Study Protocol

Official Title:

Reward-based Technology to Improve Opioid Use Disorder Treatment Initiation After an ED Visit – Phase 2

NCT Number: NCT05180669

Date of Document: 02-Sep-2019

1. TITLE
Reward-based Technology to Improve Opioid Use Disorder Treatment Initiation after an ED Visit (OARSCM)

2. EXTERNAL IRB REVIEW HISTORY*
N/A

3. PRIOR APPROVALS:
All necessary approvals will be obtained prior to commencing the research.

Conflict of Interest (COI): We will adhere to the mitigation plan developed by the campus COI Committee which includes the following:
1. Dr. Boudreaux will not be involved in enrolling or consenting subjects in this study.
2. The patient consent form shall include the following
   The study is being paid for by the National Institutes of Health. UMMS and Q2i are collaborators in this project. Any assessments or interventions that are developed as part of this project will be jointly owned by UMMS and Q2i. Both organizations and the participating scientists could potentially earn money from selling the assessments and interventions developed during this study. Dr. Boudreaux, the Principal Investigator on this study, is a faculty member at UMMS. He also is an unpaid advisor to Q2i. Dr. Boudreaux does not get paid for the work he does for Q2i.
 3. Dr. Boudreaux will disclose his relationship with the company in publications and presentations related to the product.
   4. During the course of the study, Dr. Boudreaux cannot serve as a scientific officer, director or board member of the company. The Q2i website will prominently indicate that Dr. Boudreaux is an unpaid advisor to Q2i.
   5. Dr. Boudreaux will not directly analyze the data. Instead, the study statistician or other qualified personnel will analyze the data.
   6. Dr. Boudreaux will be required to abstain from the purchase or acceptance of options for company stock during the study. This term shall also apply to immediate family members. The foregoing restrictions shall remain in effect for a period of one year after the end of the study.
   7. Dr. Boudreaux will notify the COI Committee should his financial interest or the nature of his collaboration with Q2i.

UMMS Data Core request: Electronic Health Record Integration: This is a Fast-Track STTR. This means the NIH will fund Phase 1 first, then make a decision about whether to fund Phase 2 after reviewing the progress report from Phase 1. The OARSCM software being developed with this grant will ultimately be integrated with the UMMHC EHR (Epic). However, this is not anticipated to happen in the Phase 1 part of the study. We will be submitting our data request to the UMMS Data Core, but we do not anticipate full approval of integration and resolution of data sharing and security until AFTER Phase 1 is complete. We will submit additional materials to the IRB as needed once Phase 1 is complete and the path for integration is cleared through UMMS Data Core.

4. OBJECTIVES*

The Specific Aims for Phase 2 have been modified from the original submission with approval from the program officer at NIDA. Updated Aims are as follows:

Phase 1, Aim 1: To develop the OARS+CM platform. User-centered design principles will be employed to enhance the existing OARS software to produce OARS+CM. This will culminate in a proof-of-concept study of up to 20 individuals with OUD and their providers/clinicians whose feedback and experiences will be used to iteratively improve the interface and features. The usability criterion will be reached when ≥ 3 participants in a row are able to use the program without staff assistance (with on-device support if needed, as intended) and no more substantive improvements are needed. We will also assess acceptability, and rates of treatment initiation and adherence (attending therapy, drug urine/saliva tests).

Phase 2, Aim 1: To assess the efficacy of OARS+CM in promoting MOUD treatment initiation. Using a randomized controlled trial (N=102 randomized), the efficacy of the OARS+CM (n=51) in promoting MAT initiation will be tested against TAU with MyMAT (an educational mobile app) (n=51).
> H1: OARS+CM will result in greater MOUD treatment initiation from acute care settings than TAU with MyMAT.

Phase 2, Aim 2: To assess efficacy of OARS+CM in promoting transition from MOUD Initiation to maintenance.
> H2: OARS+CM will result in greater rates of sustained abstinence for 6 months after the index visit.
> H3: MOUD therapy attendance will be increased such that OARS+CM >TAU with MyMAT.

Phase 2, Aim 3: To evaluate costs. Exploratory data on cost-effectiveness, cost avoidance and cost savings through reduced acute care visits between conditions will be collected and analyzed.

This submission is currently seeking approval for Phase 2 following successful completion of Phase 1, as the NIH will only fund Phase 2 if Phase 1 is successful. All materials for Phase 2 in this submission outline what has occurred since Phase 1 was completed successfully. Any changes to Phase 2 material have been revised and are being submitted to the IRB as a modification for review and approval when appropriate.

5. BACKGROUND*
See grant: "RESEARCH STRATEGY" (p.2-4) for details. The Procedures for Phase 2 have been modified from the original submission. Updated Procedures are as follows:

Procedures
Screening, recruitment, eligibility and training procedures are in C.2.1 and the Eligibility criteria document.

Randomization will occur following determination of eligibility using an urn procedure and stratifying on 1) other (than opioid) substance use disorder no/yes, 2) gender/sex, 3) race/ethnicity.

TAU with MyMAT (n = 51). In the acute care setting, the Behavioral Health Service run by Drs. Boudreaux and Davis-Martin provides SBIRT for substance use disorders, including OUD. They provide SBIRT as part of TAU, including, when possible, warm handoff contact with outpatient MOUD treatment that includes a scheduled outpatient appointment, optimally within 48 hours of the ED visit. Patients randomized to this group will also receive MyMAT, a mobile application with opioid treatment educational content, as an attention control measure against OARS+CM. TAU outpatient suboxone treatment consists of urine toxicology screening, group/individual therapy, and MOUD prescription continent on drug-negative (except cannabis, which is legal in MA) urine toxicology. Treatment visits are typically, weekly in weeks 1-4 and then taper over time, to every other week in weeks 5-8, and monthly in weeks 9-12 and thereafter. Nonadherence can lead to increased frequency/intensity of therapy and urine toxicology until the patient stabilizes. If increased frequency/intensity is unsuccessful, patients may be referred to detoxification and subsequently re-admitted to outpatient care when appropriate.

OARS+CM (n = 51) patients will receive the same TAU procedures described above. They will also earn chances for prizes, with the same targeted behaviors, escalation of chances for prizes for each targeted behavior in a row, and reset criteria described. Briefly, for scheduling a MOUD treatment intake patients will earn 1 guaranteed prize of $5 and for completing their MOUD treatment intake patients will earn 1 guaranteed prize of $20. After intake, patients will earn chances to win prizes for each targeted behavior completed. Chances for prizes will start at 2 and then will increase by 2 chances with documentation of each targeted behavior in a row up to a maximum of 10 draws/targeted behavior. With 38 targeted behaviors (schedule MOUD intake, complete intake, 12 opioid-negative urine toxicology/week over 12 weeks plus bonuses for cocaine-negative tests, and 12 group/individual therapy/week over 12 weeks), patients can earn up to 252 chances for prizes during the 12-week RCT.

6. INCLUSION AND EXCLUSION CRITERIA*
Inclusion and Exclusion Criteria: See grant: "HUMAN PARTICIPANTS PROTECTION" (p.17) for details. The Overall Study Design, Study Population and Randomization, and Interventions for Phase 2 have been modified from the original submission. Updated Overall Study Design, Study Population and Randomization, and Interventions are as follows:

Overall Study Design: This Fast-Track STTR includes a small proof of concept pilot study followed by a randomized controlled trial (RCT) with two conditions: 1) treatment as usual (TAU) with MyMAT, and 2) the OARS + CM. This study will use recruitment and study enrollment procedures successful in our prior SUD research (refer to Biosketches). Participants will be individuals with OUD presenting to acute care settings. They will complete a screening survey to assess for minimal eligibility criteria and confirm their interest. Once confirmed, research staff will obtain written informed consent and enrolled in the study. Participants will be randomized to one of two conditions described above. The study period begins at enrollment during their index acute care visit. Follow-up surveys and tracking through the mobile application (OARS+CM) and review of all relevant healthcare records will occur at 1, 3, and 6 months after enrollment. For scientific rigor, biochemical verification of abstinence from opioids

will be obtained from outpatient treatment records. Self-reported use will also be obtained through structured follow-up assessments.

Study Population and Randomization: We will randomly assign N=102 individuals with OUD meeting minimal eligibility criteria to one of two conditions using REDCap, allocated 1:1 to the two conditions.

Interventions:

Group A: TAU with MyMAT. For TAU participants, the usual care provided to individuals with OUD at the UMass University and Memorial hospitals will be provided. This typically consists of (1) medical stabilization and treatment, as needed; (2) brief counseling and referral to treatment by a social worker or other behavioral health provider, which includes providing a tailored referral list; and (3) when the patient is interested and treatment facility available, a "warm handoff" comprised of contact with the outpatient provider and transportation directly to the facility or a scheduled intake appointment within 48 hours, when feasible. TAU participants will also receive MyMAT, a mobile application with opioid treatment educational content, as an attention control measure against OARS+CM.

Group B: OARS+CM. Participants assigned to OARS+CM will receive the same treatment as in the TAU condition but with the enhancement of the CM features, described in detail in Section C.2.1, Proof-of-concept testing for usability section.

Table 1: Eligibility criteria	
Inclusion	**Exclusion**
◆ >= 18 years old	◆ Persistent altered mental status (not alert, not oriented, psychotic).
◆ Presenting for acute care at UMass University and Memorial hospitals, including EDs, inpatient medical units, inpatient behavioral health units, or community acute care partners for opioid addiction related health complaints, including opioid overdose, opioid related medical consequences, opioid intoxication or withdrawal syndromes, and/or seeking help for OUD	◆ Patient declines referral to UMass Bridging MAT Clinic, to CleanSlate Addiction Treatment Center, to SaVida Health, to Eleanor Health, or to Spectrum Health Systems for MOUD.
◆ Presence of a current DSM-V opioid use disorder (OUD), mild to severe	◆ Not interested or willing to participate in MOUD treatment
◆ Medically appropriate for outpatient MOUD treatment, as judged by the treating clinician and behavioral health consultant or toxicologist working with the patient clinically	◆ Unwilling to use the OARS+CM app (if assigned)
	◆ Does not have access to their own smartphone with at least iOS 7.1 or Android 4.2, the minimal technology required to run the app, or not willing to access clinic-dedicated computer to access the program

	⬥ Currently a UMMS student
⬥ Treatment provider of patient who consented to participate	⬥ Prisoner or currently in state custody or pending legal action that might lead to imprisonment
	⬥ Cannot paraphrase the study requirements
	⬥ No reliable telephone access
	⬥ Does not read or speak English
	⬥ Does not reside in the central MA region
	⬥ Already enrolled into the trial

7. STUDY-WIDE NUMBER OF SUBJECTS*
N/A

8. STUDY-WIDE RECRUITMENT METHODS*
N/A

9. STUDY TIMELINES*
Phase I of the Project was completed within the 1st year of the project (technically within 6 months of the Phase 1 notice of award), and Phase 2 tasks will be completed within years 2 and 3 of the project. See grant: "PROJECT TIMELINE" (p.16) for details.

10. STUDY ENDPOINTS*
See grant: "RESEARCH STRATEGY" (p.11-13) for details.

11. PROCEDURES INVOLVED*
Measures: For Phase 1, the System Usability Scale (SUS) (patients and clinicians), Timeline Followback (TLFB) (patients only), and Addiction Severity Index (ASI) (patients only) will be used and is included in this submission. For Phase 2, The Mini Quiz (MQ), Mini-Usability Acceptability Testing (Mini-UAT) questionnaire, Timeline Followback (TLFB), PROMIS Pain Intensity and Interference Scales (PIIS), HIV Risk Behavioral Scale (HRBS), Post-traumatic Stress Diagnostic Scale for DSM-5 (PDS), Treatment Satisfaction Scale (TSS), and the System Usability Scale (SUS) will be used and are included in this submission.

Assessments/Procedures for Phase 2	Intake	Onboarding	Transition to Suboxone	Week 1 to 12	Month 1	Month 3 / End of Tx	Month 6
Mini Quiz, Patient form, OUD	X						
Mini-UAT, Service Utilization, TLFB	X				X	X	X
PIIS, HRBS, PDS, U-Tox	X				X	X	X
Healthcare Utilization	X						X
App training, warm hand-off scheduling outpatient Suboxone intake		X					
Monitor completion of MOUD intake			X				
MOUD TAU / OARS+CM				X			
Monitor treatment attendance/u-tox				X			
Treatment satisfaction, SUS*						X	

*Only for OAR+CM group

Phase 1: Aim 1 (Develop OARSCM): 30 Clinicians (20 user testing, 10 dyads) and 30 Patients

1a. After the OARSCM is developed, patients meeting criteria and consenting to participate will be guided through using the mobile application on their personal smartphone. If the participant's smartphone is not available for use to complete the instructed tasks, the participant will be able to use a study-provided iPad.

1b. Clinicians not associated with a specific patient participant verbally consenting to participate after reviewing the User Testing Fact Sheet will be guided through using the provider portal using a test account on a study provided computer in a private office.

1c. Clinicians working at the UMass Bridge Clinic, at the CleanSlate Addiction Treatment Center at SaVida Health, and at Spectrum Health Systems associated with a patient participant (considered a dyad) verbally consenting to participate after reviewing the Dyad Fact Sheet will receive an in-person or virtual training on the provider portal on a study provided computer in a private office. After the training, the clinician will provide standard MAT treatment to patient participants and use the OARSCM provider portal to track treatment.

2a. Patient participants will complete a short survey on the iPad and a 20-30-minute interview-assessment during their hospital visit. Patient will provide their general impressions of the OARSCM mobile application (e.g., perceived appropriateness, acceptability, and feasibility), as well as any identified barriers or weaknesses. It will not interfere with care.

2b. At a later time, all clinicians (dyad or not) will complete an in-person or virtual interview to provide their general impressions of the OARSCM provider portal (e.g., perceived appropriateness, acceptability and feasibility), as well as any identified barriers or weaknesses. This clinician interview will occur outside of the acute care and outpatient visit to not interfere with any patient care. All interviews will be audio recorded with verbal consent.

3. If a dyad clinician elects to withdraw from the study but the patient chooses to remain enrolled, a research assistant will be responsible for inputting the patient data into OARSCM as to not interrupt the patient's ability to earn prizes. We would also not obtain the clinician's user testing data.

4. Patient will be connected to a community based Suboxone treatment provider, the UMass Bridging Clinic, the CleanSlate Addiction Treatment Center, SaVida Health, or Spectrum Health Systems and schedule an intake appointment. Patient will receive standard MAT treatment and will use the OARSCM mobile application to track their progress in treatment. To use the OARSCM mobile application to track their progress in treatment, patient will enter their name (first and last), email address, DOB and cell phone number when available into the application to create an account. Patient will have the option to journal free text entries about how they are thinking and feeling throughout treatment. Patient will have the opportunity to earn prizes for engaging the OARSCM program throughout treatment. Engagement in treatment is measured by scheduling and attending treatment appointments as well as urinary tox results, all of which is entered into the OARSCM program by the MAT provider using the provider portal. See "APPENDIX" for screenshots of patient application and provider portal.

5. Patient will not receive any follow up calls after the hospital visit but will have their use of the OARSCM mobile application and engagement with treatment as tracked by the OARSCM mobile application monitored for 4 weeks. Participation in this study will last about 4 weeks once the patient has started MAT treatment. After these 4 weeks, the participants will be informed that their 4-week participation has now ended and that we appreciate their participation. They will also be informed that new information related to their appointments, appointment attendance, appointment engagement and tox results will not be entered into their OARSCM mobile application profile. However, they will be able to view this DATA that had been previously entered throughout the 4-weeks. They will continue to have access to their OARSCM mobile application account in order to use their unredeemed Spins, Prizes, and eGift cards for a short time. During enrollment, patient participants will be given a handout on how to uninstall the application if they no longer want the application on their smart phone after participation. See grant: "RESEARCH STRATEGY" (p. 8). See grant: "APPENDIX" for screenshot of patient notification that their 4-week participation has now ended and handout of how to uninstall the mobile application.

Phase 2: Aims 1 and 2 (Efficacy of OARSCM): 102 patients randomized to 1 of 2 groups
If the patient agrees to participate:

1. Participants (acute care patients who meet eligibility criteria and complete consent process, see section 30. Consent Process) will be randomized to either TAU (with MyMAT) or OARS mobile application plus contingency management (OARSCM).

2. Participants will complete an interview assessment during their current medical visit. It takes about 20-30 minutes to complete. They will be asked to provide a urine sample. It will not interfere with their care.

3. Participants will be provided a warm handoff to a community-based MOUD treatment provider. All participants will be eligible to receive standard MOUD treatment per treatment as usual at the site they are referred to. If they are randomized to OARSCM, they will use the mobile application to track treatment progress and have the potential to earn prizes for engaging with the application throughout treatment.

4. Participants will receive a welcome call at 1-week post-enrollment. This call will welcome participants to the study and provide an opportunity to answer any questions they may have about participation as well as ensure they are not having any issues with study mobile applications. This call will take about 5 minutes.

5. They will complete 3 follow-up telephone calls to find out how they are doing. The calls will focus on their substance use, especially opioid use, treatment engagement, healthcare visits, health, and well-being. These calls will take about 20 - 30 minutes to complete. The calls will occur at 1, 3, and 6 months after the enrollment date.

6. The researchers will review the participants' healthcare records, including the Massachusetts Prescription Monitoring Program's EHR-integrated tool MassPAT that provides information on participant's prescriptions for MOUD through the 6 months after enrollment. We will review the

healthcare record for all participants and will only be viewing the MassPAT record for participants who do not have urine toxicity results at their outpatient MOUD provider at the 1, 3, and 6-month follow up time points. MassPAT will be used to determine if a participant is still engaging in treatment during these follow-up time points if the participant cannot be reached for their follow-up interviews or if they have stopped attending appointments at their study clinic site and have not requested to leave the study.

7. We will be seeking to collect information from medical providers or records outside of the UMMS system (a substance use treatment provider in the community that doesn't have a UMMS connection) and will require a signature on a Release of Medical Information with designated treatment facilities identified.

8. The researchers will review publicly available databases, like the participants' state's vital statistics registry (a document created by the state that tracks important health indicators, like births, deaths, and cause of death). See grant: "RESEARCH STRATEGY" (p.8-13) for details.

12. DATA AND SPECIMEN BANKING*
N/A

13. Data Safety and Monitoring Plan*
Suicidality questions will be asked in real-time during the participants enrollment in the acute care setting. If participant has identified suicide risk and treatment team is currently unaware, research staff will notify treatment team of suicide risk.
See grant: "DATA SAFETY AND MONITORING PLAN" (p.14) for further details.

14. PLANS TO MONITOR TRIAL PERFORMANCE, INCLUDING FIDELITY AND INTEGRITY OF THE DATA*
We will adhere to Investigator Guidance: Prompt Reporting Requirements (HRP-801). See grant: "DATA SAFETY AND MONITORING PLAN" (p.14-15) for details.

15. WITHDRAWAL OF SUBJECTS WITHOUT THEIR CONSENT*
Due to the sensitive nature of the topics discussed during the interview (behavioral health, substance use), the investigator's discretion will be used in deciding continued participation in the study.

16. RISKS TO THE SUBJECTS*
See grant: "HUMAN PARTICIPANTS PROTECTION" (p.19) "Potential Risk" and "Adequacy of the Protections Against Risk" for details.

17. POTENTIAL DIRECT BENEFITS TO SUBJECTS*
See grant: "HUMAN PARTICIPANTS PROTECTION" (p.20) "Potential Benefits of Proposed Research to Research Participants and Others" for details.

18. VULNERABLE POPULATIONS*
This study does not specifically recruit the vulnerable populations listed by NIH

supplemental grant instructions (i.e., pregnant women, human fetuses and neonates, prisoners, or children), and it does not exclude pregnant women and human fetuses and neonates. The study involves brief counseling, referral to treatment, and a mobile application that does not have restrictions in terms of safe use by vulnerable or other persons. No inducement, monetary or otherwise, will be offered to terminate a pregnancy. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy. Individuals engaged in the research will have no part in determining the viability of the neonate.

19. MULTI-SITE RESEARCH*
N/A

20. COMMUNITY-BASED PARTICIPATORY RESEARCH*
N/A

21. SHARING OF RESEARCH RESULTS WITH SUBJECTS*
It will be several years before the results of the research are available. If the subjects would like us to try to reach them at that time, we will request that they let us know during the consent process.

22. SETTING
We will recruit participants from two UMass Memorial Medical Center hospitals, including EDs, inpatient medical units, inpatient behavioral health units, (University and Memorial campuses), community acute care partners, and will refer participants to either the UMass Bridge Clinic, the CleanSlate Addiction Treatment Center, SaVida Health, Eleanor Health, Right Choice, and Spectrum Health Systems—outpatient MOUD clinics based on their preference. Patient interviews will be conducted in a private setting such as in an ED or inpatient treatment room or private consultation room. Clinician training and interviews will also be conducted in a private office or remotely via Zoom and will not be recorded. Data analysis will be completed in a private office on a secure served and database.

23. RESOURCES AVAILABLE
Research Personnel. Investigators and key personnel will have undergone mandatory education in human research participants' protection. Educational systems are in place to ensure that all research staff have been through such training and are approved by the IRB Human Subjects department. The responsibilities of investigators and research personnel are as follows:

Principal Investigator. The Principal Investigator will be responsible for overall project governance at UMass, leadership of the Project Team at UMass, protocol development, informing the data analytic plan, and dissemination efforts through professional presentations and peer reviewed journal publications

Co-Investigator. The Co-Investigators will be responsible for collaboration with other MOUD providers in the region and overseeing communication between research staff and community MOUD providers. Other responsibilities include overseeing contingency

management plan development and implementation and advising the team on data management and quality assurance protocols.

Project Manager. The Project Manager will be responsible for managing daily operations of recruitment and enrollment including training and supervising the research assistants. They will manage all IRB related submissions, amendments, and reporting.

Research Assistant(s). The research assistant(s) will be responsible for reviewing the electronic health record dashboard each shift and documenting potentially eligible patients on a Screening Log. They will be responsible for enrolling participants conducting interviews and completing telephone outcome assessment services for the stud(ies).

Software Engineer. The software engineer will be responsible for programming and managing the OARSCM mobile application and ensuring all data is flowing correctly between the mobile application and the secure server. They will have access to identified data within the Q2i OARSCM secure server at AWS. This data will include the patient's name (first and last), DOB, email address, cell phone number, urine toxicology results, and attendance in treatment. PHI will be directly entered into the mobile application. Q2i will have access to the server via secure shell terminal sessions. The OARSCM mobile application does not store PII/PHI locally on the device.

24. LOCAL RECRUITMENT METHODS
Patient participant recruitment will be similar in all phases of the study in which Research Assistants (RAs) will review the electronic health record dashboard and document all patients who present during their shift on a Screening Log. Additionally, they will use medical records and consultation with clinical staff to determine if an individual is appropriate to approach.

The RA will approach each patient in his/her room after the patient has been medically assessed and stabilized by medical staff. The RA will explain the nature, purpose, risks, and benefits of the study. If eligible and the patient is interested in participating, the consent process will be conducted in-person; the research staff will verbally review the consent and HIPAA forms with the participant in REDCap. We will let the participant review an electronic copy of the consent upon request. The participant and the research staff will both electronically sign through REDCap's "Signature" feature. The participant will then choose whether they would like to receive an emailed PDF copy of the consent or a PDF paper copy of the consent sent to their address. Depending on which they choose, the REDCap survey will then branch to either enter the participant's email address or mailing address. The subject's email/home address will be deleted as soon as the consent form has been sent to the subject and are not being collected as part of the study design. See grant: "HUMAN PARTICIPANTS PROTECTION" (p.19) "Informed Consent" for additional details.

For the clinician participant not associated with a patient participant, recruitment will occur via email to providers in the ED, inpatient units, and outpatient units who are X-waivered to prescribe MAT to UMass patients with OUD. The RA will send an email to these providers with the User Testing Fact Sheet and Aims of the project attached with a request to respond to the email if they are interested in learning more and potentially participating in the study. For those

who respond with interest, the RA will set up a time to meet in person in a private office to review the User Testing Fact Sheet and ask questions. After reviewing the User Testing Fact Sheet, if clinicians are interested in participating, they will verbally consent to participate.

For clinicians at the UMass Bridging Clinic, at the CleanSlate Addiction Treatment Center, at SaVida Health, at Spectrum Health Systems, Eleanor Health, and Right Choice who will be working with patient participants referred to the clinic, the RA will send an email to these providers with the Dyad Fact Sheet and Aims of the project attached with a request to respond to the email if they are interested in learning more and potentially participating in the study. For those who respond with interest, the RA will set up a time to meet in person to review the Dyad Fact Sheet and ask questions. After reviewing the Dyad Fact Sheet, if clinicians are interested in participating, they will verbally consent to participate.

Phase 1 Aim 1 (Develop OARSCM): After the RA consents the patient participant, the RA will help the participant download the OARSCM mobile application on either their personal smartphone or study-provided iPad. The participant will then enter their name (first and last), DOB, email, and cell phone number when available into the OARSCM mobile application for registration. The RA will then instruct the participant on how to use the OARSCM mobile application and guide them through tasks on the application such as reviewing their scheduled appointments, journaling and using prize draws. The RA will then interview the participants on the usability of the OARSCM mobile application. After the usability survey, the RA will also instruct the participant on how to delete the OARSCM mobile application should they no longer want the mobile application on their phone at the end of the study. If participants do not have their personal smartphone available at the time of enrollment, they will be given a handout with instructions for how to download and delete the OARSCM mobile application. Patient participant will then receive standard clinical care for their substance use, including gathering a recent history of their substance use using the timeline followback and addiction severity index to assist in the referral, connecting them to the UMass Bridge Clinic, CleanSlate Addiction Treatment Center, SaVida Health, or Spectrum Health Systems treatment provider, and scheduling an intake appointment at the Bridge Clinic, at CleanSlate, at SaVida Health, or at Spectrum Health Systems. At the end of the study period, participant OASRCM account access will be removed.

In Phase 1, all patient participants who complete the intake process and usability interview will receive $30 remuneration for enrollment during their hospital visit. In addition to the $30 they receive during their hospital visit, they are eligible for additional prizes earned in the OARSCM mobile application for engagement in MAT treatment. Prizes come in the form of electronic gift cards in the mobile application to Amazon, Dunkin' Donuts and Walmart and are available of increments of $5, $20, and $100. Patients are able to earn $1 prizes which they will need to save until they reach $5 to claim a gift card. Patient participants do not receive follow-up calls. See grant: "RESEARCH STRATEGY" (p. 3) for complete schedule of prize potential and earnings.

For the clinician participant not associated with the UMass Bridge Clinic, with the CleanSlate Addiction Treatment Center, with SaVida Health, or with Spectrum Health Systems who responded to the email with interest in potentially participating, the RA will schedule a time for the clinician participant to learn more and conduct the interview. Providers will be instructed to

access OARSCM through either a work computer or a work tablet PC, with the standard UMMHC security capabilities that are in place throughout the system, as well as the Q2i security features that are in place for the patients, such as, all confidential data is stored encrypted and is only stored in authenticated services. Prior to conducting the interview, all clinicians will be given the User Testing Fact Sheet in person and the opportunity to ask questions about the study. For those who review the User Testing Fact Sheet and verbally agree to participate, they will be given a clinician study ID that will be recorded at the top of User Testing Fact Sheet and a copy will be given to the clinician. The RA will then instruct the clinician to create a test account in the provider portal and guide them through user tasks in the portal. The RA will then interview the participants on the usability of the provider portal. The clinicians participating in usability testing will not receive remuneration for their participation.

For the clinician participant associated with the UMass Bridge Clinic, with the CleanSlate Addiction Treatment Center, with SaVida Health, or with Spectrum Health Systems (dyad) who responded to the email with interest in potentially participating, the RA will schedule a time for the clinician participant to learn more and complete a training on how to use the OARSCM provider portal to track patient participant progress in treatment. Providers will be instructed to access OARSCM through either a work computer or a work tablet PC, with the standard UMMHC security capabilities that are in place throughout the system, as well as the Q2i security features that are in place for the patients, such as, all confidential data is stored encrypted and is only stored in authenticated services. Prior to completing the training, all clinicians will be given the Dyad Fact Sheet in person and the opportunity to ask questions about the study. For those who review the Dyad Fact Sheet and verbally agree to participate, they will be given a clinician study ID that will be recorded at the top of the Dyad Fact Sheet and a copy will be given to them. The RA will then train the clinician on how to create an OARSCM provider account using their name (first and last) and email address and walk them through how to use the OARACM provider portal to track patient participant treatment progress. After the clinician has completed treatment with at least one patient participant, the RA will reach out the clinician to schedule a time to conduct the interview on the usability of the provider portal. Once the patient has completed their 4 weeks in the study, they will become archived on the provider portal, and the provider will not be able to see that particular patient's information. The provider's general portal will be active for longer than 4 weeks as they will have more than one patient who will be completing the study at different times. In phase 1, the clinical information that the provider enters (appointment attendance and tox results) are accessible to the provider through the EHR (EPIC). The clinicians participating in the dyad portion of the study will not receive remuneration for their participation.

Phase 2 Aims 1 & 2 (RCT of OARSCM): Patients will complete a screening survey to assess for minimal eligibility criteria and confirm their interest. If a potential participant is deemed ineligible for the study, they will be informed that they are not a good fit for this study and the screening form will be shredded immediately after the encounter. After the RA consents the participant, they will open a randomization envelope and randomize the patient to either TAU or OARSCM. For TAU the participant will receive SBIRT provided by the RA, a warm handoff to a community MOUD treatment facility and will be trained on how to use MyMAT (an educational mobile application). For OARSCM the participant will receive TAU as described

above with the addition of the OARSCM mobile application instead of MyMAT. Participants will be trained on how to use the OARSCM mobile application, potentially earning prizes throughout treatment as part of contingency management. After leaving the ED, participants will complete follow-up calls at 1, 3, and 6-month time periods.

In Phase 2, all participants will receive an initial $25 remuneration for enrollment during their ED visit, an additional $30 per follow-up call (1 and 3 months), and an additional $35 for completing the 6-month follow-up call for a total of $120/participant. Those randomized to the contingency management group have to opportunity to earn additional money as part of treatment. See grant: "RESEARCH STRATEGY" (p12) "Procedures" for further details.

25. LOCAL NUMBER OF SUBJECTS
Phase 1 Aim 1 (Develop OARSCM): 30 individuals with OUD and 30 providers/clinicians will be recruited to provide feedback to improve the interface and features.

Phase 2 Aims 1 & 2 (RCT of OARSCM): 102 patients will be enrolled and randomized into OARS+CM (n=51), or TAU with MyMAT (n=51) to determine efficacy of OARSCM. See grant: "RESEARCH STRATEGY" (p12) "Procedures" for further details.

26. CONFIDENTIALITY
Potential risks due to loss of confidentiality will be minimized by having all information collected and handled by research staff and Q2i employees trained to deal appropriately with sensitive clinical issues. All research personnel and Q2i employees will receive training in research ethics. All information will be treated as confidential material and will be available only to research and clinical staff, including Q2i employees working on the project. All paper-based materials, like consent forms, will be kept in locked files. All datasets will be handled in a HIPAA compliant manner, will be password protected, and the analytic dataset hosted by UMMS will be de-identified after the study is completed, data is cleaned, and primary analyses are completed. After primary analyses are completed, de-identified data will be kept by Q2i for mobile application improvement, such as predictive analytics. For additional information on processes to mitigate loss of confidentiality, please see grant "HUMAN PARTICIPANTS PROTECTION" (p.19-20) "Protection Against Risk."

Certificate of Confidentiality: As of October 1, 2017, all NIH funded research collecting or using identifiable, sensitive information will automatically be issued a certificate of confidentiality (aka applications are no longer needed). The NIH is no longer doing physical certificates, but rather the Notice of Award and Grants Policy Statement will suffice as documentation of CoC protection. See link below for the full policy details. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html

Audio recordings: Audio recordings of all interviews will be obtained, unless the participant declines. The sound files will be recorded on digital voice recorders then downloaded to a password protected folder on a secure drive hosted by UMass. After downloading to the secured drive, the recordings will be erased from the voice recorders. All data will be transcribed and stored electronically on password-protected laboratory computers and in REDCap. Audio recordings will be destroyed 5 years after the study ends.

27. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS
The following security protocols will be applied to all data: physical protections - all databases and systems will be hosted behind the firewall by UMass Medical School and employ user authentication and role-based security for access. Standard security access procedures designed by UMass Medical School will be used to ensure that only authorized research staff has access to the study data. All paper-based materials, like consent forms, will be kept in locked files; logical protections - All datasets will be handled in a HIPAA compliant manner, will be password protected, and the analytic dataset will be de-identified – All urine samples will be stored in locked medical storage containers per the MAT clinic's policy. Results of tox screens from the urine samples are secondary data for this study and urine samples will not be kept by the study team.

<u>OARSCM and MyMAT</u>: The OARSCM and MyMAT applications reside on a secure server maintained by Q2i. All transmissions are encrypted for security. No data is stored outside of Q2i's secured, encrypted, AWS environment. DATA at rest: AES – 256 encryptions, in transit: SSL. It complies with HIPAA and HiTECH Act requirements. Only the participant, study team, outpatient MOUD providers, and necessary Q2i's personnel will have access to the OARSCM program and MyMAT application. OARSCM requires multi-factor authentication to create an account and access the program for both patients and providers. OARSCM and MyMAT can be accessed as a mobile application from a smart phone or tablet or through a computer with internet connection. If using a computer, OARSCM prompts users to close their browser when logging out. See "APPENDIX" for screenshot of prompt.

A HIPAA waiver of authorization has been obtained from the IRB in order to access medical records for to determine eligibility of potential subjects for the subject interviews. Additionally, patients will sign a HIPAA authorization during the consent process for interviews.

If the patient is excluded or refuses, this information, along with the reason for exclusion, will be documented on the Screening Log to allow comparisons of those enrolled vs. not enrolled, which will allow the team to assess representativeness of the sample

28. COMPENSATION FOR RESEARCH-RELATED INJURY
This research involves no more than minimal risk or harm to subjects. However, the subjects will be informed during the consent process of the following: "The University of Massachusetts Medical School does not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available."

29. ECONOMIC BURDEN TO SUBJECTS
Participant smart phone data may be used to participate in the research. The participant would be responsible for any data charges to their phone plan during the course of participation. All insurance plans are accepted by the UMass Bridging Clinic, by CleanSlate, by SaVida Health, by Eleanor Health, and by Spectrum Health Systems. The cost of MOUD treatment is standard and covered by their insurance provider, copays will vary depending on patient's insurance provider.

Participation in this study will not cost patients any additional economic burden by going to the UMass Bridging Clinic, to CleanSlate, to SaVida Health, to Eleanor Health, or to Spectrum Health Systems compared to routine MAT treatment at any provider in the community. There will be no cost to the Acute Care or MAT clinicians to participate in the study.

30. CONSENT PROCESS

The consent process will be conducted in accordance with *HRP-802 INVESTIGATOR GUIDANCE: Informed Consent.*

Patients: The Patient consent process refers to subjects in all applicable aims. The RA(s) will approach each patient in his/her room after the patient has been medically assessed and stabilized by medical staff. They will explain the nature, purpose, risks, and benefits of the study. To assess for competency, a mini quiz will be administered to ensure that all potential subjects possess an understanding of the risks and benefits of study participation. The mini quiz consists of four multiple choice questions, which will be asked after the entire consent form has been thoroughly reviewed. Potential subjects will be given two attempts to answer all questions correctly; if a patient provides an incorrect answer, a research team member will review the corresponding section of the consent form and will give the patient another opportunity to answer the question. If a potential subject does not answer all four questions correctly after two attempts, the subject will not be enrolled in the study. The consent process will be conducted in-person; the research staff will verbally review the consent and HIPAA forms with the participant in REDCap. We will let the participant review an electronic copy of the consent upon request. The participant and the research staff will both electronically sign through REDCap's "Signature" feature. The participant will then choose whether they would like to receive an emailed PDF copy of the consent or a PDF paper copy of the consent sent to their address. Depending on which they choose, the REDCap survey will then branch to either enter the participant's email address or mailing address. The subject's email/home address will be deleted as soon as the consent form has been sent to the subject and are not being collected as part of the study design. See "HUMAN PARTICIPANTS PROTECTION" (p. 19) "Informed Consent" for additional details.

Clinicians (Phase 1): Waiver of written documentation of consent will be obtained for the clinician interviews. The research involves no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of research context. Study procedures will be described verbally. An information sheet will be provided to the clinicians informing them about the study and that their participation is voluntary.

31. PROCESS TO DOCUMENT CONSENT IN WRITING

Patients: The consent process will be conducted in-person; the research staff will verbally review the consent and HIPAA forms with the participant in REDCap. We will let the participant review an electronic copy of the consent upon request. The participant and the research staff will both electronically sign through REDCap's "Signature" feature. The participant will then choose whether they would like to receive an emailed PDF copy of the consent or a PDF paper copy of the consent sent to their address. Depending on which they

choose, the REDCap survey will then branch to either enter the participant's email address or mailing address. The participant's email/home address will be deleted as soon as the consent form has been sent to the subject and are not being collected as part of the study design.

32. DRUGS OR DEVICES
Data generated from this study will be used to support a 510k submission to seek clearance as an FDA cleared device.