

Protocol: **M**Health Incentivized **A**dherence **P**lus **P**atient Navigation (the MIAPP Study)

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Preface

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Study Overview

Background and Rationale

Polysubstance use involving opioids and methamphetamine is emerging as a new public health crisis. Patients with opioids and methamphetamine use often experience serious medical complications requiring hospitalization, which provides an opportunity to offer addiction treatment. Prior research demonstrated the feasibility and efficacy of initiating buprenorphine among hospitalized patients with opioid use disorder (OUD). Yet linkage to outpatient treatment post-discharge is suboptimal and methamphetamine exacerbates outcomes: our research showed that people with OUD who use methamphetamine have 40% lower rates of treatment linkage (Tsui JI, et al. 2023) and are 2.4 times more likely to discharge from outpatient buprenorphine treatment programs (Tsui JI, et al. 2019). Building upon the prior studies, we propose to develop an intervention for hospitalized patients with OUD and methamphetamine use that combines the flexibility and human connection of patient navigation (PN) with the efficacy and scalability of mHealth-based financial incentives for linkage and medication adherence. Guided by the Information-Motivation-Behavioral Skills (IMB) Model, we propose to pilot test “MHealth Incentivized Adherence Plus Patient Navigation” (MIAPP) to promote treatment linkage and retention for patients with OUD and methamphetamine use who initiate buprenorphine in the hospital. This pilot will provide preliminary evidence of feasibility for a subsequent R01 study to test the effectiveness of the intervention. If shown to be effective, this PN+mHealth approach could provide a transformative service model that helps reduce substantial gaps in MOUD initiation and retention for persons with opioid and methamphetamine use.

Aim 1: To perform a two-arm, pilot randomized clinical trial (n=40) comparing MIAPP + treatment-as-usual (TAU) versus TAU alone on outpatient MOUD linkage within 30 days (primary) and 90-day retention on medications (secondary) among hospitalized patients with OUD and methamphetamine use.

Aim 2: To develop health services outcome measures by performing a retrospective, observational study of hospitalized patients initiated on buprenorphine from 2019–2021 to 1) describe healthcare utilization outcomes (ED visits and hospital readmission) at 30, 90, and 180 days and 2) to examine associations between baseline methamphetamine use and healthcare utilization.

Note: This document describes the study protocol for Aim 1 (pilot randomized trial).

Study Organizations

Participating organizations/site descriptions:

University of Washington Department of Medicine, Division of GIM

Offices: Dr. Tsui has office space with full computer and network support at Harborview Medical Center. The Research Coordinator has desk space, computer, phone, and network support through the UW Division of General Internal Medicine. Conference rooms are available near offices. Standard office equipment (photocopiers, facsimile machines, etc.) are available to all personnel.

Computers: Workstations are equipped with desktop computers, monitors, networked printers, touch-tone telephones (with voice mail), and Ethernet connections that enable access to the CP LAN, FHCRC WAN, and Internet. The Division of General Internal Medicine provides administrative support for budget management, human resources and hiring, and grant submission.

Scene Health Inc. (Scene)

Scene is a small business located in Baltimore, Maryland dedicated to developing high-impact public health applications. The company has been a commercial entity for over three years and has 10 full-time staff members.

Harborview Medical Center, Addiction Consult Service

Harborview Medical Center (HMC), which is owned by King County and managed by UW, provides high-quality primary care to medically underserved patients in Seattle and King County, many of whom are immigrants and refugees with limited English proficiency and low health literacy. It is a comprehensive health care facility dedicated to the control of illness and the promotion and restoration of health. With over 50 primary and specialty clinics, HMC provides approximately 246,000 patient visits annually. HMC, UW Medical Center, Northwest Hospital & Medical Center, Valley Medical Center, and their affiliated clinics (including the International Medicine Clinic at HMC) together account for 65,000 patient admissions and 1.6 million outpatient and emergency room visits each year. As academic medical centers, these institutions provide the latest in evidence-based diagnoses and medical care. The physicians not only treat patients but also conduct scientific research and teach the next generation of medical professionals. *UW School of Medicine* was established in 1946 and has grown quickly into a highly productive, highly collaborative research community with excellent scientific resources and facilities. It receives more than \$500 million per year in research funding—fully half of all grant funding received by the UW.

Study Design

Data Collection Overview:

Research assessments will occur at baseline during hospitalization and 30 days after discharge from the hospital (“30-day follow-up”). Both assessments will ideally be in-person visits, with research staff administering assessments in an interview format. Point-of-care urine drug testing using Alere 14 Panel Drug Test iCup DX or equivalent will be administered at the 30-day follow-up visit only. Study data (including screening, assessment, urine drug testing results) will only be recorded for research purposes and will not be shared with clinical providers outside of the study team (unless there are imminent safety concerns). Participants will be reimbursed \$60 for the baseline visit and \$60 for the 30-day follow-up visit, plus another \$20 at the 30-day follow-up visit if a urine drug test is provided. This reimbursement for study participation will be provided to both study arms (MIAPP and control arm). At the 30-day follow-up visit, participants will return any study-provided smartphones, if utilized. Data extraction for secondary outcomes will occur after 180 days, which will encompass the 30-, 90-, and 180-day outcome timepoints we will report. These secondary outcomes will include outpatient visits/medications, hospital readmissions, and emergency department visits and will be obtained through partnership with WA State DSHS RDA. Data will be collected for patients who are enrolled in the pilot RCT (Aim 1), as well as for a larger, historical, observational cohort of HMC patients who initiated

treatment with buprenorphine between 2019 and 2021 (Aim 2). This will ensure the feasibility of collecting outcomes for a larger sample size and provide estimates of rates of healthcare utilization that can be used to power a larger clinical trial.

Eligibility

Inclusion Criteria:

- ≥ 18 years old
- Admitted to HMC on any inpatient service
- Initiated on sublingual buprenorphine for OUD while in the hospital or at the time of discharge and planning to continue outpatient
- Used methamphetamine within the past 30 days (any route of administration or frequency), per patient self-report at screening
- Willing to be randomized to MIAPP intervention or control condition
- Willing and able to use a smartphone (study can provide) and work with patient navigator
- Discharge setting does not preclude the use of video-DOT (i.e., nursing home, inpatient psychiatry, etc.)

Exclusion Criteria:

- Cognitive impairment (acute or chronic) resulting in inability to provide informed consent.
- Currently incarcerated and will discharge to jail or prison.
- Plans to discontinue buprenorphine in the near future (<3 months)
- Lives far away such that they cannot keep study visit 30 days post discharge.
- Not English speaking
- Researcher's discretion that participant will not be appropriate for participation in the study (e.g., participant is planning on moving away, is knowledgeable of future incarceration during the study, or has behavioral issues that may pose safety concerns for clinic and research staff, etc.)

Compensation

If a participant is in the treatment as usual condition, they can receive up to \$140 in payments. If they are in the intervention condition, they can receive up to \$660. A breakdown of the payments is listed below.

| Condition | Procedure | Amount | Method of payment | Schedule/timing of payment |
|-------------------------|---------------------|--------|--|----------------------------|
| All participants | Baseline assessment | \$60 | a reloadable prepaid debit card system that does not require participants to have a bank account, or cash or gift card | At study visit |

| | | | | |
|--------------------------|--|----------------------|--|---|
| All participants | End of study assessment | \$60 | a reloadable prepaid debit card system that does not require participants to have a bank account, or cash or gift card | At study visit (or mailed/picked-up for participants who are unwilling/unable to do the 30-day visit in-person but agree to complete remotely). |
| All participants | End of study urine drug test | \$20 | a reloadable prepaid debit card system that does not require participants to have a bank account, or cash or gift card | At study visit |
| Intervention only | Proof of linkage to an outpatient buprenorphine clinic | \$70 | a reloadable prepaid debit card system that does not require participants to have a bank account | Payments will usually be disbursed within 3-4 days after confirmation of linkage has occurred. |
| Intervention only | Video to document taking daily buprenorphine treatment | \$15 per daily video | a reloadable prepaid debit card system that does not require participants to have a bank account | Payments will usually be disbursed within 3-4 days after a video is submitted. |

Screening and Recruitment

Overview of Screening and Recruitment

Potential participants for the pilot study will be identified through the Addiction Consult Service (ACS). Dr. Bhattraju (co-I) will work with the research staff and clinical team to help identify patients for the PN to approach for screening. Research staff (patient navigator and research coordinator) will also review the Addiction Consult Service's patient list and information in the electronic health record (EHR) to perform "pre-screening" where potentially eligible participants are identified. Potentially eligible patients will be approached by the research coordinator. If the patient is eligible and agrees to participate in the study, then the research staff will obtain written informed consent, conduct the baseline assessment, and then randomize the patient using a REDCap randomization module. The study will aim to enroll 40 patients for the Aim 1 pilot RCT (20 randomized to each condition).

Pre-Screening Methods

Pre-screening Electronic Health Record Charts of Potential Participants:

Potential participants for the pilot study will be identified through the Addiction Consult Service. Dr. Bhatraju (co-I) will work with the research staff and clinical team to help identify patients for the PN to approach for screening. Research staff (patient navigator and research coordinator) will also review the Addiction Consult Service's patient list and information in the electronic health record (EHR) to perform "pre-screening" where potentially eligible participants are identified.

We have IRB approval to review electronic health record charts prior to meeting the patient. This method allows research staff to review potential eligibility and give time to notify hospital staff of a patient of interest. Research staff must record all medical record numbers (MRNs) of patients whose EHR data is accessed, regardless of whether the patient is ever approached to participate in the research. This is done in the **MIAPP Microsoft Excel Participant Tracking database** under the sheet "Potential Participants and Screening". Consistent and accurate documentation is important, and the research team should expect to always have this report ready for university/organization audit purposes. The date of chart review and which research staff member reviewed the chart needs to be documented on this form as well. Patient information such as name, date of birth, MRN, chart review date, notes, etc. will be collected in the password-protected **MIAPP Excel Participant Tracking Database** in the form "Potential Participants and Screening."

The following pre-screening data elements will be tracked in the "Potential participants and screening" tab of the Excel Participant Tracking Database:

- First and last name
- MRN
- Date of EHR review
- Initials of the staff member who reviewed the EHR
- Criteria used to determine eligibility, including whether the patient was:
 - Admitted to HMC on any inpatient service (document which location and service to make comparisons between patients admitted for trauma/surgery vs. medicine)
 - Initiated on buprenorphine for opioid use disorder while in the hospital or at the time of discharge
 - Age range (≥ 18 years)
 - Planning to continue buprenorphine treatment as outpatient*
 - Used methamphetamine within the past 30 days (any route of administration or frequency)*
- Status in hospital (admitted, discharged, etc.) per EHR, and follow-up with ACS staff
- Hospital room and hospital phone number, per EHR, and follow-up with ACS staff
- Cell phone number of patient if available (use only as back-up, not for initial approach to screen)

***Note:** During the pre-screening process, it may not be possible to confirm with complete certainty whether the patient is planning to continue buprenorphine treatment as outpatient or whether they used methamphetamine based on EHR data alone. For example, this information is sometimes missing from the EHR, or it may have been inaccurately recorded in the EHR, or patients may change their mind about continuing treatment during hospitalization. Thus, patients can still be approached for screening if

this information is missing/unknown, or if the EHR indicates that a patient does not plan to continue buprenorphine as outpatient or has not used methamphetamine in the past 30 days. The final determination of eligibility will be based on the [screening interview](#) conducted with the patient, not the pre-screening data collected from the EHR and Addiction Consult Service.

Recruitment

Hospital staff who work with the Addiction Consult Service will be educated about the study and asked to refer interested patients who may be eligible. Research staff may also notify hospital staff, via staff messages within EPIC or by face-to-face contact with ACS staff at daily meetings, of patients who, based on pre-screen EHR review, are potentially eligible for the study. This is because ACS staff may be able to provide additional information about the patient that is not available in the EHR. Messaging must be done in the EHR software (i.e., EPIC). Research staff who are recruiting patients will regularly attend the Addiction Consult Service rounds to connect with hospital staff who may help with a “warm hand off” with potential participants. Research staff may also directly introduce themselves and the research study. Hospital staff can also provide the **MIAPP study recruitment flyer** to patients if they prefer to contact staff directly or would like information to think about the study further. Research staff may also provide the flyer to participants they are introduced to if they are not be ready to screen and/or enroll at that time.

Screening Visit

The trained research staff will explain the study ([MIAPP Screening Script](#)). Discussion will be in private space, if possible, or over the phone excluding other patients or staff. If this is not possible due to multiple occupancy rooms or presence of clinical staff, we will enhance privacy through the drawing of curtains around the bedside and will offer the use of a white noise machine (**MIAPP Study Screening Form**). Further explanation and information about the **screening form and screening processes** can be found in the **TAAB REDCap Protocol**.

Screening Data Collection and Tracking

Data Collection Tools and Software:

For this study, research staff are using various software programs and web-based platforms to collect data.

Determining Eligibility in REDCap Screening Database:

Data collected during screening will be captured in a REDCap screening project that is separate from other study data. Screening data includes patient’s date of birth, basic demographic information, and other items to determine whether the patient meets inclusion criteria (see list of criteria in section 4.1.1 above). The screener form is coded to automatically notify the assessor on whether the patient is eligible or ineligible to participate in the study. An eligible or ineligible script depending on patient responses will be populated at the end of the form once all questions are asked; however, the screening assessment can be stopped at any time if the patient requests or at the discretion of the assessor (e.g., the patient seems uncomfortable or not in the best mindset to complete the assessment). The assessment can be stopped at any time based on patient request or assessor discretion regardless of potential eligibility status.

If an eligible patient is uninterested in participating, the assessor should document the reason(s) in the REDCap screening eligibility verification form (if possible). The results of a screening encounter must be

updated on the REDCap Eligibility Verification Form in the MIAPP Participant Screening database for administrative purposes. Please refer to **MIAPP REDCap Manual of Procedures** for further information and procedures when eligibility has been determined.

Excel Database – Potential Participants and Screening Form:

As explained in [section 5.1.1](#), this Excel form will be started for patients prior to screening, but will need to be updated once screening is completed with the dates of screening and the results of screening (e.g., eligible, ineligible, discharged before screened, screening not completed, etc.) included. This database is used for research administration and coordination of the study. No study data from research visits will be entered into this database.

The following post-screening data elements will be tracked in the “Potential participants and screening” tab of the Excel Participant Tracking Database after screening:

- Screening ID
- Whether patient was approached for study screening, and why not approached (e.g., appeared ineligible, discharged before being able to be approached, etc.)
- Date of approach
- Whether patient verbally consented to study screening, and why they didn’t consent (if known)
- Date of verbal consent to screening
- Initials of staff member administering screening
- Outcome of screening (eligible and interested, eligible and not interested, ineligible)
- Notes on screening encounter

Informed Consent

Consent will be obtained by trained research staff (research study coordinator or research assistant) from patients who meet all inclusion criteria. The PI/co-Is in general will not consent patients and will avoid consenting patients for whom they provide direct clinical care. The study will be thoroughly described by research staff, and the potential subject will be asked if s/he has any questions about the study procedures. If the individual agrees to participate after consideration of all options and is deemed able to provide informed consent, s/he will provide written consent.

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

Participants will sign two copies of the informed consent form. Prior to having the participants sign the informed consent the research staff will check to make sure that the most current draft of the informed consent form is being used. After the participant has signed, the research staff will review the forms to ensure that they are correctly signed and dated. One copy will be sent home with the participant and the other will be stored in a locked cabinet with the research study team. This form should never be stored with participant study data.

HIPAA Authorization Form

Research staff must have the study participant complete and sign four HIPAA Authorization Forms. Two UW HIPAA Authorization forms and two Washington State HIPAA forms. One of each forms will be given to the participant and the others will be stored in a locked filing cabinet, along with the signed consent form. This form should never be stored with participant study data.

Release of Information (ROI) Form – for discharge to outpatient treatment outside of UW system

Data will be collected on the location where continued buprenorphine treatment is planned via self-report during the screening assessment. If the patient is determined to be eligible at the time of screening, provides informed consent to participate in the study, and there is ambiguity from the patient self-report during screening regarding discharge date and location, research staff should connect with the Addiction Consult Service before the patient is discharged from the hospital to clarify where the participant will be planning to continue outpatient buprenorphine treatment. Two ways the research staff will connect with ACS staff will be by attending the morning rounds meeting which occur daily at 8:30am and through communicating via EHR staff messages within EPIC. Once the discharge location is determined and if the location is outside of the UW system, then the research staff member will fill out the necessary information in the Release of Information form, print the form and bring the copy to the participant in the hospital, and ask the participant to sign the form to obtain records. This process will need to be done for all participants regardless of which study condition they are assigned to.

Additionally, please note that this information on planned date and location of discharge for outpatient buprenorphine treatment will also need to be entered and/or updated in three places:

1. On the participant locator form (see details below)
2. Within the Enrolled participants form in the Excel Tracking Database (see details below).
3. In the Post-discharge EHR Review Form within REDCap. This can be found by abstracting data from the discharge summary (after discharge has occurred) within the EHR (see REDCap MOP for more details on this form).

Baseline Visit (prior to or at hospital discharge)

Enrollment occurs at the time the informed consent documents are signed. Ideally, the baseline assessment occurs immediately or shortly after enrollment/informed consent documents are signed and prior to randomization. The research study team should inform participants that it is important that consenting and baseline occur as close to one another if not on the same day. The baseline visit consists of completing the baseline assessment interview, then randomization and informing the participant of assignment to the MIAPP intervention or TAU condition. Patients will be assigned and given a re-loadable debit card for reimbursements/incentives at this time (see Reimbursement SOP for more information). For patients in the MIAPP intervention, the research staff member should introduce the patient navigator (PN) using a “warm handoff” if it is a different person. If the patient navigation is to be provided by the same research staff person, they will then notify the patient they will be fulfilling that role and switch to using patient navigator procedures/protocols to conduct visit or arrange to come back at a later time prior to discharge.

Baseline Assessment

Data will be collected primarily via interview format using REDCap, but research staff conducting research visits should have, at all times, paper copies in case of any technical difficulties. Additionally, research staff will carry a small binder of Assessment Cards. These Assessment Cards display the response options to all assessment items in large, printed font to assist participants during the assessments.

Below is a study schedule table that describes the study information that is collected in REDCap and at what point during the study:

| Procedure | Baseline | At hospital discharge | 30-days post hospital discharge |
|---|----------|-----------------------|---------------------------------|
| Screening script and data collection form | X | | |
| Screening eligibility verification form | X | | |
| Baseline assessment | X | | |
| Enrollment verification form | X | | |
| Post-discharge EMR review form | | X | |
| Video submission review form | | X | X |
| 30-days post-discharge assessment | | | X |

After the assessment and randomization, the research staff member should review and check off the items in the Research Checklist that is provided at the end of the study assessment in REDCap and on paper, and once back in the Pat Steel Building office should file all paper forms in their appropriate locations:

- Disbursed reloadable credit card to participant
- Incentive receipt form signed by participant, physical copy with research staff
- Entered data into REDCap
- Consent signed by participant, (one copy given to participant, one copy filed, signature and date checked prior)
- HIPAA Authorization form signed by participant, in hand
- Contact form and ROI completed, in hand
- Phone agreement contract signed by participant (for those randomized to PN+mHealth), in hand

Randomization

Once a participant has signed the informed consent form, HIPAA Authorization form, provided contact information for the participant locator form, and completed the baseline assessment, the research study member who consented the participant can move forward with randomizing the participant to either the treatment as usual (TAU) or MIAPP study conditions. When explaining randomization, the research staff informs the participant that the decision of which condition they are assigned to is random – like the flip of a coin – and that the research team does not control who is in which condition. Participants

should only be randomized if they are able to complete the entire baseline assessment. Research staff will notify the participant of condition assignment immediately after the randomization is completed. Details about completing the randomization process through REDCap can be found in the MIAPP REDCap Manual of Procedures.

Treatment as Usual

TAU will include the usual services provided to patients who receive buprenorphine induction from the Addiction Consult Service while hospitalized at Harborview. TAU typically includes offering patients several days of buprenorphine medication for use after discharging from the hospital and coordination with an outpatient buprenorphine treatment provider (e.g., an outpatient buprenorphine appointment is scheduled before discharge from hospital) and, for some patients (if the Addiction Consult Service attending feels indicated), an encounter with a peer support specialist, social worker, and/or OBOT Registered Nurse. These activities will be performed by hospital staff (not the research team).

Enrollment Data Collection and Tracking

REDCap MIAPP Study Database

This is a web-based HIPAA compliant platform used to conduct assessment interviews and to collect research data. The study will use a REDCap database to complete baseline and final visits. Data collection at baseline and final visits will be collected through interviews between research staff and participants, which ideally will be conducted in person (in order to obtain biospecimens) but if needed can be conducted by phone. Research staff will read the questions from REDCap forms and then directly enter patient responses on the REDCap forms on a tablet, laptop or desktop computer. However, all research staff in charge of administering visits should have paper copies of all assessments in case of technical issues with REDCap (e.g., loss of wifi connection). Further information about REDCap can be found in the **MIAPP REDCap Manual of Procedures**.

If time allows, consenting, enrollment and the baseline visit will directly follow the screening visit on the same day. However, please be mindful that patients who are hospitalized may be fatigued due to medications, injuries, medical treatments, etc., and they may need frequent and/or lengthy breaks. The researcher conducting the screening, consent, and baseline assessment should routinely check in with patient about whether they would like to take a break, even if the patient does not appear fatigued. They should also utilize their own judgment on this (e.g., taking a break if the patient appears to become somnolent, irritable, etc.). Also, there may be interruptions to when patients are taken away for procedures, tests, etc. In that case, the research staff should offer to come back and complete the visit at a later time. Or, if the patient is transported to a similarly private location awaiting care, the research staff may be able to complete the interview in a different location.

Research staff will collect the participant's contact information and location of planned outpatient buprenorphine treatment after discharge ([MIAPP Participant Locator Form](#)). Participants will also be asked to provide information about additional contacts in case a research staff person is unable to reach the study participant. Research staff will attempt to obtain at least one-- but ideally up to 3 contacts--to potentially reach out to in the scenario that they are unable to get ahold of the participant directly. This

form will be stored in a locked filing cabinet with the research team and will not be stored with participant study data.

REDCap Forms will be labeled with study ID numbers; No personal identifying information will be entered into the REDCap Study Database where study assessment/questionnaire data will be entered.

Excel Database – Enrolled Participants Form

Research staff will use the MIAPP Microsoft Excel Database to complete administrative related tasks to ensure proper tracking of every participant. This includes keeping track of dates of completed and scheduled research visits.

Enrolled participants and their information are stored on the Excel database form “Enrolled participants.” This form tracks each visit including the research visit dates for each visit and payment verification tracking. It also logs contact information, if they borrowed a study phone and when it should be returned, etc. This form is also used as the cross-linking file that connects the participant’s MIAPP screening ID, MIAPP study ID, and, if randomized to MIAPP arm, Scene Health patient ID.

The following data elements will be tracked under the “Enrolled participants” tab of the Excel tracking database after enrollment:

- Screening ID
- Study ID
- Date enrolled in study
- Initials of staff member who enrolled participant
- Scene Health patient ID
- Contact information: phone, email, address, etc. (from [Participant Locator Form](#))
- Date of hospital discharge per self-report at screening, or EHR abstraction
- Location of clinic for discharge to outpatient buprenorphine treatment, per self-report at screening or per EHR review by research staff, or per ACS staff if ambiguity in self-report or EHR.
- Planned 30-day follow-up visit date (ideally schedule with participant before leaving the hospital, but if not possible the participant may be contacted after discharge to schedule the visit)
- follow-up visit status (completed / not completed)
- Money dispersed for BL and FU visits and FU urine test, etc.
- Credit card number of distributed PEX card for video upload incentives (if applicable and randomized to PN+mHealth arm)

Follow-Up Assessments

Follow-up Research Appointment (30 days post-discharge)

At the final visit, participants will complete a research interview and have the option to complete a urine drug test. The research interview will include questions for feedback on study experience, and satisfaction with the application (for MIAPP condition only). We will query patients at the 30-day follow-up visit to determine whether they have successfully engaged in outpatient treatment, which included medications, and we will obtain medical records from the setting they report receiving treatment from to substantiate. If patients are unable to complete a 30-day follow-up visit in person, we will obtain this

information over the phone. Similar to the baseline assessment, the follow-up assessment will be completed via interviews with research staff, with the staff directly entering participants' responses into REDCap. A participant should be scheduled to complete the follow-up visit 30 days after discharge from hospital (or longer). These can be completed up to 90 days after discharge, if necessary. Ideally, they will be completed as close to 30 days as possible, but no less than 28 days after discharge.

Participants who were loaned phones for use during the study will be expected to return phones (and accessories- charger, case) at the final research visit. The following study checklist, that is provided at the end of the study assessment in REDCap and on paper, should be reviewed and checked to ensure all study closeout tasks are completed with the participant or after the final visit is completed.

- Retrieved study provided phone from participant, if possible
- Incentive receipt form signed by participant, physical copy with research staff
- TLFB form completed during visit, physical copy with research staff
- UDT form completed during visit, physical copy with research staff
- Entered follow-up assessment data into REDCap
- Entered in final visit tracking data into Excel database under "Enrolled Participants."

Data from Self-Report Buprenorphine Adherence Timeline Follow-back

Self-Reported OUD medication adherence will be assessed at the final visit and is determined by using a monthly calendar and an approved study timeline follow back process. Research staff will work with participants to document their total daily amount of buprenorphine and determine if they adhered to that daily amount every day for the 30 days after their hospital discharge date. This should be completed on paper and research staff person should note the participant study ID on the paper form. The calendar form will need to be printed prior to the final visit and brought to the visit, and the assessor should mark the date that the participant was discharged from the hospital at the top of the form. Additional instructions on the TLFB procedures will be provided within the REDCap final assessment. The paper forms should be stored in a locked filing cabinet within a folder that matches the study ID.

Data from Urine Drug Test

At the final research visit, the participant will be asked to provide a urine sample to be tested for illicit substances and for the presence of buprenorphine. Research staff will have multiple Alere iCups and fentanyl strips at all times in case of an invalid test. Data results from these tests will be captured on paper UDT form labelled with the correct participant ID before being entered into the REDCap database (**See Appendix for UDT Forms**). This is to ensure that the study tablets are not damaged in the lab, in addition testing protocols with these tests cannot sit for longer than 5 minutes. Results of these tests are not to be shared with the participant or their providers. The paper forms should be stored in a secure and locked filing cabinet in a folder labelled with the participant's study ID.

Within the study binder, research staff should have printed out the [UDT Step-by-Step instructions](#). The test results for the POC UDT will also need to be entered in on the REDCap form. Additionally, the UDT package inserts are also electronically stored in study files for easy future reference.

Research Reimbursements and Incentives

Pre-paid Debit Card for Financial Reward/Incentives (PEX or equivalent)

Participants in the TAU arm can receive up to \$140. They will be reimbursed \$60 for the baseline visit, \$60 for the follow-up visit, and \$20 for completing a urine drug screen at the follow-up visit. This reimbursement for study participation will be provided to both arms. We encourage participants to complete their 30-day visit in person by offering an additional \$20 reimbursement for completion of urine tests (in addition to \$60 for the assessment), but patients may complete the visit remotely if needed (e.g., via telephone).

Participants in the MIAPP + TAU arm can receive up to \$660 (\$140 for research assessments previously stated + \$520 financial incentives). Financial incentives will be provided for linking to outpatient buprenorphine programs and documenting daily medication adherence. Patients will receive a one-time reward of \$70 for linkage to an outpatient buprenorphine clinic, as evidenced by medication refill by outpatient provider (either demonstrated by medical records or patient providing a video of showing medication script or package/bottle), and \$15 for submitted video documenting daily adherence to buprenorphine (one reward available per day, for days 1-30 after hospital discharge). Reimbursements and incentives may be deposited by the Patient Navigator (or Research Coordinator if Patient Navigator is unavailable) onto a reloadable debit card, which research staff will add funds to throughout the study using an online account dashboard. We will use a reloadable prepaid debit card system that does not require participants to have a bank account. If necessary, the Research Coordinator/Patient Navigator will disburse cash to the participant in replacement of the reloadable debit card. Patients must meet study staff at Harborview Medical Center or Pat Steele Building to receive their funds. Research staff should strive to administer rewards as soon as possible to maximize reinforcement (ideally, the same day the videos were submitted or linkage was confirmed), and payments should be dispersed no more than 3-4 days after a video is submitted/confirmation of linkage has occurred.

Partial or prorated payments will not be offered, as we anticipate that in nearly all cases participants will either fulfill each activity (e.g., 30-day post-discharge visit, urine test, linkage to outpatient buprenorphine clinic, etc.) or not complete it at all. Therefore, we will offer full payment even if an activity is only partially completed (e.g., if a participant partially completes a 30-day post-discharge visit but leaves before it is fully completed, the participant will still receive the full payment for that activity).

It is important that research staff track this and document that the participant did in fact receive their payment, along with information about the payment that was issued (e.g., type of incentive, gift card serial numbers).

Electronic payments will be tracked using the electronic records in the re-loadable debit card database. Cash payments will be tracked using the [MIAPP Participant Payment Verification Cash Payments \(1\).docx](#) form. Along with that, payment dates will be tracked using the **Microsoft Excel MIAPP Participant Tracking** database.

Patient Navigation

The PN role will include care coordination supported by brief motivational interviewing skills and focused discussions on buprenorphine medication adherence aimed at enhancing patients' knowledge and motivation to take their buprenorphine.

For patients in the MIAPP intervention, the PN will train the participant on the use of the Scene application. They will help participants download and log into the application, then show how to use the mHealth application to record daily videos of themselves taking buprenorphine. If discharge occurs >3 days after the instruction, then the PN will perform a “booster” session to review details of using the app just prior to discharge. The PN will provide m-Health assisted services for 30 days post-discharge. To ensure intervention fidelity: 1) All PN checklists and logs that are filled out for each patient, and the submitted videos for the first week of the first 10 patients will be reviewed by the PI or co-I, and 2) and at least 3 initial visits in the hospital or until competency is achieved. See **MIAPP Patient Navigator Manual** for more information.

During the informed consent process, all participants will be made aware that videos will be made available to research staff for mandatory review. Research staff will review all videos within 7 calendar days but will target the review period for within less than 24 hours of upload. The PI or co-I supervisor will review the submitted videos for the first week of the first 10 patients. The research staff member providing informed consent will inform participants that they will be disbursed \$70 for providing evidence of linkage to an outpatient buprenorphine visit and \$15 per day for uploading a video that demonstrates buprenorphine adherence for the first 30 days after discharge, totaling up to \$520 if linkage occurs and videos for all 30 days are completed.

Participants randomized to the MIAPP intervention will utilize their personal smartphones or tablets, or be provided with a smartphone for use during the study period if they do not have access to a personal device or choose not to use their personal device. The patient navigator or other research staff will help patients obtain a study phone when needed. Phones will be returned at the end of the study period. Participants needing a study phone will sign two copies of a [Phone Agreement Contract](#). If the study phone is lost, damaged, or stolen, there is no penalty to the participant; the study phone will be replaced up to one time. If the second phone is lost, damaged, or stolen, participants can continue to upload videos using a personal device if able and willing. Alternatively, they can continue participating in all remaining study procedures without uploading videos – i.e., they can receive a financial reward for linking to an outpatient buprenorphine provider, and they can complete the 30-day follow-up assessment. Participants who choose to utilize their own device will not be reimbursed for data plan costs and will utilize their device's memory.

Protection of Human Subjects

Involvement of Human Subjects

This study will conduct a randomized controlled trial of 40 participants with opioid and methamphetamine use at Harborview Medical Center (HMC) who are initiated on buprenorphine while in the hospital to determine effects of the intervention on post-discharge outcomes of linkage to outpatient treatment, retention on medication, use of opioids or methamphetamine, and hospital

readmissions and ED visits. Patients will be assigned to one of two arms (20 per arm) using a stratified randomization procedure.

Research Material Obtained from Participants

Individuals who are eligible and enroll in the RCT will complete a baseline and a 30-day post-discharge study visit. Data to be collected at those visits include information on demographics, co-morbidities, current and past addiction treatment, medication adherence and knowledge, motivation and skills for adherence, current and past-year substance use, HIV risk behaviors, mental health symptoms, and satisfaction and trust in provider (both for physician and patient navigator). Urine drug testing will occur at the 30-day post-discharge visit using Alere 14 Panel Drug Test Cup iCup DX or equivalent multi-drug point-of-care test, and a fentanyl urine test strip. A review of medical records (electronic and faxed records from outside hospitals) will be conducted to record information on hospital readmissions and outpatient treatment for 90 and 180 days post-discharge. Assessment data will be collected directly onto netbook computers used by research assessors. We will utilize the Research Electronic Data Capture (REDCap) system through the University of Washington's Institute of Translational Health Services (ITHS). Hospital readmissions and Emergency Department visits within 90 and 180 days of discharge will be extracted by WA State DSHS RDA from statewide Medicaid claims data.

Consent Procedures

The informed consent process will be conducted by staff members trained in the ethical treatment of human subjects. This process involves presenting a detailed verbal description of the study as it is described on the printed, IRB-approved consent form. Subjects will be advised of the purpose of the research and will be asked to provide their verbal informed consent for screening. Answers will be recorded anonymously. Eligible subjects will then be informed of the details of the study and will provide written consent if they wish to participate. Research assessors will review the elements of consent with participants, including the purpose and duration of the study; a description of the study procedures; the risks, discomforts, and benefits; the procedures to ensure confidentiality (including use of unique, non-personally identifying ID numbers instead of names on research materials and maintenance of data in protected computer databases and locked filing cabinets in locked rooms); and that participation is voluntary and their decision whether or not to participate will not impact their clinical care in any way.

Risks to Human Subjects

Participation in this study involves no physical risks. Potential risks for participants include psychological stress from the research interviews and loss of confidentiality. We will take steps to protect participants from these risks as described below.

- *Psychological stress* could be caused by the interview, in which they will be asked sensitive questions regarding substance use. Distress caused by the length of the interview is also possible. Research staff will be rigorously trained on study protocols and will receive close supervision by the investigators. The research assessors will be trained to address these issues with a calm, non-judgmental attitude. We will take steps to minimize any psychological discomfort by ensuring confidentiality as described below. We will only enroll patients who understand the study procedures and are willing to participate.

- *Loss of confidentiality* related to study visits or contacts is potentially the most serious risk of the proposed study. We take this risk seriously, and we will take steps to protect participants' confidential data and anonymity. All subjects will be informed of risks and provide their consent prior to enrollment. All study staff will also receive human subject research training.

The alternative to participation in the proposed study is not to participate.

Adequacy of Protection Against Risks

Risks of psychological distress from the research assessments will be minimized by using trained interviewers and a standardized interview process. Participants may choose to discontinue the interview at any time. In the event of an adverse event during the interview, Dr. Tsui will be on call to assist subjects and make referrals as appropriate. The study will take place in or in proximity to a medical setting where standard procedures are in place to assist patients who experience acute events. If consequences arise due to research procedures (e.g., distress, anxiety, suicidal thoughts), then the physician investigators will be available to assess subjects and make appropriate interventions or referrals based on the clinical circumstances.

Loss of confidentiality is very unlikely given the structures that will be put in place to avoid inadvertent disclosure. These structures to assure confidentiality include the following: each subject will receive a unique identification number, and research data collection and data entry forms will be electronic and identified only with this number. Only the master enrollment list, written informed consent forms, and participant locator information will have identifying information on them. These documents will be kept in a secure computer hard drive or in a locked file cabinet, accessible only to the Principal Investigator (Dr. Tsui) and the Research Coordinator. Tracking information will be kept similarly. Computer data will be password protected and accessible only to research staff needing the information for follow-up and monitoring purposes. Files stored on UW servers will be protected by electronic firewalls that restrict access to designated users.

Another possible threat to confidentiality could arise if a participant indicates an imminent danger to self or others or if a participant discloses abuse of vulnerable persons such as children, the elderly, or the disabled. Ethical and legal requirements may force us to disclose this type of information to relevant authorities. We will attempt to minimize this threat to confidentiality by clearly informing participants of the risks involved during the informed consent process.

Potential Benefits

There are no known health benefits to subjects from participation in the proposed study. All subjects may benefit from discussing their health with an assessor.

Importance of Knowledge to be Gained

The study will inform us about the ability of an intervention that combines Patient Navigation with an mHealth adherence tool with video-DOT and financial incentives to improve adherence and retention for patients with opioid and methamphetamine use who have initiated buprenorphine for treatment of opioid use disorder while hospitalized. If the study demonstrates a benefit of the intervention, then this would provide evidence of efficacy of a new adjunct for opioid and methamphetamine use disorder treatment that could improve patient outcomes. The risks to subjects are reasonable in relation to

anticipated benefits and in relation to the importance of the knowledge expected to result from the proposed study.

Scene Health

Data captured on Scene and data review will happen asynchronously (i.e., not in real-time). Participants will have unique login username and password. The videos uploaded will be protected via data encryption. When research staff go to review the uploaded video data, the video will be decrypted and then be determined to be either approved or rejected. Research staff will be given administrative access to the Scene provider platform (www.platform.emocha.com) to review the videos and determine if they meet set criteria. Whether the video is rejected or accepted, the participant will be able to review this on their phone via the application's adherence calendar feature.

Electronic Health information

EHR data that is collected prior to screening, at baseline, and 30-days post enrollment will be entered into the **MIAPP Screener Database** and the **MIAPP Study Database** EHR event forms in REDCap. Other data, such as the patient's MRN, will be entered into **the MIAPP Participant tracking Excel database** to report to university research audit teams on which electronic health records will be accessed.

Incarcerated Participants

As per NIH guidance, research participants who become incarcerated during the study will be temporarily withdrawn from the study until OHRP guidelines are met. When subjects are incarcerated their buprenorphine treatment is not continued, and they do not have access to cell phones, so they cannot continue participation for these reasons. When subjects become released from incarceration, we will resume study procedures. If research staff members are unable to contact a participant who has missed an appointment or cannot be reached to remind them of an upcoming research visit, research staff should check the local law enforcement databases to determine if the study participant is incarcerated.

Important Definitions

Adverse Event (AE)

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

Serious Adverse Event (SAE)

Any adverse event that results in any of the following outcomes:

- Death
- Life-threatening
- Event requiring inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/incapacity
- Results in birth defect

Unanticipated problems/events

They must meet all of the following criteria (per UW definition):

- 1) Unexpected-- The harm (or potential harm) is inconsistent with risk information previously reviewed and approved by the Institutional Review Board (IRB) in terms of nature, severity, or frequency as well as the characteristics of the study population
- 2) Related or probably related to participation in the research
 - a. Probably related: there is reasonable (more likely than not) that the incident, experience or outcome may have been caused by the procedures involved in the research, or that it is associated with the use of any drug, biologic, or medical device that is part of the research.
- 3) Suggests that the research placed (or did place) one or more subjects or other a greater risk of harm than was previously know or recognized. This includes physical, psychological, economic, educational advancement, or social harm.

Classifying adverse events

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

Severity

Classifications often include the following:

- **Mild:** Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
- **Moderate:** Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning
- **Severe:** Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating

Severity is not synonymous with seriousness. A **severe** rash is not likely to be an **SAE**.

Likewise, a **severe** headache is not necessarily an **SAE**. However, **mild** chest pain may result in a day's hospitalization and thus is an **SAE**.

Expectedness

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

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

Relatedness

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

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

Adverse Event Reporting

Research staff may learn about Adverse Events AEs (including Serious Adverse Events/SAEs) during planned study visits or when contacting participants for reminders or to check on use of the intervention application. AEs and SAEs have specific reporting procedures. AEs will be collected via REDCap. If REDCap is down, research staff should use the paper form **Adverse Event Reporting Form**.

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

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

Serious Adverse Event Reporting

All SAEs, unless otherwise specified in the protocol and approved by the IRB or DSMB (as applicable), require expedited reporting by the Principal Investigator to the study's safety monitoring bodies. Serious adverse events will be reported to the site PI within 24 hours of research staff becoming aware of the event. SAEs that are unanticipated problems will be reported to the NIDA PO and DSMB Chair within 24 business hours of becoming aware by email and a written follow up will be submitted within 2 days of awareness of the event; reporting/submitting supplemental forms to UW should be according to most current requirement, currently within 10 business days (within 24 hours if there was a breach of confidentiality).

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

Suicidality

It is possible that participants may disclose suicidal ideations (SI) with research staff when conducting study activities. Any participant who voices current suicidality or is experiencing a psychiatric emergency

at study visit will be reported to the site PI, or another doctor on-site, immediately. That physician will determine the appropriate course of action, which will depend on the clinical situation.

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 is administered at the study baseline visit and the 30-day post discharge follow-up visit. Question number 9 of the PHQ-9 asks the participant: *“Over the past 2 weeks, how often have you been bothered by any of the following problems? Thoughts that you would be better off dead, or thoughts of hurting yourself in some way?”* If a participant answers the question with an answer of “several days,” “more than half the days,” or “nearly every day” research staff then ask the participant the below follow-up questions:

1. "Which of the two statements, ‘better off dead’ or ‘thoughts of hurting yourself’ were you endorsing?”
2. If yes to “thoughts of hurting yourself,” ask follow-up question “are you currently (i.e. right now) having those thoughts?”
3. If answer to question #2 is “no,” respond by saying “I’m glad to hear that” and research staff will provide information for the 988 Suicide and Crisis Hotline and emphasize that the participant can go to the Emergency Department or inform their current medical providers for help.
4. If answer to question #2 is “yes,” the PI and one of the study medical providers will be notified immediately for assessment.

If a participant indicates current SI to research staff during a remote interaction, such as a phone call or video chat session, the research staff will remain on the phone with the participant to: (1) provide encouragement to utilize the 988 Suicide and Crisis Hotline, (2) encourage the participant to visit the Emergency Department if they believe they may act on suicidal or self-harm thoughts, and (3) notify the study PI or a medical provider on site, who will determine the course of action.

Data Safety and Monitoring Plan

The Principal Investigator (PI) will be responsible for ensuring participants’ safety on a daily basis. The PI Dr. Tsui and a Data Safety Monitoring Board (DSMB) will oversee the safety of the participants and the validity and integrity of the data. The DSMB will be led by an individual who is selected at the discretion of the funding agency and Dr. Tsui. Individual members of the DSMB will be named at the time of award.

Responsibilities of the DSMB

Responsibilities will include:

- Evaluating the research protocols and plans for safety and data monitoring prior to start of participant enrollment
- Evaluating the progress of the study, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, performance of the trial site, and other factors that can affect study outcome
- Evaluating evidence for treatment harm or benefit that might necessitate consideration of modification or termination of the study
- Considering factors external to the study when relevant information becomes available, such

as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics or practicality of the trial

- Reviewing study site performance, making recommendations, and assisting in the resolution of problems reported by study team
- Ensuring the confidentiality of the trial data and the results of monitoring

DSMB Meetings

The PI will meet annually with the DSMB by teleconference or in person. After the initial meeting, the DSMB will meet again when the study has enrolled 50% (i.e. 20 participants) or in a year, whichever comes first, and at least annually thereafter. At each meeting the DSMB will review study progress, recruitment, randomization integrity, data quality, and outcomes by treatment arm, as well as individual SAEs and cumulative AE reports. Following each meeting, the DSMB will make recommendations on continuation, modification, or termination of the study. Aside from these regular meetings, an unanticipated AE may prompt an ad hoc report to be distributed and may result in an ad hoc teleconference for the entire DSMB.

DSMB Reporting to NIDA

A report following annual meetings and activities will be sent to the NIDA PO within a month after each meeting. The report will contain the following:

- Meeting dates (past and upcoming if known)
- Meeting minutes or summary
- DSMB recommendations regarding the research project (continuation, modification or termination and any other specific recommendations)

SAEs that are unanticipated problems will be reported to the NIDA PO within 24 hours by email and a written follow-up will be submitted within 2 days of the event.

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

DSMB Reporting to IRB

A Supplement RNI form will be completed and submitted to the IRB within 10 days of a DSMB meeting.

Statistical Analysis Plan

Descriptive statistics will be calculated for all baseline variables; variables will be assessed for any differences between the two randomized arms using chi-square tests, t-tests, or the Mann-Whitney U test depending on the distributions. Baseline variables that differ between the two arms and potentially confound tests of intervention effects will be included in analyses as covariates. This study will use an intent-to-treat analysis including all subjects according to their randomized assignment, regardless of their follow-up status and their level of compliance with intervention components. The investigators will provide regular written reports to the Data Safety Monitoring Board including outcome data by the unblinded treatment group.

Primary Outcome Analyses

We hypothesize that participants randomized to MIAPP + treatment as usual compared to treatment as usual alone will be more likely to link to outpatient treatment with medications for OUD within the 30 days of hospital discharge. To evaluate the primary hypothesis, we will use modified Poisson regression analysis (53) with robust standard errors to compare intervention arms on the proportion of participants who link to outpatient treatment with medications for OUD within 30 days of hospital discharge, while potentially controlling for any baseline variables that differ between the two groups as described above if they could confound the hypothesis test. The results of this analysis will be presented as the proportion of patients in each group who link to outpatient treatment and the (adjusted) risk ratio (RR, i.e., ratio of the two proportions) with a 95% confidence interval computed by exponentially transforming the coefficient of the treatment effect in the modified Poisson regression model. We will also report the difference between proportions with a 95% confidence interval, as recommended by CONSORT guidelines (54). The RR and difference are two different ways of quantifying the intervention effect that have meaningful clinical interpretations. Results from the Poisson regression will be used for primary interpretation and conclusions.

Secondary Outcome Analyses

We hypothesize that participants randomized to MIAPP + treatment as usual compared to treatment as usual alone will a) have more days of medications for OUD treatment within the 90 days post-discharge (secondary), b) have lower rates of readmissions to the hospital and emergency department visits within 90 days (exploratory), and c) have fewer days using opioids or methamphetamine 30 days post-hospital discharge (exploratory). Analyses of secondary outcomes will use modified Poisson regression similar to those described above for binary outcomes (readmissions to hospital and emergency department) and linear regression for continuous outcomes (e.g., days of medications for OUD treatment; days of opioid or methamphetamine use).

Sample Size and Power

The primary goal of this pilot trial is to develop and pilot test the MIAPP intervention. This pilot work will provide evidence of the feasibility/acceptability of the MIAPP intervention and research procedures that will be used to inform a future, larger study, as assessed by our ability to fully recruit the planned sample and deliver the intervention to the majority of those randomized to the intervention arm. The sample size of 40 for the pilot randomized controlled trial was chosen as we projected we could enroll and complete the study procedures and analyses within the available funding period. Although the sample size was not selected for the purpose of providing a fully-powered study, with our sample size of 40 we are nonetheless powered at 80% to detect some effects if they are large in size. For binary outcomes, power depends on the base rate of the outcome measured, and based on prior studies (38, 55), we anticipate that anywhere from 20% to 50% of participants in treatment as usual successfully linking to outpatient medications for OUD services post-discharge. For binary outcomes, including the primary outcome measure, our pilot study will be powered to detect intervention effect sizes of $RR \geq 1.89, 2.05, 2.40, \text{ or } 3.10$, if linkage rates for treatment as usual are 50%, 40%, 30%, or 20%, respectively.

For continuous outcomes (days of buprenorphine coverage, days of opioid or methamphetamine use), we will be powered to detect standardized effect sizes of Cohen's $d \geq 0.91$ with 40 participants.

Appendix

MIAPP Pre-Screen Script

Information completed before screening encounter

Screening ID Number: _____

Date of screening: _____

Initials of person conducting the screen: _____

Introduce yourself:

- Hi, my name is _____. I'm a research coordinator here at Harborview.
- I'm letting people know about a research study we're doing here in the hospital, which you might be eligible to participate in.
- I'm wondering if I could tell you about the study today, in case you're interested in participating in it?

If no: No problem. Is there another time that might be better for me to come by?

If yes:

- Great, thank you.
- I'll tell you about the study. Then, if you think you're interested in participating, I'll ask some questions to see if you're eligible.
- This can take anywhere from 10-30 minutes. Will that be okay?

Purpose of study:

- The purpose of this study is to test a new program that we think may be helpful to people in the hospital here at Harborview. In particular, we want to test whether this new program can be helpful to people who use opioids and methamphetamine, who have started a medication called buprenorphine while they are here in the hospital. We're conducting a study where we're offering this program to patients here in the hospital. The study is a clinical trial, where some patients receive the program, and some patients don't.

Description of study:

- You can choose whether or not you'd like to participate in the study. Choosing to participate (or not participate) won't affect the medical care you receive while you are here in the hospital.
- If you participate in the study, you will be randomly assigned to 1 of 2 conditions.

- The first condition is called “treatment as usual.” If you’re in the “treatment as usual” condition, I’ll invite you to complete two interviews with me – one before you leave the hospital, and one 30 days after you leave the hospital. During these interviews, I’ll ask you questions about your medical conditions, mental health, and substance use. You’d have the option of also providing a urine sample that we would use to see if buprenorphine or other drugs are in your system. You’d be compensated for your time and can receive up to \$140 for completing these two interviews and providing a urine sample.
- The second condition is called “MIAPP.” If you’re assigned to the MIAPP condition, I’ll invite you to complete the same two interviews with me and you’d have the option to provide a urine sample. In addition, we’d offer you financial incentives (i.e., money) if you demonstrate that you’re continuing to take buprenorphine after you leave the hospital. For example, we’d pay you \$70 if you initiate treatment in a buprenorphine program after you leave the hospital. We’d also pay you \$15 for every day that you submit a video of yourself taking your buprenorphine medication after you leave the hospital, for up to 30 days. We’d provide you with a reloadable debit card and a smartphone app to help with this. We’d also connect you with a “patient navigator” who will help you with these things. If you’re in this MIAPP condition, you could receive up to \$680 for participating. As a basic rule, the more you continue to take buprenorphine (and upload videos of yourself taking it), the more money you’d receive.
- If you decide to participate in this study, you’ll will be randomly assigned to one of these two conditions. The condition you would be assigned to is determined by a coin flip.

What questions do you have so far?

Determine Interest in Participating:

Great. Now that you have a basic understanding of the study, do you think you might be interested in participating?

- Yes
- No

If No:

No problem. If you feel comfortable sharing why, that information is really helpful to us. But it’s totally fine if you don’t want to share why.

Reason for not wanting to participate, if given: _____

If Yes:

Great! Before we can enroll you in the study, I need to determine if you are eligible. I would like to ask you a few questions about your demographics, your substance use, and your medications. Would now be a good time to ask these questions?

- ☐ Yes
- ☐ No

If No:

No problem. Is there another time I could come back that might be better?

Scheduled date and time: _____

If Yes:

Some of these questions may be sensitive. You are free to skip any questions you don't want to answer. Please also let me know if you need a break.

Ensure that patient has adequate privacy.

- *If visitors are in the room: Ask the patient if they'd like the visitors to leave for a few moments while you complete the eligibility screening.*
- *If there are multiple patients in the room: if there is a private area available: ask patient if they would like to move to a more private area if feeling well enough to move. Or, if there is a curtain or partition available, ask if they would like to have the curtain closed for privacy.*

Confidentiality Reminder

- I really appreciate you taking the time to be with me today.
- As a reminder, the information you give me today will be used for research that can potentially help future patients in the hospital.
- Please be as honest as you can when answering the following questions.
- You are free to skip any questions you do not want to answer.
- The information you give us won't be shared with your doctors or anyone else here in the hospital, except in rare circumstances, such as if we're worried about potential harm to you.
- If you have any question, feel free to ask! I'm here for you.

Participant Locator Form

Participant information:

| | |
|---|--|
| Name | |
| Date of Birth | |
| MRN | |
| Social Security Number | |
| Address (Street, Apt #) | |
| City, State, Zip | |
| Phone 1 | |
| Phone 2 | |
| Email | |
| Scene App Username | |
| Scene App patient ID # | |
| Planned outpatient buprenorphine clinic location | |

Alternate contact #1

| | |
|---------------------|--|
| Name | |
| Relationship | |
| Phone 1 | |
| Phone 2 | |
| Email | |

Alternate contact #2

| | |
|---------------------|--|
| Name | |
| Relationship | |
| Phone 1 | |
| Phone 2 | |

| | |
|-------|--|
| Email | |
|-------|--|

If possible, collect two more contacts from participant

MIAPP Phone Contract

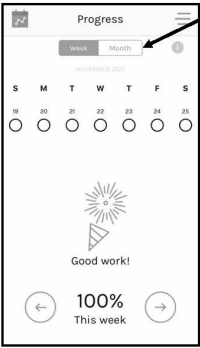
MIAPP Phone Agreement

By signing this document, I, _____, acknowledge I am receiving this phone (MIAPP Phone ID # _____) for use during the MIAPP research study. I understand this phone should be returned to the research staff in good, working condition at the final visit date so it can be used by future participants. This phone is expected to be returned on ____ / ____ / ____

| | | |
|--------------------------|-----------|------|
| Participant Printed Name | Signature | Date |
|--------------------------|-----------|------|

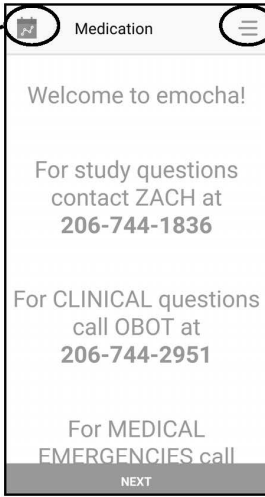
| | | |
|--------------------|-----------|------|
| Staff Printed Name | Signature | Date |
|--------------------|-----------|------|

Review video upload progress

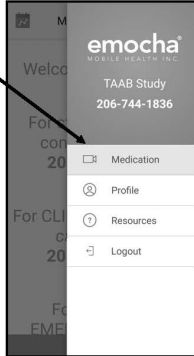


- Click calendar icon in upper left corner
- Switch between weekly and monthly views to view progress
- A green check mark means you uploaded at least 1

Medication



Access resources, weekly survey and change settings



Resources


- Access UW Medicine's ecare
 - Login to see upcoming medical appointments, review test results and message your care team
- Links to local resources and medication information

Settings


- Click "Profile"
- Option to enable "touch ID" or passcode in place of a password
- Start or stop medication alerts (you can enable 1 reminder per day)
- Change your email or password

Steps for daily upload


1. Log-in with username@uwtaab



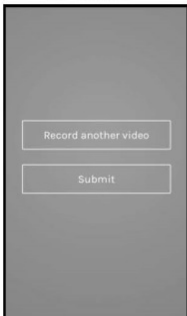
5. Start video by clicking red button



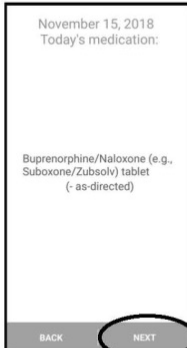
3. Home Screen: Click "next" to start



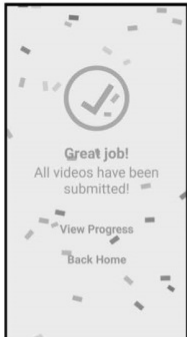
6. Choose "record another video" (if needed) or "submit"



4. Screen shows medication




7. End screen



Download app

- Open app store
- Search for "emocha video"
- Download app



Notes

- Connect to wifi when available to use less data.
- If you do not have wifi or cellular service, videos will be stored in your device until you return to service.
- If you submit another video at the same time, all videos will be uploaded.

MOUD Adherence

I would like to ask you about your use of ____ [medication for OUD] _____ in the 30 days after you left the hospital.

Note to Assessor: using the calendar help orient participants to specific window of time, ask them about any special events (i.e., Holidays such as Thanksgiving, Christmas, etc., vacations, birthdays, holidays)

[Calendar - use to help specify days and recall, including the date of discharge from the hospital]

In the past 30 days after your discharge from the hospital, did you ever take _____ when it was prescribed to you?

YES (continue to daily questions below)

NO (report “none taken” for all days below)

Assessor: “During this time period, are there any days that you were in jail or the hospital?” (Mark those days as institutionalized days)

“On mm/dd, did you take your _____ as prescribed, took less than prescribed, more than prescribed, took it in a way different than prescribed (e.g., intranasal), or did not take any _____ that day?” [Card 3]

| | | | | | | |
|--|--------|---------|-----------|--|--------|----------|
| Study ID: _____ Today's Date: _____ Participant Discharge Date: _____ | | | | MIAPP Medication Adherence TFLB Calendar | | |
| <p>Current Total Daily (<i>insert name of medication for OUD</i>) Dose: _____ mg</p> <p>Note to assessor: Collect information on past 30 days beginning with <u>the day after the hospital discharge date</u></p> | | | | <ol style="list-style-type: none"> 1. Mark the day of hospital discharge with an X – then number the past 30 days. 2. Ask participant what their total daily buprenorphine dose is 3. Ask participant if any special events or a holiday, etc. occurred between the dates of the day after the Discharge Date (Day 1) and Day 30 4. Ask if between dates of Day 1 and Day 30, if they took their total daily dose every day – if yes, mark Day 1-30 with total dose in mg. Do step 5 and stop. 5. Ask if between dates of Day 1 and Day 30, if they took any of their medication in a way other than prescribed i.e. intranasal 6. If didn't adhere – ask participant starting with “ On MM/DD how much buprenorphine did you take?” document amount (in mg) of how much Buprenorphine for each day of the past 30 days. | | |
| | | | | | | |
| Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

UDT Step-by-Step Instructions

Alere iCup and Fentanyl Strip test

1. Collect fresh urine in the specimen cup. Make sure urine is above the minimum line
2. Remove fentanyl strip from canister
3. Holding the strip vertically by the end (where product name is printed). Avoid contamination by NOT touching the strip membrane.
4. Dip the test strip in urine specimen cup for 10-15 seconds. Do not immerse strip past the maximum line.
5. Set strip aside on a non-absorbent flat surface.
6. Open Alere iCup lid foil pouch. Remove test lid from pouch. Discard pouch
7. Twist lid onto the cup. The cup lid must be closed tightly
8. Tilt the cup on its legs to activate the test.
9. Set timer for 5 minutes. Read test results for both the Alere iCup and Fentanyl test strip at 5 minutes.

DO NOT READ RESULTS FOR ALERE iCUP PAST 8 MINUTES
DO NOT READ RESULTS FOR FENTANYL STRIPS PAST 10 MINUTES

Reading Alere iCup Results

Test Control – region is designated with “C”

Test Assays – 7 columns (2 substances per column); 2 test regions (T1 and T2)

Invalid Urine Test: C region line is absent – Rerun test

Negative Urine Test: All lines are present – even a very faint test line is considered negative result

Positive Urine Test: Missing line in T1 and/or T2 region

Reading Fentanyl Test Strip Results

Negative Urine Test – All lines are present for both Test and Control

Positive Urine Test – Missing line in the Test Region, but Control line is present

Invalid Urine Test – Missing a line in the Control region; Or missing lines in both Test and control regions. Rerun test

Documenting UDT Results

All UDT Test results will be documented on dated and participant ID labelled UDT Form

Once assessor is back to computer, they may enter the results on REDCap in the final visit UDT Form.

The paper form should be stored in a locked filing cabinet along with the participant’s Adherence TFLB Calendar.

Adverse Event Reporting Form

MIAPP Adverse Event Report Form

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

This form is to be completed by MIAPP Research staff upon notice of an adverse event and updated until event is resolved and all necessary parties are notified of the specific singular event.

| | |
|---|---|
| Adverse Event Record ID: | — — — |
| Date of Report: | Date report was written. |
| Name of staff completing report: | First and Last Name of Research Staff Person |
| Research Role of staff completing initial report | <input type="checkbox"/> Research Assistant <input type="checkbox"/> Research Coordinator/Patient Navigator <input type="checkbox"/> Co-Investigator <input type="checkbox"/> Primary Investigator |
| Date Research Staff became aware of event: | Date Staff became aware of event |
| How did Research Staff become aware of event: | <input type="checkbox"/> Electronic Medical Record <input type="checkbox"/> Informant: Who was the informant? <input type="checkbox"/> Other: How did you become privy to the event? |
| | |
| Date of Event: | When did the event occur? |
| Participant's MIAPP Study ID: | — — — — |
| Participant's Condition Assignment: | <input type="checkbox"/> PN+mHealth <input type="checkbox"/> TAU |
| Description of Event: | Describe the event – what happened, how did it happen, how upset does the participant seem, etc. |
| | |

| | | |
|--|--|---|
| 1. Was the event serious? <input type="checkbox"/> YES (please indicate reason) <input type="checkbox"/> NO | <input type="checkbox"/> Death <input type="checkbox"/> Life-Threatening <input type="checkbox"/> Hospitalization <input type="checkbox"/> Persistent or significant disability/incapacity <input type="checkbox"/> Result in birth defect <input type="checkbox"/> Breach of Confidentiality <input type="checkbox"/> Other – Specify the other serious outcome | |
| 2. Was the event related to study participation? <input type="checkbox"/> YES (please indicate degree of relatedness) <input type="checkbox"/> NO | <input type="checkbox"/> Possibly Related <input type="checkbox"/> Definitely Related | <u>Justification for degree of Relatedness</u> Refer to DSMP to explain reasoning for selected degree of relatedness. |
| 3. Was the event expected? | <input type="checkbox"/> YES <input type="checkbox"/> NO | |
| What is the severity of the event? <input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe | <u>Justification for degree of Severity</u> Refer to DSMP to explain reasoning for selected degree of severity | |
| <p>Event meets Severe Adverse Event Criteria – If the answer to Q1 and Q2 above are “YES” And Q3 is “NO” (i.e. SAE that is an unanticipated problem), then:</p> <ul style="list-style-type: none"> - Research staff should notify and report to Site PI within 24 hours of becoming aware of the event (as for all SAEs), and - Research Team or PI should then notify the NIDA PO and DSMB Chair within 24 business hours of the event by email and then submit a written follow-up plan to the PO within 2 days of the event. - Research Team should also plan to report the event/submit forms to their Site IRB within 10 business days (within 24 hours if there was a breach of confidentiality) | | |

| | |
|--|--|
| Action taken by research staff following notice of event: | <p align="center"><u>Describe action taken</u></p> <p>Describe any actions staff took once they became aware of the event.</p> |
| Is a planned follow-up need? <input type="checkbox"/> YES (please indicate follow-up plan) <input type="checkbox"/> NO | <p align="center"><u>Description of Follow-up Plan:</u></p> <p>What is the Follow-up plan to resolve any issues?</p> |
| Date of Follow-up plan implemented | What date was the follow-up plan implemented? |
| | |
| <p align="center"><u>To be completed by Site PI upon notice of an event</u></p> | |
| Has the Site PI been notified of the event? <input type="checkbox"/> YES (Please provide dates of notification and reviewed) <input type="checkbox"/> NO (notify Site PI immediately) | <p>Notified: Click here to enter a date.</p> <p>Reviewed: Click here to enter a date.</p> <p align="center">(Completed by Site PI)</p> |
| Does the Site PI believe that the event put greater than minimal risk than was previously known or recognized? | <input type="checkbox"/> Yes <input type="checkbox"/> No |
| | |
| <p align="center"><u>If the event is determined to be a Severe Adverse Event that is an Unanticipated Problem, then the NIDA PO needs to be notified in addition to UW IRB.</u></p> | |
| NIDA PO Notified? <input type="checkbox"/> YES (please note dates of contact) <input type="checkbox"/> NO | <p>Initial Email Date: Click here to enter a date.</p> <p>Follow-up plan Email: Click here to enter a date.</p> |
| | |
| Has the site IRB been notified of the event? | <input type="checkbox"/> Yes <input type="checkbox"/> No |
| Date of Site IRB notified: | Click here to enter a date. |

| | |
|---|---|
| Action Requested by IRB: <input type="checkbox"/> YES (please describe IRB action) <input type="checkbox"/> NO | <u>IRB Requested Action</u> Describe the requested IRB action. |
| Date of IRB Action Request: | Click here to enter a date. |
| Date of NIDA PO notified of IRB Action Request | Click here to enter a date. |
| | |
| Outcome of Event: | <input type="checkbox"/> Unresolved – yet to be reviewed by PI <input type="checkbox"/> Ongoing – PI reviewed, waiting for responses from necessary parties <input type="checkbox"/> Unknown (lost to f/u) <input type="checkbox"/> Resolved – No more further action required (Resolved Date: Click here to enter a date.) <input type="checkbox"/> Death (Date: Click here to enter a date.) |
| Will the participant continue study involvement? | <input type="checkbox"/> YES <input type="checkbox"/> NO |

Additional Notes

Actions to be taken by Research Staff for Serious Adverse Events

SAEs that are Unanticipated Problems

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

- Report to Site PI within 24 hours of becoming aware of the event
 - o Judith Tsui (tsuij@uw.edu)
- Report to NIDA PO and DSMB chair within 24 business hours by email and submit a written follow-up within 2 days of the event
- Report to Site IRB
 - o Any IRB action response will be reported to NIDA PO and DSMB chair within 3 business days of site study team’s notice of the action.
 - UW – ([link to UW HSD IRB Reporting Guidelines](#))
 - If the event is a breach (risk or loss) of confidentiality – report event to IRB within 24 hours.
 - If the event did not result in breach of confidentiality but still an unanticipated event UW Research Team must report to IRB within 10 business days of the event (and submit “Supplement RNI form”

Events that are not unanticipated problems

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

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

DSMB Reviews and Reports

All individual SAEs and cumulative AEs are to be reviewed by the project’s designated DSMB annually. Following the annual DSMB AE Review, reports and, if needed, plans of action to modify study design to improve participant safety will be submitted to the IRBs. Reports are to be shared with the NIDA PO within a month of DSMB review.

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