a positive response to PHQ-9 item #9, the study team will:

- Provide a crisis line number in the payment letter with their check.
- Additionally, crisis line numbers may be texted, emailed, or sent via private social media messaging, at subject's request or approval.
- Inform study clinical team (via electronic log, email, in person, phone, etc.) so they can review that procedures have been properly adhered to and address any remaining safety concerns.

Should the subject inform the follow-up interviewer that they are having suicidal thoughts at any other time during the assessment, even if the response to the PHQ-9 item 9 is 0, the interviewer will inform the clinical team to assess the subject's need for further suicide risk intervention.

There are other ways that the research study team members who conduct follow-up assessments with subjects may become aware of suicidal ideation or behavior besides during a study assessment. For instance, a study team member may be told by a subject while contacting the subject to schedule a study assessment that the subject is suicidal or having thoughts of taking his/her own life. In this case, the study team member will follow the protocol for a 9a = Yes above (i.e., warm handoff to the clinical team).

A study team member may find out that a subject has attempted suicide or died by suicide during attempts to find and contact a subject through a public records search (e.g., WA state death records), from public posts or private messages sent through the subject's social media (e.g., Facebook), or even relayed by an alternate point of contact for the subject. In this case, research study team members will notify the clinical team, who will address any patient safety concerns.

Suicidality or Suicidal Behavior Discovered During Study Intervention Delivery
Intervention team members interacting with subjects, such as the social worker or peer interventionists, may become aware of subject suicidality, such as through care management phone calls or other intervention-related activities, assessing symptoms, or when viewing the subject's medical record. If a non-clinical team member becomes aware of subject suicidality they will inform the clinical team members via the 24/7 study cell, so that they can assess suicidality severity and make decisions about how to address patient safety concerns for those subjects deemed to be at risk for suicide. The intervention team will address suicidality as it occurs as a normative part of the ED-LINC intervention. Actions may include additional assessment regarding a subject's suicidal ideation, plan, means, intent and history of attempts, discussion of subject's suicidality and overall recovery during weekly case reviews, safety planning, and referrals to treatment if deemed necessary.

Tracking and Reporting of Subject Suicidality
Adherence to this protocol and patient suicidality concerns will be tracked; however, this will not be reported to the DSMB unless it reaches the level of an SAE (i.e., suicide attempt, hospitalization due to suicidal ideation or attempt, or death).

Suicide Prevention Resources

- **Crisis Connections**
  24 hour, toll-free, telephone hotline provides immediate, confidential assistance to people in distress in the King County area. Call 1-866-4-CRISIS (1-866-427-4747) or 206-461-3222.

- **National Suicide Prevention Lifeline**
  Provides 24 hour, toll-free, telephone support for anyone in suicidal crisis or emotional distress and provides information to locate crisis clinics and resources throughout the U.S. 1-800-273-TALK (8255)

- **Veterans Crisis Line**
  Veterans and family members can receive confidential help by calling 1-800-273-8255 (then PRESS 1). Visit online to access confidential online chat help.