Encouraging Opioid Abstinence Behavior: Incentivizing Inputs and Outcomes

4/1/21

NCT04235582

AURORA HEALTH CARE, INC.

PROTOCOL TITLE: **Encouraging Opioid Abstinence Behavior: Incentivizing Inputs and Outcomes**

PRINCIPAL INVESTIGATOR: **Mindy R. Waite, PhD, MS**
Behavioral Health Research Scientist
960 N. 12th Street, 4120
Milwaukee, WI 53233
414.219.7803
Mindy.Waite@aah.org

INVESTIGATORS AND KEY PERSONNEL:

Rebecca Dizon-Ross, PhD,
Associate Professor of Economics
University of Chicago

Ariel Zucker, PhD, Post-doctoral Fellow (under Jeremy Magruder, PhD)
UC Berkeley

Varun Satish, Research Associate
University of Chicago

TBD, Research Associate

This protocol was designed and developed by the University of Chicago, University of California - Berkeley University, and Aurora Health Care. It is intended to be used only in conjunction with institution-specific IRB approval for study entry.

The Aurora IRB requires that this protocol be conducted according to U.S. and international standards of Good Clinical Practice (International Conference on Harmonization (ICH) Guidelines), Common Rule, WI and the Aurora IRB policies and procedures. All Human Participant Research and all Clinical Investigations conducted at Advocate Aurora Health or by researchers employed by Advocate Aurora Health will be

guided by the ethical principles set forth in the Belmont Report of the National Commission for the Protection of Human Participants of Biomedical and Behavioral Research.

I. Background and Significance

Numerous studies have tested whether providing incentives to encourage abstinence from drugs can further reduce drug abuse in a drug-treatment setting. The results are promising: Incentives to reduce opioid abuse increase the average duration of abstinence by 25 – 60% relative to medication and counseling alone (Petry et al., 2006; Schottenfeld et al., 2005). Similar effects have been demonstrated repeatedly across a wealth of populations, substance-abuse disorders, and payment methodologies (see Lussier et al., 2006; Higgins et al., 2011; Davis et al., 2016; and Higgins et al., 2016 for reviews of providing incentives for managing addiction).

Despite evidence that incentives are effective and the increasing need for effective approaches to combat the addiction crisis, incentive programs have not been widely implemented. A key barrier is that while the benefits are largely borne by patients and taxpayers, there are large logistical costs that must be borne by clinics: most existing incentive programs involve manual, in-person measurement of behaviors, and prize or voucher purchase and delivery by clinic staff. The significant clinic-level legwork necessary to set up these programs, including setting up behavioral and payment tracking systems, training staff, etc., have prevented the programs from scaling widely (Benishek et al., 2014). In sum, prior experience has consistently shown that incentives increase duration of treatment and decrease substance abuse, but the logistical complications remain a hurdle to implementation.

We propose to conduct the first randomized evaluation of an innovative, scalable incentives program for opioid addiction delivered through a mobile application. The application, which was developed by our implementing partner, DynamiCare Health, provides a "turnkey" solution that health clinics can easily prescribe. The app enables remote monitoring of behavior; for example, drug tests can be administered in patients' homes, as patients submit "selfie-videos" showing them taking saliva drug tests, which are then verified by trained remote staff. Treatment adherence can similarly be checked through GPS tracking for on-site methadone pharmacotherapy. The efficacy of this approach has not been tested rigorously before.

This study will address two key knowledge gaps in the *logistics* of existing incentive program design for opioid addiction. First, we will test the first technology that we know of for *remote monitoring* of abstinence behavior for opioid use. Remote monitoring of abstinence from cigarettes and alcohol has been integral in reducing the costs and extending the potential reach of incentive programs for people with nicotine/tobacco and alcohol use disorders (e.g. to vulnerable or rural populations), and our study promises to do the same for opioid addiction (see for a review of remote monitoring technologies for incentive delivery). Our second gap is in *remote delivery* of incentives. After a behavior is verified, the app will deliver incentives to patients as cash available on a linked debit card. The delay between monitoring of the target behavior and the delivery of financial incentives has been shown to be a significant moderator of treatment effect size (Lussier, Heil, Mongeon, Badger, & Higgins, 2006). Our technology allows patients to receive

incentives almost immediately following the undertaking of the incentivized behavior: a first in incentives for opioid addiction.

Another novel feature of our design allows us to address a gap in the literature on incentive delivery: we compare both the isolated effects of incentives and of the monitoring needed to implement an incentive program. In addition to a control group, our full experiment includes both *monitoring groups* and *incentives groups.* While existing literature on incentives for addiction has included *either* a monitoring group or a control group, to our knowledge we are the first to include both, such that a comparison can be made between incentives that are distal (inputs) and proximal (outcome) to the targeted abstinence behavior.

Finally, our experiment will directly address two key open questions in the literature on incentives for drug-users. The first question is whether it is more effective to directly incentivize the outcome of interest – drug abstinence – or to incentivize behaviors that are inputs into the production of abstinence. In a similarly designed study, Petry et al. (2012) did not detect different effects on abstinence from incentivizing treatment attendance and incentivizing cocaine abstinence among cocaine users (both were effective): however, not only was this study for a different substance use disorder, but because of differential rates of test submission among these two groups, the results were not conclusive. We will similarly compare two versions of the incentive program: one that incentivizes inputs to achieving abstinence, and one that incentivizes the outcome of abstinence. To address differential test submission rates, we will measure the impacts of the intervention with urine drug-tests administered identically to patients in both treatments. In addition, we will use a novel combination of baseline survey data and preferences among future incentive programs to inform our understanding of why, and for whom, incentives for inputs and outputs are differently effective.

The second question is how to optimize the *size of incentives over time* to maximize incentive effectiveness. We propose to do this by randomly varying the size and timing of incentives offered to participants in both the Inputs and Outcomes groups. We will then use the variation in incentive amounts across participants and time to fit a structural model of abstinence behaviors over time. We will then use the model to describe the optimal shape of incentives over time.

The results of this intervention will be directly relevant for potential users of this or similar mobile applications for incentive provision among people with opioid-use disorders, including insurers, treatment facilities, and governments.

II. Specific Aims

Research Question:

Our *first research question* is whether two incentive delivery approaches, one targeting *inputs to* abstinence and one targeting the *outcome of* abstinence*,* are effective in promoting abstinence *from non-medical opioids*. We will also investigate how incentive *amounts and timing* influences its effectiveness. Our primary hypotheses are listed below.

Hypothesis 1: Providing mobile-app-based incentives will increase the *longest duration of abstinence from non-medical opioids* relative to a control group receiving *treatment as usual*.

To assess this, we will compare abstinence outcomes (longest duration and percent negative urine/saliva samples) between the pooled Inputs and Outcomes groups and pooled Monitoring and Control groups, during the intervention period.

Hypothesis 2: Incentives have persistent effects on abstinence from non-medical opioids, even after the incentive program ends.

We will compare abstinence outcomes between pooled Inputs and Outcomes groups and pooled Monitoring and Control groups, during the follow-up period.

Hypothesis 3: Abstinence is differentially affected by whether incentives are provided for inputs to abstinence or for the outcome of abstinence.

We will compare abstinence outcomes between the Inputs and Outcomes groups during the intervention period

Hypothesis 4: The differential impact of inputs vs. outcomes incentives depends on underlying characteristics of *patients* and their *environment.*

We will analyze the heterogeneity of the effectiveness of the two incentive treatments according to baseline measures of *risk aversion, risk exposure, impatience,* and *knowledge of the pathway to abstinence.*

Hypothesis 5: The time-path of incentives can be modified to increase their cost-effectiveness.

We will model how patients respond to incentives of different amounts at different times and use the model to predict the optimal time path of incentives.

The objective of this research is to assess the efficacy of two new incentives programs for abstinence behavior, thereby contributing to general knowledge on treatments for addiction.

III. Study End Points

The primary endpoint is the longest period of continuous abstinence from non-medical opioids, where abstinence is measured using lab-verified in-person urine-tests or video-verified saliva tests.

The secondary endpoints include the percent of three (3) scheduled urinalyses/saliva test results classified as negative, the percent of psychotherapy visits attended, the rate of discharging from treatment before completion (discharge against medical advice), and the adherence to medication assisted therapies.

There are no intervention-related safety endpoints that we expect will cause participants to end participation due to safety concerns.

IV. Study Design

To answer our research questions, we will conduct a randomized controlled trial pilot of temporary incentives to encourage either abstinence, or inputs to abstinence, among 600 adults with opioid use disorders in Milwaukee, Wisconsin. Participants will be recruited from outpatients (partial and day treatment programs) with substance use disorders in treatment at the Adult Behavioral Health Program within the Aurora Health Care system. Incentivized behaviors will be monitored and rewarded through a mobile application developed by our implementing technology partner, DynamiCare Management. We will evaluate the incentives using a combination of administrative data and surveys. In preparation for this experiment, we will conduct a Phase 1 pilot of 36 individuals to test and fine-tune our study protocols. Any significant alteration to the protocol or any change that affects Human Participants concerns will be submitted to the IRB as a modification.

Pilot Timeline:

- The total duration of an individual participant's participation in the pilot (including follow-up) is 3 months.
- The anticipated duration to enroll all study participants is 3 months.
- The estimated date for the investigators to complete this pilot (complete primary analyses) is September 30, 2020.

Study Timeline:

- The total duration of an individual participant's participation in the study (including follow-up) is 9 months: a 3-month intervention, and a 6-month follow-up.
- The anticipated duration to enroll all study participants is 30 months.
- The estimated date for the investigators to complete this study (complete primary analyses) is June 1, 2023.

In addition to the prospectively collected data, we will pull EHR data for patients whose records indicate that they were treated for an opioid use disorder in the relevant treatment programs (SUD PHP, IOP, or outpatient) during similar dates of service to the pilot study. Dates of service for these retrospective patients will be between April 1 March 31, 2021. We will use data from these individuals for two purposes: First, to better understand potential enrollment rates going forward, as there may be seasonal variation in treatment enrollment. Second, to form a "Control" group of similar patients to our pilot program. Comparisons between "Control" and "Treatment" patients will allow us to estimate a treatment effect, which we will input into power calculations for assessing the necessary sample size for the full study.

V. Experimental Design and Methods (or Study Procedures)

Interventions

Pilot: During the pilot, the study population will be randomly divided into three treatment groups: Inputs, Outcomes, and Combined. The study will include a twelve-week intervention period, during which each group will receive different interventions in addition to their standard of care treatment through AAH.

Inputs Group: During the intervention period, the "Inputs" group will receive incentives for behaviors that are inputs to abstaining from drug use. Patients in this group will receive the same services and urine drug-test schedule as standard of care. Additionally, patients will be registered for a mobile phone application (app) provided by DynamiCare Health and provided with a linked debit card. The debit card does not display the participant's name and has restricted access for purchases of approved products (e.g., cannot be used for purchasing alcohol). The app will prompt patients to complete actions that are inputs to abstinence an average of three times per week. These actions will be tailored to the patient's individual needs, and may include:

- Drug adherence to prescribed drug-maintenance therapy.
- Attendance at individual and group psychotherapy sessions (monitored by phone GPS for patients attending in-person or via EHR records for patients attending virtually).
- Mobile Cognitive Behavioral Therapy (CBT) Modules offering patients self-guided addiction counseling.

Patients will receive immediate financial rewards for completing a subset of these actions prompted by the app.

Control Group: This group will not have received any opportunity to enroll in the study because they were in treatment during times outside of the study enrollment period. As a result, they will not have had access to the DynamiCare app or any surveys/study data collection.

The incentive amounts offered in the inputs group will vary randomly across participants in order to understand how effectiveness varies according to incentive amount.

Outcomes Group: During the intervention period, the "Outcomes" group will receive incentives for abstaining from drug use. Patients in this group will receive the same services and urine drug-test schedule as standard of care and a similar mobile app and debit card as the Inputs group, as well as access to Mobile Cognitive Behavioral Therapy (CBT) Modules. However, the app will prompt patients in this group to submit saliva drug tests through their mobile phones on a random schedule (averaging three tests per week). Patients will receive immediate financial rewards in exchange for submitting drug-negative samples. Saliva tests typically have a window of detection between 24-48 hours after drug use.

Combined Inputs/Outputs Group: This group will receive interventions from both Inputs and Outputs groups, as well as standard of care therapy services and urine drug tests. Interventions include incentives for a combination of the following actions:

- Drug adherence to prescribed drug-maintenance therapy.
- Attendance at individual and group psychotherapy sessions (monitored by phone GPS for patients attending in-person or via EHR records for patients attending virtually).
- Mobile Cognitive Behavioral Therapy (CBT) Modules offering patients self-guided addiction counseling.
- Random saliva tests.

Patients will receive immediate financial rewards if they complete each action prompted by the app.

Other Procedures

All participants in the study will continue to receive Aurora's standard opioid use disorder treatment, which may be virtual or in-person. Standard of care treatment consists of pharmacotherapy, individual psychotherapy, group psychotherapy, and urine drug screens (if in-person). As part of in-person standard of care, urine drug screens are typically performed 3-4 times per 2-week period for both partial and day treatment.

All patients will have access to mobile Cognitive Behavioral Therapy (CBT) Modules through DynamiCare Health offering patients self-guided substance use counseling, which will not be incentivized.

Patients in all groups will be asked to submit saliva drug tests at Weeks 4, 8, and 12 through the app, in addition to the routine clinical urine drug screens (and, for the Outcomes group, randomized saliva samples) mentioned above. The pre-scheduled saliva samples will be rewarded $20 *non-contingent* on positive/negative status. If no saliva tests are submitted, patients can be asked to submit a non-clinical urine sample in-person (incentivized with $20), their records will be checked for recent clinical urine samples (no incentive provided), or they will be asked about their recent drug use (no incentive provided).

Any saliva/urine samples collected for research purposes over and above the routine urine testing that occurs in treatment as usual are not performed as part of clinical care and will not be shared with the clinical care team.

Surveys: All patients will receive a baseline and endline survey. In addition, we will electronically administer the WHOQOL-BREF survey through the DynamiCare app at weeks 4, 8, and 12. The WHOQOL-BREF is a validated, commonly used survey to measure quality of life.

No other procedures are performed on the participants of this study.

We do not anticipate any risks associated with the saliva test. However, tests will be administered through the DynamiCare Rewards app and will be checked by trained remote staff.

Incentives

Payments will be made to all participants as part of the evaluation activities: We plan to provide incentives to all participants for completing the subset of non-standard-of-

care saliva/urine tests completed during the course of the intervention period – those at 4, 8, and 12 weeks after enrollment. Any urine tests administered as part of standard-of-care treatment at Aurora will not be incentivized; these could be on weeks 4, 8, and 12 as needed. The incentive will be provided to participants in all groups in the form of $20 via the app (if saliva) or via Amazon gift card (if in-person). In addition, we plan to provide $20 Amazon gift cards to patients for completing the Endline survey. The maximum that can be earned from primary outcomes saliva/urine collection and surveys (3 urine/saliva samples + 1 endline survey) is $80.

Further, we are adding on $2/survey for secondary outcomes of the completing the WHOQOL survey at baseline, Weeks 0, 4, 8, and 12. Therefore, subjects could earn an additional $8for surveys.

Payments made to participants assigned to one of the incentives groups as part of the incentives intervention: Patients in all Pilot groups will be awarded payments through the DynamiCare Rewards application. With up to 13 random tests per month, up to $130 can be earned per month; however, on average only about 70% of that amount is earned ($91). The debit card can only be used for restricted purchases; for example, it cannot be spent at bars, liquor stores, casinos, etc.

The application has two types of reward schedules. For some tasks, the application uses an escalating rewards schedule with a hard reset (i.e., completing the first task earns a predetermined amount of money with an escalation at each successful step, and missing or failing a task reduces/resets the reward). This type of schedule is consistent with previous contingency management protocols.

Rewards schedule for behaviors on the streak (i.e., saliva tests and medication adherence)

- Amount of first reward: $2
- Reward escalation interval: $2 (i.e., each time the behavior is successful, the incentive amount goes up by $2 for the next behavior)
- Maximum reward for a single behavior: $10
- Reward reset value: $2 (i.e., if a behavior is unsuccessful, the incentive amount for the next behavior resets to $2)
- If action unverifiable/cancelled: no escalation/no reset

Rewards schedule for non-streak behaviors (i.e., appointments)

The application also allows for an independent rewards schedule (i.e., the reward received for a given task is determined independently of how the patient has performed on other tasks). In the independent rewards schedule, patients earn a preset number of dollars for activities. Missing or failing an independent-rewards task does not impact the reward for future tasks or depend on performance of previous tasks. *Amount of each reward: $5*

This was necessary because the app cannot currently incorporate appointments into their streak formula, so every appoint is worth a fixed $6.

The incentivized behaviors differ among the three groups.

- “Outcomes” patients *only* receive incentives for illicit opioid-negative saliva tests

- "Inputs" patients *only* receive incentives for drug adherence and appointment attendance (including virtual appointments)
- "Combined" patients receive incentives for *all* behaviors above

Schedule 1: Example Escalating Schedule Only (i.e., Outcomes Group)

	Task 1	Task 2	Task 3	Task 4	Task 5	Task 6	Task 7	Task 8	Task 9	Task 10
Pass/Fail	Pass	Pass	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Pass
Dollars earned	2	4	6	8	10	10	0	2	4	6
Accumulated earned	2	6	12	20	30	40	40	42	46	52

Schedule 2: Example Escalating Schedule + non-streak behaviors (i.e., Inputs Group)

	Task 1 steak	Task 2 streak	Task 3 non-streak	Task 4 streak	Task 5 non-streak	Task 6 streak	Task 7 streak	Task 8 non-streak	Task 9 streak	Task 10 streak
Pass/Fail	Pass	Pass	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Pass
Dollars earned	2	4	5	6	5	8	0	5	2	4
Accumulated earned	2	6	11	17	22	30	30	35	37	41

Schedule 3: Example Constant Schedule (not currently planned to be used in the pilot)

	Task 1	Task 2	Task 3	Task 4	Task 5	Task 6	Task 7	Task 8	Task 9	Task 10
Pass/Fail	Pass	Pass	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Pass
Dollars earned	4	4	4	4	4	4	0	4	4	4

	Task 1	Task 2	Task 3	Task 4	Task 5	Task 6	Task 7	Task 8	Task 9	Task 10
Accumulated earned	4	8	12	16	20	24	24	28	32	36

Task examples: saliva test, attend group meeting, take pharmacotherapy

a. Screening Visit (T = 0)

- Treating therapists will briefly describe the study to their psychotherapy groups receiving AODA treatment.
- Screening will be performed at Aurora (APH) or virtually via HIPAA-compliant zoom meeting, depending on the patient's treatment type (in-person or virtual) and preferences. Potential participants will be referred to the RA and/or principal investigator by their clinician, APH intake, other APH professional, or will be identified from the EMR. Virtual enrollment is necessary for patients who are receiving virtual treatment or who prefer virtual enrollment as a way to maximize social distancing for safety.
- The RA and/or PI will conduct a preliminary screening survey. If patients are eligible for the study, the RA and/or PI will then explain the study and obtain informed consent to participate from willing participants. Only patients whose potential participation is approved by the person responsible for their treatment plan will be approached, per WI DHS 94.
- Per RSPP requirements, if the subject is being enrolled virtually (via Zoom platform), the RA must make a determination on the identity of the subject by having the subject show a viable form of identification. The consent may be signed either physically or via approved e-signature (Adobe Sign), which is owned by the AARI Research Business Services team.
- Following informed consent, the RA and/or PI will conduct a Baseline survey using a tablet or computer.
- The RA will send an invitation link to the subject's email and help the subject download, log into, and navigate the app. This can be done either in person or via Zoom.
- Treatments will be assigned via stratified randomized lists generated in statistical software. Participants will be provided with instructions pertinent to their treatment group following the baseline survey. Subjects will be offered $2 on their debit card to complete the baseline WHOQOL survey.Participants in all Pilot groups will receive a debit card, either in-person or in the mail, on which to receive their rewards.

b. Visit 1 (T = 4 weeks)

- Visit 1 will occur 4 weeks after the screening visit with +/- one (1) week.
- Participants may receive urine tests as part of usual in-person treatment.
- If participants do not receive urine tests as part of usual treatment, they will be contacted by the research associate to complete a research-only saliva or urine test either in-person or via DynamiCare. If they complete the saliva/urine test, they will receive a $20 incentive.
- If they refuse to complete the saliva/urine test, they will be briefly asked about their recent non-medical drug use (presence/absence and type) but will not be provided a financial incentive.
- The WHOQOL survey will be delivered using RedCap. Completed surveys will be incentivized with $2 on their debit card .

c. Visit 2 (T = 8 weeks)

- Visit 2 will occur 8 weeks after the screening visit with +/- one (1) week.
- Participants may receive urine tests as part of usual treatment.
- If participants do not receive urine tests as part of usual treatment, they will be contacted by the research associate to complete a research-only saliva or urine test either in-person or via DynamiCare. If they complete the saliva/urine test, they will receive a $20 incentive.
- If they refuse to complete the saliva/urine test, they will be briefly asked about their recent non-medical drug use (presence/absence and type) but will not be provided a financial incentive.
- The WHOQOL survey will be delivered using RedCap. Completed surveys will be incentivized with $2 on their debit card..

d. Visit 3 (T = 12 weeks)

- Visit 3 will occur 12 weeks after the screening visit with +/- one (1) week.
- Participants may receive urine tests as part of usual treatment.
- If participants do not receive urine tests as part of usual treatment, they will be contacted by the research associate to complete a research-only saliva or urine test either in-person or via DynamiCare. If they complete the saliva/urine test, they will receive a $20 incentive.
- If they refuse to complete the saliva/urine test, they will be briefly asked about their recent non-medical drug use (presence/absence and type) but will not be provided a financial incentive.
- The RA will conduct an Endline survey using a tablet (if in-person) or via phone or Zoom. They will receive a $20 gift card for finishing the survey.
- The WHOQOL survey will be delivered using RedCap. Completed surveys will be incentivized with $2 on their debit card..

Study Procedure	**Screening Visit**	**VISIT 1:**	**VISIT 2:**	**VISIT 3:**
Sign Informed Consent	***X***			
Incentive for Saliva/Urine Drug Screen and WHOQOL		***X***	***X***	***X***
Survey Interview	***X***			***X***

VI. Risks

The purpose this study is to measure the effectiveness of Contingency Management (as delivered by the smartphone-based DynamiCare Rewards system) as an adjunct to standard treatment for opioid use disorders. This is a low-risk study, as the proposed

intervention is a mobile application, which does not provide any diagnosis or treatment for any disease. This project does not involve invasive tests or procedures. Saliva and urine samples will be collected, but these procedures pose no direct risk to participants, and aside for our research use, could be considered standard clinical practice in addiction treatment. However, mild stress may occur when performing self-administered saliva testing. Since participants have the potential to earn money for abstinence, they may become distressed if they believe that the equipment is not performing accurately. Although these indirect risks tend not to be of a large magnitude, participants may experience discouragement if they don't meet their goal, or if they do meet the goal but do not get appropriately rewarded due to rare but possible false positive results in the tests. In addition, although we purposefully mitigate risk by constraining the use of debit cards only to certain activities (e.g., not for payment at a liquor store), participants may still use the debit card for contra-therapeutic purposes and engage in harmful behaviors such as purchasing alcohol or cigarettes.

A final potential risk is that participant confidentiality could be breached, in regard to patient health information, during transmission of electronic data including patient names or exercise adherence. Participants can decline to be in the study or leave the study early if they have any concerns and, as an alternative to study participation, they can continue in usual care.

It is not expected that participation in the study will contribute any significant cost to participants. However, requisite to participation in the study, their smart phones must have a data plan in order to run the application. Each saliva test video is ~60 MB. In the app settings there is an option, "Upload only over Wi-Fi." This will store the video on their phone until the participant's phone establishes a Wi-Fi connection, at which point the app will automatically upload the video (even if the phone is just in their pocket). As such, participants with low data caps can choose to use that feature to avoid potentially adding extra data charges.

Risk Associated with a Breach of Confidentiality

To protect confidentiality, all research participants will be assigned unique participant identification codes that will be used on all study-related forms and online websites. Documents that include the participants' full names (e.g., signed informed consent forms) will be stored in an independent binder, consistent with FDA Good Clinical Practice Guidelines, and will be kept in a locked area. Confidential information will never be shared with anyone outside of the research program without the explicit written permission of the research participant, and a Certificate of Confidentiality will be obtained from the NIH for the study in order to protect participant data. Only selected designated staff members will be approved to share confidential information after explicit written permission is obtained from the participant and the participant will be able to revoke written permission at any time. In accordance with IRB requirements, all research staff will be formally trained in these procedures. No identifying participant information will be used in written reports, manuscripts and/or conference presentations.

Dr. Waite (PI), behavioral economist Lead Investigators (Dr. Dizon-Ross and Dr. Zucker), and the AAH research associate will be the only individuals who will have access to cross-linking information that connects the study identification number to

identifiable personal information, such as participant name or email address. Even though the final dataset will be stripped of identifiers prior to release for sharing, we believe that there remains the possibility of deductive disclosure of participants with unusual characteristics. Thus, we will make the data and associated documentation available to users only under a data-sharing agreement that provides for: (1) a commitment to using the data only for research purposes and not to identify any individual participant; (2) a commitment to securing the data using appropriate computer technology; and (3) a commitment to destroying or returning the data after analyses are completed.

In addition to written participant data, videos of participants are uploaded into the DynamiCare platform for saliva assessments. DynamiCare Rewards is a HIPAA-compliant platform designed for use in healthcare settings. It protects patient information with encryption in-transit and at-rest, and limits visibility of patient data to only those with authorized access. These data are automatically uploaded to the DynamiCare HIPAA-compliant server. Only staff working on the research project at the various sites (i.e. DynamiCare Health, Aurora Health Care, University of California-Berkeley, and University of Chicago) will have access to participant data.

Further, accounts for DynamiCare access will be issued, tracked, and removed/added by the Aurora PI if personnel leave or are added to the study. If the Aurora PI is scheduled to leave the study, then a replacement (interim) PI will be identified and put in place before the original PI leaves to ensure that a PI is always available to add/change personnel access. In an emergency situation (e.g., the PI in incapacitate), the Aurora research associate is authorized to make these changes.

If the subject is receiving virtual behavioral health therapy, it is likely that interactions between the subject and RA will occur via Zoom. AAH has access to a HIPAA-compliant Zoom platform, which is currently used for providing behavioral health therapy. This same platform will be used to offer Zoom meetings with subjects; no videos or photos will be recorded during these Zoom meetings. Zoom links will be sent either to personal emails or personal phone texts as provided by the client (in other words, the patient will provide these emails/phone numbers).

Zoom meetings with potential subjects may or may not immediately follow their group therapy meetings; this depends entirely on the patient's availability. Zoom meetings may be scheduled at other times, and the scheduling agreement with the patient may be done via personal email or via phone call. Zoom meeting confirmations will If done via email, the email will be generic and not point to the study purpose (e.g., the email may be titled: "Zoom Meeting: AAH Research Study" or something similarly vague and not mentioning substance use or any other diagnosis/disorder category. The consent form will be provided during the Zoom call via Zoom download and via link to DocuSign. The patient may sign the consent form via DocuSign during the meeting or, if the patient provides approval, the consent form or DocuSign link may be emailed to the patient's personal email. There are no clinical parameters for arranging these meetings as they are not clinical visits.

Provisions for Research Related Harm/Injury

Although this study involves minimal risk and no adverse events are expected, the resources of Aurora Health's clinical team are available to handle any unforeseen events, as they would be for patients not involved in a research protocol. Each of Aurora's OTP sites is medically staffed to assess acute issues that may arise in the context of OUD treatment, and the programs have access to standard psychiatric and counseling services.

VII. Benefits

By incentivizing inputs to opioid abstinence as well as opioid abstinence itself, this project aims to improve the outcomes of participants in this study with severe opioid use disorders by reducing the barriers to abstinence. This may lead to direct long-term improvements in health and employment, as well as wellbeing of the participants and their friends and families. Several previous studies have suggested these benefits are likely to occur.

If the study endpoints are positively affected, it will serve as evidence of the effectiveness of the DynamiCare mobile application: the first scalable, turnkey solution for incentives for healthy behaviors among people (i.e., contingency management) among people with opioid-use disorders.

In addition, the study will push the frontier of knowledge on how incentives in general can be more effectively applied in similar populations, leading to potential improvements in the design of contingency management broadly. This will result in more efficacious interventions for people seeking treatment for substance use disorders.

VIII. Sample Size

We will recruit 36 participants to pilot the incentive programs during the Pilot.

IX. Study Population

Include	*Exclude*	*Vulnerable Population Type*
	✓	*Adults unable to consent due to cognitive impairment (i.e., current diagnosis for psychosis or non-English speaking)*
	✓	*Individuals who are not yet adults (e.g. infants, children, teenagers)*
	✓	*Wards of the State (e.g. foster children)*
✓		*Mentally ill*
✓		*Women, including pregnant women*
✓		*Economically disadvantaged*
✓		*Minorities*
	✓	*Prisoners*

The study will be conducted among outpatients with opioid use disorders at Aurora Health. This population includes a number of vulnerable population types that will be included in the study. For example, economically disadvantaged individuals, people with mental-health comorbidities, women (including pregnant women) and minorities are included in the category of vulnerable populations.

That stated, the potential risks of this minimal-risk study are far outweighed by the potential benefits of study participation, both for the individuals involved and for the vulnerable populations as a collective. First, participants will have the chance to receive contingencies for abstinence-promoting behaviors, which may both reduce substance abuse. Second, the results of the study will be published. These results will inform the academic and treatment community of the availability and effectiveness of smartphone-based contingency management, and whether inputs- or outcomes-based reinforcement has larger clinical effect sizes. Third, the study results will inform the further refinement of the mobile app, which will increase its effectiveness in helping people with substance use disorders (and perhaps make it more effective for the participants themselves if they choose to use the app later). It is critical that solutions for opioid use disorders be studied among the multi-faceted populations who can benefit from treatment, and these populations naturally include a number of vulnerable groups.

Because this is minimal-risk research, there is comparatively greater upside benefit for participants than there is any research-related risk of harm.

The benefit of non-exclusion of vulnerable populations from research participation is the improvement in understanding strategies to encourage abstinence among the populations where these strategies are needed most.

In order to protect the welfare of vulnerable populations, individuals in the study must be already enrolled in Aurora Health's Behavioral Treatment Program for treatment of their opioid use disorder and any co-occurring mental health diagnoses. This will ensure they already have access to standard-of-care treatment necessary for their medical needs.

Qualifying candidates meet the following Inclusion and Exclusion criteria:

a. Inclusion Criteria

1. Age at least 18 years old;
2. Meet DSM-5 opioid use disorder criteria as evidenced by an opioid disorder CPT code F11 (opioid related disorders) or other clinical notes indicating illicit opioid use for treatment;
3. Have access to a smartphone (iOS or Android) with data plan and willing to download DynamiCare app;
4. Are in day (PHP), partial day (IOP), residential, or outpatient AODA treatment in Aurora Health's Behavioral Health Program;
5. Are currently prescribed or will be prescribed within 1-4 days buprenorphine, naltrexone, or methadone for their OUD;

6. Are likely to be helped by contingency management because at least ONE of the following conditions is true:
    a. Were first enrolled in day or partial day opioid treatment no longer than 2 treatment weeks (14 days/encounters of treatment) prior to providing informed consent.
    b. Currently using non-medical opioids.
    c. Regularly missing scheduled AODA appointments.
7. Understands English.

b. Exclusion Criteria

1. Have evidence of active (non-substance related) psychosis that might impair participation as determined by the PI.
2. Has significant cognitive impairment that might confound participation as determined by the PI or are so significantly cognitively impaired that they have a legal guardian.

Note that pregnant women are not excluded from participating in the study.

X. Recruitment and Screening

Participants will be actively recruited into the study in one of two ways. Either patients will be recruited at patient intake at Aurora's Behavioral Health Program or referred to the study by their clinician at Aurora with the patient's assent.

The first stage of recruitment (eligibility screening) will be conducted by the research team. This team will determine if potential participants (who have or have not yet expressed interest in the study) meet all inclusion criteria below *except* Smartphone and data plan access, and no exclusion criteria. Qualifying potential participants will then be directed to the Research Associate to determine whether their phone and data plan access meet study requirements.

If an interested patient meets inclusion criteria (specified above), the Research Assistant will arrange for the patient to complete research consent as described in Section XV below. Patients will be offered the opportunity to consent to participation. However, eligible patients that are not prepared to give informed consent on the same day will be given the contact number of the Research Associate and may consent at a later date as long as they are within eligibility timelines.

There are no materials needed for recruitment.

We do not anticipate withdrawing participants from the study without their consent. However, participants can decline to be in the study, or leave the study early if they have any concerns, and as an alternative to study participation they can continue in usual care.

Research participants who wish to fully withdraw from the study can do so by contacting the research associate or Principal Investigator. Contact details will be given in the

informed consent at the consent stage. In the event that a participant wishes to fully withdraw, all survey and drug test data will be removed from research databases, and the mobile app will be deactivated. In the event that a participant wishes to discontinue use of the app, but allows continued analysis of their data, the mobile app will be deactivated, but we will analyze and, where possible, continue to collect urine samples and other available outcome data from that participant.

XI. Privacy Plan

All communication with the participants during the study will be through in-person appointments, through the DynamiCare application, via patient-provided email, phone, and/or AAH-purchased Zoom. DynamiCare will execute a Business Associates Agreement with Aurora Health Care to provide a HIPAA umbrella over the patient-generated data. The smartphone application requires the user to input a username and password, allowing for their control over their private information.

Questions asked will be minimally intrusive. However, participants will be told in advance that they may refuse to answer any question at any time. Research Assistants who are trained in working with patients with substance use disorders, and who are culturally sensitive, will conduct enrollment. Examinations and procedures, such as urinalysis, will be no more intrusive than standard care as provided in the Aurora substance use disorder treatment programs.

The geographical locations system within the app only tracks the location of the participant within a small window of time related to their programmed clinical appointments. As a result, the data collected on phone location are specific and minimal.

XII. Data Collection

Data Sources & Description

Survey data, mobile application data, and clinic data will be used during the study.

Baseline survey data will measure characteristics such as risk aversion, time preferences, knowledge about the pathway to abstinence, and a real-stakes measure of preferences for inputs-based versus outcomes-based incentive programs. Administrative data will include urine test results, medication compliance measures, appointment attendance, and CBT module usage in groups randomized to use the app. Baseline survey data will measure characteristics such as risk aversion, time preferences, knowledge about the pathway to abstinence, phone and data plan access, and a real-stakes measure of preferences for inputs-based versus outcomes-based incentive programs. Periodic surveys administered through the DynamiCare app will measure other behaviors such as avoidance of “trigger” situations and stress-relieving activities. Endline survey data will measure self-reported drug use, drug avoidance behavior, health, and quality-of-life data.

The survey instruments are currently under development with the intent to be administered digitally through participants’ smart phones. We will begin piloting in

Phase I without survey instruments. Mockups and screenshots of the final surveys will be submitted to the IRB in a protocol amendment before they are implemented.

DynamiCare Rewards is a HIPAA-compliant platform designed for use in healthcare settings. It protects patient information with encryption in-transit and at-rest, and limits visibility of patient data to only those with authorized access. In this study, data will be collected on saliva tests, medication adherence, treatment attendance, and self-guided Cognitive Behavioral Therapy (CBT) modules; these data are automatically uploaded to the DynamiCare HIPAA-compliant server. Data on participant utilization of the smart debit card will be available from True Link Financial, Inc., via a confidential data-sharing agreement.

Administrative data will be collected from Aurora Health Care clinical records, *including alcohol and/or substance use records*. These records will be integral to the study for a number of reasons. First, we will stratify our randomization by dosage history and number of times in treatment, and conduct sub-analyses based on these variables. Second, we need to verify upcoming appointments at the Aurora Behavioral Health Program (to be incentivized or prompted in the app in the Inputs or Combined groups). Third, we will use clinical urinalysis results to measure non-medical drug use in the construction of our primary outcome measure.

Only designated staff working on the research project at Aurora Health Care will have access to participant PHI. All personal data collected will be used for research purposes only, including determination of study eligibility and to characterize the sample. All records and data will be kept strictly confidential and will only be released to research staff with the specific written consent of the participant. Participants will be assigned a unique identifying code at the time of study enrollment to help ensure confidentiality. All data will be stored in RedCap, which is an encrypted program designed specifically for research and clinical trials. The RedCap database is only accessible to AAH employees.

Data to be collected for prospective participants:

Purpose	**Variable**	**Potential sources**
Eligibility/analysis	Identifiers (MRN, Patient Name)	clinical data
Eligibility/analysis	Dates of service	clinical data
Eligibility/analysis	Demographics (age, gender, race/ethnicity)	patient interview, clinical data
Eligibility/analysis	Opiate use in the past 30 days (yes/no)	patient interview, clinical data
Eligibility/analysis	Current opioid use	clinician interview, clinical data
Eligibility/analysis	ICD 10 opioid use diagnosis (F11)	clinician interview, clinical data
Eligibility/analysis	Other significant psychiatric disorders and mental illnesses and whether they currently have a legal guardian	clinician interview, clinical data, patient interview

Eligibility/analysis	Other substance-use disorders	clinician interview, clinical data
Eligibility/analysis	Access to smart phone and data plan and willing to download DynamiCare app	patient interview
Analysis	Appointment adherence, program length of stay, and reason or discharge	clinician interview, clinical data, app
Analysis	Standard-of-care drug test outcomes and EHR notes regarding recent substance use	clinical data
Analysis	Study-specific drug test outcomes	app data
Analysis	Distance to clinic	patient interview, clinical data
Analysis	Standard-of-care drug quality of life survey (Wisconsin Recovery Pulse): https://www.dhs.wisconsin.gov/publications/p01922a.pdf)	clinical data
Analysis	Pregnancy status	patient interview, clinical data
Analysis	Commute time to clinic	patient interview
Analysis	Medication-assisted therapy drug, dosage, schedule, and adherence (e.g., buprenorphine, vivitrol, methadone)	clinician interview, clinical data, app
Analysis	Receipt of previous treatment for opioid dependence (yes/no)	clinician interview, patient interview, clinical data
Analysis	Psychotherapy type (level enrolled across time) and attendance	clinician interview, patient interview, clinical data
Analysis	Therapy appointment schedule and adherence (updated realtime during intervention period)	clinician interview, clinical data, app data
Analysis	Reinforcement activity from app (updated realtime during intervention period)	app
Analysis	Average medication adherence during intervention period	clinician interview, clinical data, app data
Analysis	Admissions to substance use treatment during three time periods: 12 weeks before enrollment, 12 weeks during DynamiCare access, and 12 weeks after DynamiCare access is turned off. Treatment = inpatient admission for SUD reason, SUD residential admission, SUD IOP, SUD PHP, and	clinical data

	SUD outpatient. Will include reasons for treatment.	
Analysis	App reward amounts and reward expenditures (purchases from DynamiCare debit card)	App data

Data to be collected for retrospective subjects:

Purpose	**Variable**	**Potential sources**
Eligibility/analysis	Identifiers (MRN)	clinical data
Eligibility/analysis	Dates of service	clinical data
Eligibility/analysis	Demographics (age, gender, race/ethnicity)	patient interview, clinical data
Eligibility/analysis	Opiate use in the past 30 days (yes/no)	clinical data
Eligibility/analysis	Current opioid use	clinical data
Eligibility/analysis	ICD 10 opioid use diagnosis (F11)	clinical data
Eligibility/analysis	Other significant psychiatric disorders and mental illnesses and whether they currently have a legal guardian	clinical data
Eligibility/analysis	Other substance-use disorders	clinical data
Analysis	Appointment adherence, program length of stay, and reason or discharge	clinical data
Analysis	Standard-of-care drug test outcomes and EHR notes regarding recent substance use	clinical data
Analysis	Standard-of-care drug quality of life survey (Wisconsin Recovery Pulse): https://www.dhs.wisconsin.gov/publications/p01922a.pdf)	clinical data
Analysis	Drug urine test outcomes during similar timeframe of enrolled subjects (e.g., 12 weeks plus 3 month follow-up)	clinical data
Analysis	Distance to clinic	clinical data
Analysis	Pregnancy status	clinical data
Analysis	Medication-assisted therapy drug, dosage, schedule, and adherence (e.g., buprenorphine, vivitrol, methadone)	clinical data
Analysis	Receipt of previous treatment for opioid dependence (yes/no)	clinical data
Analysis	Psychotherapy type (level enrolled across time) and attendance	clinical data
Analysis	Medication schedule (updated realtime during intervention period)	clinical data
Analysis	Therapy appointment schedule	clinical data

	(updated realtime during intervention period)	
Analysis	Admissions to substance use treatment during three time periods: 12 weeks before enrollment, 12 weeks during DynamiCare access, and 12 weeks after DynamiCare access is turned off. Treatment = inpatient admission for SUD reason, SUD residential admission, SUD IOP, SUD PHP, and SUD outpatient. Will include reasons for treatment.	clinical data

Secure Data Storage and Transmission

The PHI will be collected digitally by a Research Associate and will be stored in RedCap at Aurora Health Care. De-identified data will be stored in encrypted files on a secure server at the University of Chicago. Data will be shared only among the key project personnel, using hard encryption methods.

After data analysis and publication, all available study data will be permanently stripped of identifiers. The de-identified data will be kept until 7 years after the data analysis is complete per BCBA ethics guidelines (https://www.bacb.com/wp-content/uploads/BACB-Compliance-Code-english_190318.pdf). After 7 years, the data will be destroyed. However, if at any point there is no PI to lead the study, the data may be destroyed at that time.

Only certain selected members from the research team will have access to the delinked data.

The Research Associate and PI are responsible for the receipt and transmission of administrative clinical data. The principal investigators are responsible for the receipt and transmission of survey data, as well as for data collected through the DynamiCare Rewards app.

The data will be shared only among the key project personnel and shared using encryption methods. DynamiCare Rewards is a HIPAA-compliant platform designed for use in healthcare settings. It protects patient information with encryption in-transit and at-rest and limits visibility of patient data to only those with authorized access. In this study, data will be collected on saliva tests, medication adherence, treatment attendance, and self-guided Cognitive Behavioral Therapy (CBT) modules; these data are automatically uploaded to the DynamiCare HIPAA-compliant server. Remote testing data will be verified through inspection of "selfie-videos" to guarantee quality. Data on participant utilization of the smart debit card will be available from True Link Financial, Inc., via a confidential data-sharing agreement. Only staff working on the research project at the various sites (i.e. DynamiCare Health, UC Berkeley, University of Chicago, Aurora

Health Care) will have access to participant data. Names that are linked to identifiers will be stored in independent binders as well as the password-protected, encrypted electronic database separate from the data.

Personally-identifying information will be delinked completely from the data set and all data will be presented in aggregate in any report.

XIII. Statistical Plan

For the pilot, we will descriptively analyze the Inputs versus Outcomes versus Combined groups. The treatment groups will also be compared to the historical control group.

For the full study, the randomized design allows us to directly compare abstinence (longest duration and percent negative urine samples) between our different treatment arms as follows:

1. Inputs Group vs. Outcomes Group
2. Pooled Inputs and Outcomes Groups vs. pooled Control and Monitoring Groups
3. Pooled Inputs and Outcomes Groups vs. Control Group
4. Pooled Inputs and Outcomes Groups vs. Monitoring Group

We will test for differences in the mean of our primary outcome variables – longest duration of abstinence and percent negative urine samples - using a two-tailed t-test at a 95% confidence level. We will control for baseline characteristics (e.g. time since most recent non-medical drug use at baseline, total time in treatment, and distance from clinic). We will also look at the heterogeneity by measures collected in the baseline survey and described above. Finally, we will conduct exploratory sub-analyses according to dosage history and number of times in treatment.

Our target sample size of 200 patients in each of two incentives groups (Inputs and Outcomes), and 100 each in the Control and Monitoring groups is based on power calculations using patient outcome data from a similar patient population in a different health system. This sample size gives us power to detect minimum effects between the incentive groups of one additional week of continuous abstinence in our 12-week intervention, and a 7.5 percentage point increase in opioid-negative urine samples.

XIV. Monitoring Plan

Not applicable: the human research involves minimal risk to participants.

The study has no premature stopping rule: it will continue until the target sample size is reached.

XV. Regulatory Requirements

Consent will be acquired by a trained Research Assistant or the PI, who identifies eligible patients by assessing the Partial Hospitalization Program (PHP) or Intensive Outpatient (IOP) schedules or by clinician referral. Eligible persons will be provided a copy of the IRB-approved informed consent form to review.

If prospective participants wish to consider the opportunity and weigh more information before signing consent in person or electronically, they will be permitted to do so without time constraints. However, they must be eligible to enroll at the time of enrollment.

- The prospective participant will sit in a private space and have a chance to read through the consent with a study staff member present. Participants will be invited to discuss any questions or concerns with a study staff member who is authorized to witness the informed consent and will be provided as much time as they need to make an informed decision about study participation. The staff member will answer questions posed by the potential participant and clarify any issues that are brought up.
- Prospective participants will be informed that neither study participation, voluntary withdrawal from the study, or discharge from the study will have any impact on any past, present nor future medical treatment they may receive at any Aurora Health Care treatment facility.
- Prospective participants will be invited to include outside parties (e.g., spouse, family members, advocate, legal counsel, and/or independent specialist) to participate in the consenting process discussion, if desired. The site will not assume anyone external into the consenting process nor contact an external party without a prospective participant's permission.
- The study coordinators will review the consent document with potential participants, will answer questions about study treatments, and potential risks, conduct a review that indicates the potential participant's understandings, and complete the signing process. Any identified gaps in understanding will then be addressed until resolved.
- At that point, the patient and staff performing the consent will sign a physical or HIPAA-compliant virtual consent form.
- All participants will be provided with a copy of their signed informed consent form to keep and will be encouraged to contact study staff with any questions that may arise at any time during the study. The original, signed informed consent form will be kept with the participant's research chart. Individuals who are unable (for any reason) to provide voluntary informed consent will not be enrolled.
- The PI will oversee and be responsible for the consenting process.
- The PI and staff that are involved in the consenting process adhere to rigorous ethical principles in the conduct of research.

XVI. References

Benishek, L. A., Dugosh, K. L., Kirby, K. C., Matejkowski, J., Clements, N. T., Seymour, B. L., & Festinger, D. S. (2014). Prize-based Contingency Management for the Treatment of Substance Abusers: A Meta-analysis. *Addiction (Abingdon, England)*, *109*(9), 1426–1436. https://doi.org/10.1111/add.12589

Kurti, A. N., Davis, D. R., Redner, R., Jarvis, B. P., Zvorsky, I., Keith, D. R., … Higgins, S. T. (2016). A Review of the Literature on Remote Monitoring Technology in Incentive-Based Interventions for Health-Related Behavior Change. *Translational Issues in Psychological Science*, *2*(2), 128–152. https://doi.org/10.1037/tps0000067

Lussier, J. P., Heil, S. H., Mongeon, J. A., Badger, G. J., & Higgins, S. T. (2006). A meta-analysis of voucher-based reinforcement therapy for substance use disorders. *Addiction*, *101*(2), 192–203. https://doi.org/10.1111/j.1360-0443.2006.01311.x

Petry, N. M., Alessi, S. M., Carroll, K. M., Hanson, T., MacKinnon, S., Rounsaville, B., & Sierra, S. (2006). Contingency management treatments: Reinforcing abstinence versus adherence with goal-related activities. *Journal of Consulting and Clinical Psychology*, *74*(3), 592–601. https://doi.org/10.1037/0022-006X.74.3.592

Schottenfeld, R. S., Chawarski, M. C., Pakes, J. R., Pantalon, M. V., Carroll, K. M., & Kosten, T. R. (2005). Methadone Versus Buprenorphine With Contingency Management or Performance Feedback for Cocaine and Opioid Dependence. *American Journal of Psychiatry*, *162*(2), 340–349. https://doi.org/10.1176/appi.ajp.162.2.340