Official Title: Increasing Women's Engagement in Medication Treatment for Opioid Use Disorder through Digital Intervention

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Mass General Brigham

Institutional Review Board
Intervention/Interaction Detailed Protocol

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Project Title:	Women's Opioid Treatment Follow-up Study
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For Intervention/Interaction studies, submit a Detailed Protocol that includes the following sections. If information in a particular section is not applicable, omit and include the other relevant information.

4. Background and Significance

From 1999 to 2017, opioid overdose fatality rates increased 642% among women compared to 439% for men. (Centers for Disease Control and Prevention, 2013) Women with opioid use disorder (OUD) have more medical problems, greater functional impairment, and greater psychiatric severity than men with OUD. (Back et al., 2011; McHugh et al., 2013) Medication treatment for OUD (MOUD) is effective but underutilized. (Volkow, Jones, Einstein, & Wargo, 2019) While longer retention in MOUD is associated with better outcomes and reduced mortality, drop-out is common, particularly in the early stages of treatment. (Morgan, Schackman, Leff, Linas, & Walley, 2018) With rising rates of fatal opioid overdoses in women, it is critical to develop specific sustainable strategies to engage and retain women in MOUD. Evidence-based gender-specific substance use disorder (SUD) treatments for women have been associated with increased engagement, greater satisfaction, and improved outcomes. (McHugh, Votaw, Sugarman, & Greenfield, 2018; Dawn E. Sugarman, Reilly, & Greenfield, 2017) However, these treatments have not specifically targeted women with OUD. Furthermore, the impact of existing gender-specific treatments is restricted by in-person delivery requiring intensive clinician training thereby limiting dissemination and implementation. Despite this need, there is a paucity of research demonstrating effective strategies to implement this care for women in mixed-gender settings and especially targeting their engagement in MOUD. Prior research shows that digital interventions are effective in reducing substance use and increasing treatment engagement. (Bickel, Marsch, Buchhalter, & Badger, 2008; Guarino, Acosta, Marsch, Xie, & Aponte-Melendez, 2016) In previous studies (IRB# 2019P003747, IRB#2022P001902), we gathered data that informed the development of a digital platform to deliver gender-specific care that addresses the individualized needs of women with OUD in mixed-gender settings. In this study we aim to pilot test the digital intervention and collect data on feasibility, satisfaction, and engagement.

2. Specific Aims and Objectives

Aim 1: To demonstrate feasibility of delivering a gender-specific digital intervention (GSDI) to women with OUD.

Aim 2: To collect preliminary estimates on the effect of the GSDI on engagement in MOUD.

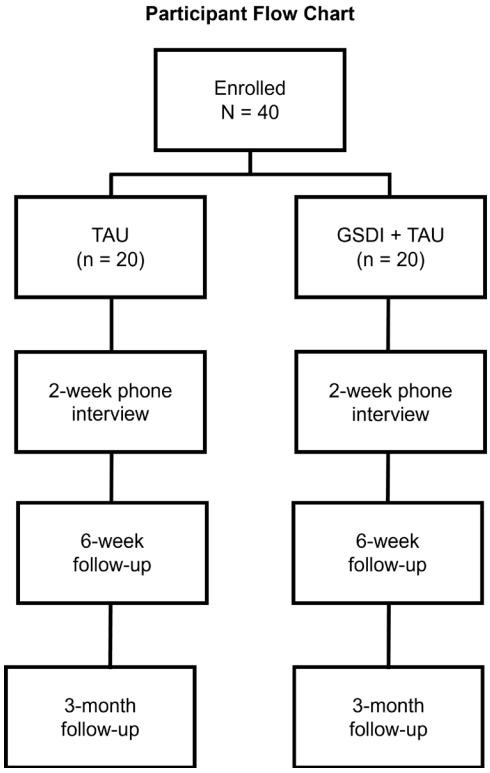
To achieve these aims, we will conduct a pilot randomized controlled trial (RCT). Feasibility, satisfaction, and engagement with the GSDI are the primary outcomes and will be measured post-intervention and at

two-week, 6-week and 12-week follow-ups. MOUD adherence will be assessed at 12-weeks post-enrollment to collect preliminary estimates on the effect of the GSDI on MOUD engagement.

3. General Description of Study Design

Figure 1 outlines the study schema. We will conduct a pilot RCT to evaluate the feasibility of delivering the digital intervention to women who have recently initiated MOUD (within 30 days). Participants will be randomized to receive either the GSDI+TAU (gender-specific digital intervention + treatment as usual) or TAU-only. Because TAU varies across levels of care (inpatient, residential, outpatient), randomization will be stratified based on level of care.

Figure 1. Study schema



4. Subject Selection

We will enroll up to 40 women.

Inclusion/Exclusion Criteria

Women will be included if they (a) are 18 years of age or older, (b) have a current OUD diagnosis (moderate or severe by DSM-5 criteria), (c) have initiated MOUD in the past 30 days, and (d) are able to provide informed consent. Women will be excluded if they (a) have an acute psychiatric or medical condition, or cognitive impairment, that would impair the ability to complete study procedures, or (b) are admitted to their current treatment episode on an involuntary status.

Participants with co-occurring other substance use will be permitted to enroll due to the high prevalence of polysubstance use in this population. Pregnant women will not be excluded from participating. Medication treatment for opioid use disorder (specifically methadone and buprenorphine)

is the standard of care for treating pregnant and postpartum women with opioid use disorder, yet rates of initiation in this population are low. Thus, women with opioid use disorders would benefit from strategies for increasing initiation on methadone and buprenorphine, and therefore should not be excluded from this research. None of the study procedures pose additional risk to pregnant women, and therefore, the protections against risk described below are adequate.

Due to the gender-specific focus of this study, participants who do not identify as women will be excluded. No other group of persons, with the exception of minors under 18 years of age, will be categorically excluded from the study provided individual members of any group meet the eligibility criteria.

Local Recruitment Procedures
Participants will be recruited from McLean Hospital's Alcohol, Drug, and Addiction Treatment (ADATP) Services continuum of treatment programs and from other local community treatment programs. No information from the study will be entered into the medical chart.

Study staff will identify potential participants in several ways: self-selection based on posted flyers and presentations by research staff at clinical groups, review of the current census in EPIC, or referral from clinical staff.

The RA will check Epic regularly for eligible participants from the McLean Hospital's Alcohol, Drugs, and Addiction Treatment Programs (ADATP) and will coordinate with the patient's clinical care team to confirm eligibility and introduce the patient to the research assistant (RA). Recruitment flyers will also be distributed by clinical staff to patients, as well as posted in waiting areas in the ADATP as well as other local treatment programs, including clinics that serve pregnant women with OUD, and the study will also be listed on the MGB Rally site. The study RA will also attend weekly rounds with clinicians and inquire about eligible participants and correspond via email and phone with clinicians throughout the week about potential participants. The RA may also present the study to patients in group therapy when clinicians are agreeable. The RA will exclude any patients that the clinical staff indicates has a psychiatric or medical condition that would prevent them from completing study procedures. In order to help clinicians assess the eligibility of their patients, clinicians will be provided with an information sheet that includes the inclusion and exclusion criteria.

To recruit and enroll participants from the ADATP inpatient detoxification unit, study staff will first check in with a member of the inpatient clinical team (typically, the case manager) to determine whether the patient is appropriate to approach (e.g., that they are sufficiently stable to be approached for research purposes). This discussion will be documented on the *McLean Hospital: Documentation of Discussion of Clinical Appropriateness Form* (attached). If the clinical staff determine that the participant can be approached, a member of the clinical staff will then approach the patient to ask whether they would be interested in discussing research with a member of the research staff, and if interested, will introduce the participant to the study staff member. This is an established procedure on the Proctor 1 inpatient unit that has been implemented successfully in several previous and ongoing studies by our research group with minimal burden on clinical staff.

To recruit and enroll participants from telehealth clinics serving addiction clients nationwide, telehealth providers will electronically distribute IRB-approved study flyers to patients. Patients who are interested will reach out to the study team to set up a screening appointment.

To recruit and enroll participants from the MGB Rally site, the RA will complete a screening visit with respondents in addition to confirming their medication for opioid use disorder with their provider. To confirm their medication, respondents will be routed to a REDCap form from the Rally website. The form will include HIPAA authorization language detailing how their protected health information will be used. It will also include a brief survey asking for their date of birth, full name, and permission to access their electronic medical record. The study staff will use this information to look up their medical record in Epic to confirm their use of medication for opioid use disorder. If they are not an MGB patient, the RA will call them to ask for their provider's name and contact information and their permission to contact their provider. The RA will then have them sign a release of information (ROI) form so that the study staff can speak with their provider about their medication. This process will ensure that respondents who are not referred to study staff by a clinician meet all eligibility requirements.

For patients referred by clinical staff, the clinician will ask the patient's permission to be contacted by an RA about the research study. Patients who agree to be contacted will be asked to provide phone number and/or email address. The RA will then reach out to coordinate a time to explain the study to the patient. The patient will be offered the opportunity to ask questions. Patients who express interest will be screened for eligibility.

5. Subject Enrollment

Potential participants will first be approached by a clinical staff member to see if they are interested in meeting with study staff, unless participants self-identify to study staff. If a patient wants to participate, they will complete an initial eligibility screening checklist (pages 2-4 of attached screening form) and if eligible, research staff will collect contact information (page 1 of attached screening form) and a study session will be scheduled and they will be invited to complete the Informed Consent process.

For this study, we (study staff) will implement the Mass General Brigham REDCap (Research Electronic Data Capture) eConsent. All potentially eligible subjects will be asked to complete electronic Informed Consent process, at which point the subjects will read through the IRB-approved consent form with a research staff member to answer any questions, explain the study procedures, and review the risks and benefits of the study. Subjects will be informed about the experimental nature, purpose, risks, and benefits of the study in accordance with procedures of the Mass General Brigham IRB. There will be no time-limit placed on the consenting process. Research staff members understand that the consent is a process and not simply a matter of signing and dating the consent form. Either the PI or one of the Co-Investigators (serving as designees of the PI) will be available to help explain the study and answer questions. Once the subject consents to participate in the study, the subject, along with a member of the research staff, will use REDCap to sign and date the consent. The subject will be provided with a copy of the fully executed consent form to their provided email address or receive a printed copy if they do not have an email address. A copy will also be maintained in the subject's source study binder.

Participants will be fully informed of the nature of the risks involved during the informed consent process and will have the ability to discontinue and withdraw consent at any time without penalty. All study personnel will be trained in the appropriate care of human participants and will have completed the Collaborative Institutional Training Initiative (CITI) human subjects training, and research assistants will be closely supervised by the study PI. As part of the informed consent process, participants will be informed that if they feel uncomfortable responding to any question or survey, they are free to choose not to respond or to express their discomfort.

In line with the Mass General Brigham system-wide policy, "Procedure: Requests to Receive Unencrypted Email" (original approval date 7/18/2017), study staff will follow procedures/proper documentation regarding sending encrypted emails to protect PHI. The statement, "*The Mass General Brigham (MGB) HealthCare standard is to send email securely. This requires you to initially set up and activate an account with a password. You can then use the password to access secure emails sent to you from MGB HealthCare. If you prefer, we can send you "unencrypted" email that is not secure and could result in the unauthorized use or disclosure of your information. If you want to receive communications by unencrypted email despite these risks, MGB HealthCare will not be held responsible. Your preference to receive unencrypted email will apply to emails sent to you from research staff in this study. If you wish to communicate with other research staff at MGB regarding additional studies, your reference will have to be documented with <u>each</u> research group,"* required by Mass General Brigham Healthcare will be stated in the contact sheet. Similarly, the statement, *"Text messages by mobile/cell phones are a common form of communication. This research study involves sending you text messages that are relevant to the research study. Texting over mobile/cell phones carries security risks because text messages to mobile/cell phones are not encrypted. This means that information you send or receive by text message could be intercepted or viewed by an unintended recipient, or by your mobile/cell phone provider or carrier,"* will be stated in the contact sheet, followed by a bulleted list of important points regarding texting. Participants will have the opportunity to acknowledge understanding of, and agreement to receiving an encrypted or unencrypted email, and to receive unencrypted texts.

After completing the informed consent process, subjects will be randomized into one of two groups: treatment as usual (TAU) or gender-specific digital intervention (GSDI) + TAU.

(1) **TAU**: TAU for opioid use disorder consists of a mix of medication treatment and individual and group therapy services across varies levels of care: inpatient, residential, and outpatient. Residential treatment is for adults who have completed detoxification and require additional treatment in a structured environment. Inpatient treatment includes short-term care and detoxification treatment and incorporates a combination of group, family, and individual therapy targeted at medical stabilization, reducing the severity of the patient's symptoms, and providing resources and ongoing support to prevent relapse. Outpatient treatment is focused on comprehensive evaluation and stabilization. Participants randomized to TAU will complete assessments at two-week, 6-week and 12-week follow-ups.

(2) **GSDI + TAU** includes the addition of a gender-specific digital intervention (GSDI) to treatment as usual. The GSDI has a web-based component and a mobile component. The web-based portion of the GSDI will be delivered using REDCap, and the GSDI mobile component will be delivered, and have data collected through, the Catalyst app. Catalyst has been previously approved by RISO and the MBG IRB. Both programs are encrypted and use HIPAA compliant software.

- The *web-based* portion of the GSDI includes: (1) gender-specific psychoeducation on substance use disorders, (2) specific education on opioid use disorder, including information about medication treatment for opioid use disorder, and (3) information on relapse-prevention skills. Participants complete the web-based portion immediately after completing baseline assessments.
- The *mobile componen*t will contain three parts: (1) weekly self-report surveys of opioid and other substance use and medication adherence, (2) twice weekly skills-practice

exercises, and (3) daily motivational messages encouraging self-care. Participants engage with the mobile component after completing the web-based portion until the end of the study (12 weeks).

6. Study Procedures

Participants will be screened for inclusion/exclusion criteria (see Screening Form) by study staff and those who are initially determined to be eligible will be offered the opportunity to participate in the study. Those who express interest will be scheduled for a baseline study session. In the baseline session, participants who provide informed consent will then complete a series of baseline measures (described below) to evaluate key clinical and demographic variables. Participants in the GSDI+TAU group will also complete the web-based component of the GSDI. All participants will receive a handout that includes information on crisis and domestic violence hotlines, as well as treatment information. Following the baseline session, participants will complete assessments at 2 weeks-, 6 weeks-, and 12-weeks-post-baseline. During the follow-up period, participants in the GSDI+TAU group will engage with the mobile component of the GSDI. Specifically, participants in the GSDI+TAU group will use Catalyst for (1) weekly self-report surveys of opioid and other substance use and medication adherence, (2) twice weekly skills-practice exercises, and (3) daily motivational messages encouraging self-care (sent via push notifications in Catalyst app).

The first 5 enrolled participants assigned to the GSDI condition will be asked to engage in a "think aloud" process as they navigate through the web-based portion of the GSDI. Specifically, they will be asked to describe their experience and any expected challenges with using the GSDI. The RA will take notes on participants' comments.

The baseline session will be conducted in person or via Zoom and may be conducted over two sessions if needed to accommodate patients' schedules. The 2-week visit will be conducted via phone or Zoom. The survey portion of the 6 and 12-week follow-up visits will be completed on participants' own time on their devices, in person, over the phone, or via Zoom. The interview portion of the 12-week follow-up visit will be conducted in person, via phone, or Zoom. For participants who attend visits in person, an iPad will be available to access REDCap surveys and the GSDI. A research staff person will be with the participant while she is using the iPad, and all study iPads are encrypted and secured via MobileIron Mobile Device Management. Participants who attend visits remotely, will use their own devices to access REDCap.

The GSDI is being tested as an add-on to standard care (i.e., treatment as usual). As described above, standard care for OUD consists of a mix of medication treatment and individual and group therapy services across varies levels of care: inpatient, residential, and outpatient. As a requirement of eligibility for the study, all participants will be receiving medication treatment for OUD.

Measures

Self-report assessments will be administered via REDCap. Data from the 2-week phone interview will be entered into a REDCap database by the research staff.

The following measures will be administered to participants. The schedule of assessments table below demonstrates at which timepoint measures will be administered, and to which group.

Demographics Questionnaire: Participants will be asked to self-report sociodemographic information on this brief 12-item questionnaire.
Technology Use Questionnaire: Technology use/acceptability will be measured using the "Technology Use Questionnaire", a 10-item questionnaire modified from the Smartphone App Use survey used in the Behavioral Health Partial Program. (Beard et al., 2019)
Brief Addiction Monitor (BAM): The BAM (Cacciola et al., 2013) is a 17-item self-report measure of substance use and associated problems. The BAM has demonstrated acceptable internal consistency reliability, strong retest reliability, and predictive validity, and will be used to identify patterns of substance use and severity of substance use disorders.
Opioid Use History Questionnaire: This measure will be used to track lifetime opioid use histories and will capture characteristics such as age at first use and the most prevalent opioids being used. This measure was adapted from the Prescription Opioid Analgesic Use History Questionnaire used in a previous national clinical trial (Weiss et al., 2011).
MOUD Stigma Questionnaire: This measure will be used to assess stigma associated medication for opioid use disorder (MOUD). with This 15-item measure was adapted from the Stigma Measure of the Pharmacist Knowledge Questionnaire (Davenport, Arnett, Nichols, & Miller, 2020).
PTSD Checklist for DSM-5 (PCL-5): The PCL-5 (Weathers et al., 2013) is a 20-item self-report measure that assesses symptoms of PTSD corresponding to DSM-5 criteria. At Baseline, the PCL-5 will be administered with the included Life Experiences Checklist and Criterion A questions; at all other follow-ups timepoints, only the 20 PCL-5 questions will be administered.
Patient Health Questionnaire (PHQ-8): The PHQ-8 is an 8-item measure assessing how often participants have been bothered by certain health symptoms over the last 2 weeks.
PROMIS Anxiety Scale: The Anxiety Short Form is a 6-item measure of anxiety developed as part of the PROMIS measurement system. This will be used to measure anxiety symptoms.
Treatment Utilization Questionnaire: This questionnaire assesses current substance use disorder treatment, such as pharmacological medications and behavioral treatments.
2-week Residential Treatment Utilization Questionnaire: This is a short questionnaire assessing how many days the participant has spent in inpatient/residential treatment in the past 2 weeks.
Client Satisfaction Questionnaire (CSQ): The CSQ (Attkisson & Zwick, 1982) will be used to assess participant satisfaction of the digital intervention. The original CSQ is 8 items and we have added an additional 8 items to gather satisfaction with specific aspects of the digital intervention.
Mobile Application Rating Scale (MARS-Section F): This measure was adapted from the full MARS questionnaire (Stoyanov et al., 2015). Section F assesses the perceived impact of the app on the user's knowledge, attitudes, intentions to change as well as the likelihood of actual change in the target health behavior.
System Usability Scale (SUS): The SUS (Brooke, 1995) is a 10-item questionnaire with five response options for respondents from Strongly agree to Strongly disagree. The SUS is used to measure usability of products and services, including hardware, software, mobile devices, websites and applications.
Timeline Follow-back (TLFB): Self-report of MOUD and Opioid use will be collected using the Timeline Follow-Back (TLFB) method, which has demonstrated good reliability and validity with adults (Sobell L. C. & B., 1996).
Catalyst Check-in: At the 2-week follow-up, participants in the GSDI-TAU group will be asked 2-3 questions about any issues they are having with the app. If they report having issues, the RA will troubleshoot and provide guidance.
Qualitative Interview: Participants in the GSDI+TAU group will be asked to complete qualitative exit interviews at the 12-week follow-up. Exit interviews will be follow a semi-structured interview format where patients will be asked questions regarding their experiences with the digital intervention.

Questions are modified from exit interviews conducted in our previous studies (Greenfield, Cummings, Kuper, Wigderson, & Koro-Ljungberg, 2013; D. E. Sugarman, Meyer, Reilly, & Greenfield, 2022)

Schedule of Assessments

	Baseline	Post-Intervention	2-week Follow-up	6-week Follow-up	12-week Follow-up
All participants	- Demographics - Technology use - BAM - Opioid Use History - MOUD stigma - PCL-5 - PHQ-8 - PROMIS Anxiety - Treatment utilization		- TLFB - 2-week Residential Treatment Utilization Questionnaire	- TLFB - BAM - PROMIS Anxiety - PHQ-8 - PCL-5 - Treatment utilization	- TLFB - BAM - PHQ-8 - PROMIS Anxiety - PCL-5 - MOUD stigma - Treatment utilization
GSDI-TAU participants only		- CSQ	- Catalyst Check-in		- CSQ - SUS - MARS-F - Qualitative Interview

In addition to the data being collected from participants as part of this study, patient charts (EPIC) will be used to collect data on MOUD adherence at each of the follow-ups. Further confirmation of MOUD adherence will be obtained from participants' prescribers at week 6 and 12 follow-ups for those who complete a release of information (ROI). Completion of the ROI is optional and not a condition of study eligibility. For participants who complete an ROI, the study RA will reach out to the identified prescriber to collect information on MOUD adherence (see Prescriber Confirmation Form). Engagement data will be retrieved from Catalyst including number of logins, number of completed check-ins and skills practices, and time spent on each of these activities. Time spent on the web-based portion of the GSDI will be calculated from REDCap.

Remuneration

Participants in the TAU group will receive up to $150 in remuneration and participants in the GSDI+TAU group will receive up to $230 in remuneration (see detailed breakdown below). The difference in compensation is due to the imbalance in time commitment between the two groups. Specifically, the baseline and 12-week visits will take longer for the GSDI+TAU participants to complete, compared to the TAU participants. In addition, the GSDI+TAU participants will receive remuneration for downloading and logging into the Catalyst app.

	TAU	GSDI+TAU
Baseline visit	$35	$70
Catalyst download and initial log-in	N/A	$20
2-week follow-up	$20	$20
6-week follow-up	$20	$20
12-week follow-up	$50	$75
Bonus for completing all 3 follow-up visits	$25	$25
Total	**$150**	**$230**

Partial Payments

Partial payments will be given for any incomplete visits. Any visit that is not 100% completed is considered to be incomplete. Partial payments will be given for each visit as follows:

	TAU	**GSDI+TAU**
Incomplete Baseline visit	$17.50	$17.50 (incomplete surveys), $35 (completed surveys, but incomplete GSDI)
Catalyst download and initial log-in	N/A	No partial payment
Incomplete 2-week follow-up	$10	$10
Incomplete 6-week follow-up	$10	$10
Incomplete 12-week follow-up	$25	$25 (incomplete surveys), $50 (completed surveys, but incomplete exit interview)
Bonus for completing all 3 follow-up visits	No partial payment	No partial payment

Participants will be given the choice to be compensated via check, re-loadable credit card or online gift card. Re-loadable cards are distributed using an approved, outside vendor called Advarra. This secure system is similar to a gift card or credit card. If participants choose this system, they will be given an Advarra Payments Visa card when they enroll in the study. Once this card is activated, the study team will add a payment after each paid visit completed. In order to make these payments, study staff will need to collect participants' Social Security number, and it will be shared securely with the company that runs the card-based system. If participants choose to receive a check, the check will be mailed to their home address. Online gift cards are distributed using an approved, outside vendor called Tango. If participants choose to be compensated via gift card, they will be sent a link to select a vendor from over 60 retail stores. They also have the option to choose a Visa gift card. After selecting a gift card vendor, they will be sent a link to their card. Participants will be sent a link to select a new card after completion of each session.

Participants will be offered a smartphone with a prepaid, unlimited data plan to use for the duration of the study. The primary purpose of the phone is to ensure participants can fully engage in the study, regardless of their access to a smartphone or reliable data plan. Participants can choose to accept this offer or decline it if they have a smartphone that they would prefer to use. Similar to participants who use their own phone, participants who opt to receive a phone from the study will receive communications from the RA to their smartphone, including text messages, phone calls, voicemails, and emails regarding their follow-up visits and other study-related information. Participants may also complete REDCap surveys on their phones at the 6- and 12-week follow-ups. Additionally, participants in the GSDI + TAU group will use the phone to access the Catalyst app and, if necessary, to participate in the 12-week exit interview via Zoom. Above and beyond study activities, participants may utilize the smartphone however they choose throughout the study. Study staff will not place any restrictions on the phone's functions or monitor their use of the phone. Participants will not be required to return the phones at the end of the study or if they drop out of the study.

After the study is complete and the data plan expires, participants will keep their smartphones. They will not be responsible for paying for the device; however, if they choose to keep using the phone with data, they must purchase their own data plan or insert a SIM card from a different phone to connect to a

network carrier. They will be responsible for the costs of the data plan after the study period, as well as phone repairs. Phones will not be replaced if they get lost or stolen.

7. Risks and Discomforts

As in any study involving assessment of psychiatric symptoms, there is some risk of discomfort from discussing emotional topics (e.g., symptoms of substance use). However, we anticipate that this discomfort will be transient. Nonetheless, subjects will be closely monitored for evidence of excessive or enduring distress following assessment and precautions to protect against this risk will be taken.

Another potential risk includes the possibility that subjects may experience dangerous or suicidal behavior. We do not anticipate that our study procedures will increase this particular risk. If a subject becomes very upset, is intoxicated, or is suicidal during the study, she will be evaluated by one of the study clinical staff. An assessment will be conducted, and the appropriate clinical recommendation will be made; this could involve treatment either at McLean Hospital or elsewhere. Participants in the GSDI condition will be informed by study staff during enrollment (see Catalyst Participant Information Sheet), as well as by a message that appears at each Catalyst login, that study staff will not review participants' answers on a continuous basis. Participants will therefore be explicitly instructed to call their treatment provider(s), the national suicide hotline, go to the nearest emergency room, or call 911, if they require clinical assistance and/or are at risk of harming themselves/others. A list of crisis and treatment resources will always be available to participants in the Catalyst app. In addition, participants in both conditions will receive a list of crisis and treatment resources at the baseline visit.

Breach of confidentiality is a potential risk. To protect against the loss of confidentiality, we will keep all study data locked in a separate file, coded by a unique study code number (with names and other personal identifying information stored separately). Only research staff who need access to personal identifying information for research purposes will have access to information linking the code to the participant's identification. This information will be stored in a separate password protected file on a password protected computer and will be destroyed upon completion of the study to minimize the risk of linking identifying information to research data. We will be using REDCap, a free, secure, HIPAA-compliant, web-based application, to collect data from the GSDI and survey measures. REDCap has secure web authentication, data logging, Secure Sockets Layer (SSL) encryption, and resides on secure servers behind a robust firewall. Access to the servers is tightly regulated and password-controlled. Electronically-stored data will be de-identified with use of the study code number and will be stored in a password-protected file on a password-protected computer located in a locked office in accordance with all local institutional policies. In addition, the consent form will clearly inform subjects of the limits of confidentiality, including the circumstances in which confidentiality may be breached, such as in cases of suspected child abuse or neglect, suspected abuse of a disabled person or an elderly person, and dangerousness to self or others.

The Catalyst app was designed to protect participants' privacy, confidentiality, and data security (see below for more information, as well as the Data Privacy and Security Documents). Only research personnel will have access to study information. Data collected by the Catalyst app is encrypted, and downloaded by the researcher to the local research server in a de-identified format (i.e., subject ID number). The local research server is only accessible by study staff. Study staff will provide orientation to the app and answer any questions regarding the assessments and data collected.

Should participants experience distress associated with assessment procedures that exceed a moderate intensity or transient duration, the PI will be contacted, and appropriate clinical assessment will be conducted to determine the need for intervention. If intervention is indicated, the PI and study staff will facilitate either provision of intervention on-site or arrangement of an appropriate referral. Dr. Sugarman (PI) is a trained clinical psychologist and licensed health service provider in the Commonwealth of Massachusetts, and Drs. Weiss and Greenfield (Co-Investigators) are licensed addiction psychiatrists.

Individuals will be excluded from participating in the study if they exhibit acutely dangerous or suicidal behavior at the time of screening. This helps protect against the risk of enrolling subjects who would pose a greater likelihood of experiencing acute suicidal or dangerous behavior.

In the event that subjects experience discomfort when completing the study procedures, they will be free to refuse answering any questions or surveys that make them uncomfortable, to discontinue an assessment session at any time, or, if they wish, to withdraw from the study.

8. Benefits

There are no direct benefits to study participants. Potential benefits to participating in this research investigation include contributing to the understanding of the treatment needs of women with opioid use disorder and advancing future research in this area, including ultimately the development of a novel intervention to improve outcomes for women with opioid use disorder. Given the minimal risks associated with the proposed investigation, we believe this is a very acceptable risk-benefit ratio. We believe that the minimal risks to subjects are reasonable considering the immediate and long-term benefits of the knowledge to be gained.

Due to the marked public health impact of opioid use disorder on women and a need for research on identifying the treatment needs and barriers to evidence-based medication treatment, the proposed investigation has the potential to contribute significantly to both research and public health agendas. The results of this study will further contribute to the understanding of the treatment needs of women and inform the development of a gender-specific digital intervention for women with opioid use disorder.

9. Statistical Analysis

Power Analysis and Sample Size

The sample size was selected to provide the necessary degree of precision for estimating the rates of loss to follow-up (at 2 weeks, 6 weeks, and 12 weeks), and the rates of engagement with MOUD at 12 weeks; note, this pilot RCT is not powered to detect treatment group differences in the rates of engagement with MOUD at 2-weeks, 6 weeks, or 12 weeks.

Data Analysis Plan

Qualitative data from the “think aloud” process of the first 5 participants assigned to the GSDI condition will be reviewed by the PI and the RA. Based on these data, minor modifications may be made to the web-based portion of the GSDI to improve usability. No major content changes will be made to the GSDI.

Qualitative exit interviews will be transcribed and coded for themes in NVIVO software using inductive thematic analysis (Braun & Clarke, 2006). These procedures have been used previously by the PI (Dawn E. Sugarman, Reilly, Rodolico, & Greenfield, 2019).

Quantitative data analysis will proceed as follows. Descriptive statistics will be used to summarize the sample and the GSDI+TAU's engagement, usability, and satisfaction with the intervention. Treatment Effectiveness Scores (TES) will be calculated from the TLFB data for (1) MOUD adherence and (2) opioid abstinence. The TES method was chosen because implicit in its measurement is patients' acceptance of the treatment. Specifically, the TES acknowledges that both treatment acceptability and effects on opioid use, are key elements of treatment effectiveness. Participants receive 1 point for each day they report taking MOUD and 0 points if they did not take MOUD. For opioid abstinence participants receive1 point for each day they report no opioid use, and 0 points for opioid use days. This approach is well-suited to measure the effect of the intervention on MOUD treatment engagement, as every subject who is randomized receives a TES score and missing data are assigned a value of 0, providing an indirect indicator of engagement. Scores range from 0 - 84, with 84 representing the best adherence/abstinence. Due to the small number of participants and skewness of the data, comparisons between groups on MOUD adherence and opioid abstinence will be conducted using Mann-Whitney U Tests.

10. Monitoring and Quality Assurance

In this study, safety monitoring will be conducted continuously by both study staff and Dr. Sugarman. Adverse events will be monitored by study staff and the study PI and reported in accordance with all Mass General Brigham (MGB) IRB policies and procedures. Monitoring and quality assurance will occur throughout the study period. Data collection will be reviewed by Dr. Sugarman along with other research staff at weekly meetings. At the time of continuing review, we will provide the MGB IRB with a summary of any unexpected and related adverse events as well as any other unanticipated problems that have occurred since the last continuing review. We will also follow the MGB IRB policies for expedited reporting of Adverse Events and Serious Adverse Events.

All research staff have completed CITI training and are informed about the importance of confidentiality of data. Confidentiality will be strictly protected. Participants will read the Consent Form, which explains their privacy and confidentiality. Additionally, all participants will be assigned a numeric code that is then used to associate the participant with their data. Study data will be stored separately from any identifying information (i.e., informed consent forms). Only research staff affiliated with this proposal will have access to any identifying information. Data being analyzed will not include identifying information. The identity of the participants will not be revealed in the presentation or publication of any result from the project.

Qualitative interviews will be audio-taped on digital audio-recorders. No directly identifying information will be recorded during the interview. The RA will also take notes during the interview, as a back-up in case there are issues with the recording device. All written notes will be stored in a locked file cabinet, in a locked office. Only the participant's ID number will be on the notes. There will be no identifying information recorded in the written notes. The digital files will be uploaded to a password protected file on the study computer. Once the file is uploaded, it will be deleted from the recording device. After all interviews are complete, the PI and the RA will transcribe the tapes into a written version, which will also be stored in a password protected file on the study computer. All personal identifiers (e.g., names of people, places, etc.) will be excluded from the transcript. The transcripts of the interviews will be

analyzed to find common themes. Digital audio recordings will be deleted from the computer after transcription is completed.

Electronic data will be collected using REDCap, a secure, HIPAA-compliant, web-based application and through the Catalyst App, which has been previously approved by RISO and the MGB IRB. Catalyst has been designed to ensure data security, privacy, and confidentiality. Data are encrypted on the phones and uploaded to a secure server (using HIPAA compliant software which has been reviewed and approved by MGB RISO) and downloaded by the researcher to the local research server in a de-identified format. All subject names will be coded. The master key (linking deidentified IDs to identifying information) will be stored securely on the MGB network and will only be accessible to study staff. No identifiable data will be stored on mobile devices. The attached document provides further information regarding data privacy, confidentiality, and security features of the Catalyst app. In addition to assigning participants a deidentified subject ID, study staff will also create a deidentified unique email address for each participant to create their Catalyst account and ensure confidentiality.

Data exported from both REDCap and Catalyst will be saved to McLean Hospital's ADATP Research File Area Shared Drive (RFA). Access is restricted to the ADATP RFA Volume using Partners Authorization System Groups but additionally permissions have been applied to the subfolders as well. The Servers themselves are running Windows 2012 Server and configured in a Cluster mode for redundancy. They are running TrendMicro Deep Security for Antivirus and are behind the MGB Firewall. Windows updates are run monthly. The servers are physically located in the Needham Data Center. The disks are configured in RAID 6-10 for redundancy and incremental backups are performed on a nightly basis and stored for 90 days.

11. Select the Privacy and Confidentiality measures that apply to this research:

- ☐ Study procedures will be conducted in a private setting
- ☒ Only data and/or specimens necessary for the conduct of the study will be collected
- ☒ Data collected (paper and/or electronic) will be maintained in a secure location with appropriate protections such as password protection, encryption, physical security measures (locked files/areas)
- ☐ Specimens collected will be maintained in a secure location with appropriate protections (e.g. locked storage spaces, laboratory areas)
- ☒ Data and specimens will only be shared with individuals who are members of the IRB-approved research team or approved for sharing as described in this IRB protocol
- ☒ Data and/or specimens requiring transportation from one location or electronic space to another will be transported only in a secure manner (e.g. encrypted files, password protection, using chain-of-custody procedures, etc.)
- ☒ All electronic communication with participants will comply with Mass General Brigham secure communication policies
- ☒ Identifiers will be coded or removed as soon as feasible and access to files linking identifiers with coded data or specimens will be limited to the minimal necessary members of the research team required to conduct the research
- ☒ All staff are trained on and will follow the Mass General Brigham policies and procedures for maintaining appropriate confidentiality of research data and specimens
- ☒ The PI will ensure that all staff implement and follow any Research Information Service Office (RISO) requirements for this research
- ☐ Additional privacy and/or confidentiality protections

Describe below:

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