Mayo Clinic Protocol Template for Minimal Risk Research

General Study Information

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Study Title: Senyo Health app - Connecting Primary Care to Substance Use Disorder Treatment Using a Telehealth Collaborative Care Platform

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Research Question and Aims

Hypothesis:
We built a digital platform called Senyo Health to deliver evidence-based mechanisms of behavioral change virtually to patients struggling with substance use disorder (SUD) in their primary care clinics. This mixed methods trial will include an implementation aim and a clinical trial aim. During the implementation stage we will adapt and pilot a novel screening, brief intervention, and referral to treatment (SBIRT) strategy in primary care clinics using this digitally native Senyo Health platform, as the treatment modality. **In the clinical trial stage,** the Senyo Health app platform will remotely deliver an Integrated Behavioral Health (IBH) Care Coordination (CC) model for treatment of SUDs. We hypothesize this intervention will be an acceptable intervention that will reduce frequency and intensity of substance use and help promote recovery.

Aims, purpose, and/or objectives (primary, secondary, and exploratory):
Specific Aim 1: To examine the barriers, facilitators, and optimal processes for implementing a digitally enhanced SBIRT model for SUD treatment among Mayo primary care clinics.

Specific Aim 2: To examine the effectiveness of a digital IBH platform in improving substance use outcomes, including treatment retention and substance use frequency and severity.

Background:
Poor access to Substance Use Disorder (SUD) treatment was a problem long before the pandemic. According to the National Institute of Health (NIH), around 22 million Americans need SUD treatment each year, yet only 1 in 10 people receive SUD specialty care.[1] Untreated or undertreated SUDs are estimated to cost the United States over 4 billion dollars annually.[1] Unfortunately, SUD prevalence rates have increased during the COVID-19 pandemic while treatment programs were restricted or closed.[2] NIH has described the compounding effects of the opioid epidemic and COVID-19 pandemic as a national emergency.[3]

Rural populations struggle with an even greater disparity in SUD treatment access. Pre Covid-19, the significant vulnerabilities that rural patients faced included fewer healthcare providers and a lack of mental health services.[10] Covid-19 increased the incidence of SUD in rural areas, where there is a higher likelihood of suffering from isolation, stress, and boredom—these factors pose a risk to psychological health and addiction recovery.[3] Recovery Capital is a biopsychosocial model of recovery from addiction, which encapsulates these and other interpersonal strengths and resources that can support substance use cessation.[38] The shortage of SUD providers, particularly in rural areas, impairs individuals from receiving SUD treatment and growing their recovery capital.[5-7] In the case of OUD, access to medications, especially buprenorphine, is scarce, with approximately 50% of rural counties without an identified buprenorphine prescriber (this is data from pre-

waiver removal). Moreover, those capable of prescribing are often unwilling to prescribe.[8] Primary Care Providers (PCPs) indicate that the lack of SUD-related referral resources and a limited understanding of management standards are major factors limiting their willingness to prescribe buprenorphine.[9] Due to these vulnerabilities and the potential accentuation of existing disparities in care for rural populations, the gap in treating SUD requires urgent attention.

Integrated behavioral health collaborative care (IBH) model is a system-based approach to treating psychiatric disorders in primary care settings. IBH integrates behavioral health care managers into primary care clinics The care managers serve as the primary point of contact for the patient and function as the liaison between the patient, the PCP, the supervising psychiatrist, and other mental health providers, both imbedded into primary care and outside primary care. IBH allows PCPs to manage mental health disorders effectively with less time-intensive use of psychiatric providers.[13] IBH requires a caseload registry and measurement-based care tools to track how patients are doing. Historically, SUD-specific monitoring and data have not been a standard part of IBH programs. It can also be difficult for IBH programs to comply with federal and state regulations on confidentiality and consent for SUD information sharing, which are often stricter than other psychiatric conditions.[14-16]

Telemedicine (virtual care) has been shown to improve access to specialty providers, improve PCPs' confidence in specialty mental health care delivery, decrease stigma for SUD patients and staff, enhance the utilization of technology, and assist with centralized administrative efforts. The incorporation of digital technologies within telemedicine, such as mobile phones, has markedly increased in rural areas. A recent meta-analysis on telemedicine's effectiveness in treating alcohol use disorders found that video visit interventions effectively decrease multiple adult drinking problems in community and healthcare settings.[23] Compared to face-to-face interventions, another review found that video-based interventions performed similarly on a broad range of substance-related outcomes (e.g., abstinence, total use per day).[24])

Screening, brief intervention, and referral to treatment (SBIRT) is the most common strategy to address problematic substance use in rural primary care clinic settings and is currently considered the standard of care. It was developed to close the gap between primary care patients needing SUD care and available SUD treatment providers. Twelve years ago, Mayo participated in a QI effort to spread SBIRT into primary care sites under the guidance of the Institute for Clinical Systems Improvement (ICSI) within one Mayo Clinic Health System site. Unfortunately, that trial did not lead to adoption of SBIRT into regular practice. There was hesitancy on the part of primary care team members to refer patients to the brief intervention and confusion about roles regarding team members providing the intervention. Also noted was that younger patients who might be eligible were less likely to come into the clinic. These and other barriers have been presented in the literature.[11] We learned many lessons from this experience, but two were the most important. First, we had inadequate pre-implementation training and engagement for PCPs at the site, preventing buy-in and collaboration from clinicians. Second, inadequate SUD referral resources stunted the enthusiasm of PCPs to treat an issue they felt they could not adequately address.[12] Nationwide, SBIRT is also woefully underutilized. Many studies have cited challenges similar to our experience but have also noted limited clinician time, competing clinical priorities, and no integration with the care delivery model are significant barriers to SBIRT utilization in primary care.[12]

Study Design and Methods

This is a mixed-methods study. The first stage is an implementation feasibility stage focusing on implementing SBIRT into primary care on top of IBH and making sure it is accepted and supported as

an ongoing process. The second stage is a wait-list controlled intervention study testing the efficacy of the Senyo platform in decreasing substance use.

Methods Aim 1:

The implementation phase, described below, will start with a pilot site with the Integrated Behavior Health (IBH) care coordination model fully active in regular practice. This will test the planned implementation and recruitment strategy and allow for adjustments prior to working with the future three sites. Sites will be selected with the goal of two rural Mayo Clinic Health System locations and one non-rural Primary Care Practice at Mayo Clinic Rochester. Priority will be given to sites actively using the IBH care coordination program.

Stakeholder engagement implementation design and evaluation

Pre-implementation

Once a site is selected, engagement will begin by recruiting a primary care champion. Other primary care clinic key stakeholders (nurses, integrated behavioral health staff, medical staff, and administrative staff) will be included as appropriate. We will conduct focus group interviews to assess attitudes and perceived barriers towards SBIRT, medications for addiction treatment (MAT; buprenorphine, acamprosate, etc.), and whether the site would be agreeable to their patients receiving SUD treatment through virtual delivery (the Senyo Health platform) for integrated behavioral health interventions.

Program Training and Supervision

Upon agreement, the site will promote awareness of the program and the associated referral procedures. Research team members with experience treating SUD in primary care clinics will provide education to providers at the participating site. The care manager/licensed alcohol drug counselor (LADC) will support training on brief intervention, motivational interviewing, and the referral process.

Primary care champions in each participating site will encourage providers to attend training and initiate MAT for patients with confirmed moderate- and severe-SUD diagnoses. These champions will also liaise with the LADC .

Through the implementation approach described, we will gather feedback from the primary care team on SBIRT, the Senyo Health platform, and Senyo care manager/LADC to evaluate the processes. Primary care clinicians, nurses, key administrators, and clinic staff from each of the sites will be identified for interviews. Feedback on these components will be utilized to iterate and refine our strategy.

Processes of SBIRT:

1. Screening

Our a pre- screening process will use Tobacco, Alcohol, Prescription medication, and other Substances (TAPS) Tool, Vermont Treatment Needs (VTN) Questionnaire, or Health History Questionnaire to identify patients who are at high risk for substance use. With primary care approval, patients will be approached to discuss the study. Medical charts will be searched for clinically collected questionnaires (TAPS, VTN) responses related to substance use. A smart phrase, containing the recruitment flyer language, will be available for physicians to add to the after visit summary for patients they talked to about the study.

Patients interested in participation will be screened for eligibility using the Drug Abuse Screening Test (DAST)[38] or the Alcohol Use Disorders Identification Test (AUDIT-C)[20] instruments to determine the need for treatment referral using the Screening, brief intervention, and referral to treatment (SBIRT) pathway of care. Versions of the AUDIT-C are more routinely (but not always) implemented across primary care, but the DAST is not. The patient's medical record will be reviewed for AUDIT-C and DAST-10 scores. If no scores are

found in the past month, the patient will be sent screening instruments via Mayo Portal. The cadence of this screening will depend on feedback from clinic staff.

2. Brief Intervention

The brief intervention stage is where the SBIRT pathway often stalls out. Implementation of a brief intervention will be collaborative and iterative with the initial pilot site. FRAMES[36], which consists of feedback, responsibility, advice, menu for change, empathy, and enhancing self-efficacy, will be the primary component of this intervention. Primary Care/IBH staff members can provide this type of intervention, including physicians, nurses, social workers, etc. But if granted, an LADC can provide a brief intervention to the patient. The goal of this interaction will be to facilitate the referral process.

3. Referral

Patients will be informed about local treatment options for treatment as usual (TAU) and about the option to participate in this study. They will be allowed to choose which option (participation in research or community treatment) is best for them. Once the process runs smoothly at the site, we will expand to the next selected site.

4. Treatment

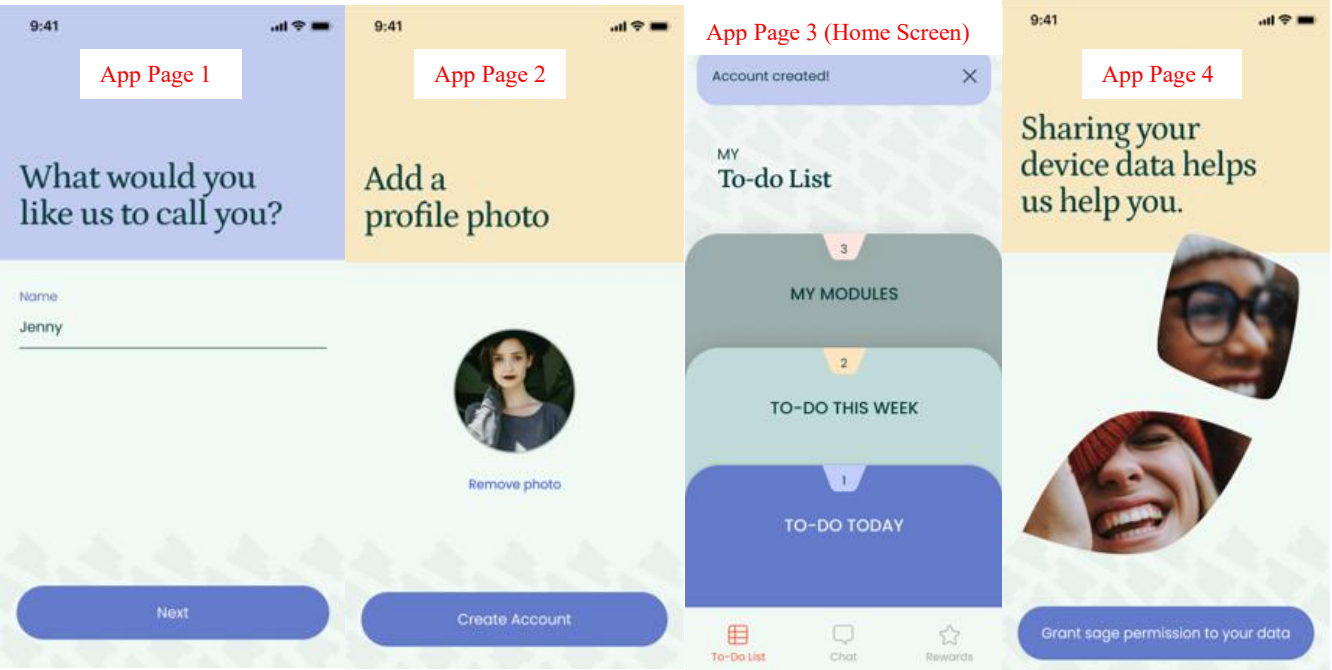
Providers will track patients based on the referral they choose: TAU versus participating in this study. As part of data gathering for quality improvement, we will reach out to patients that have chosen TAU to see how they are doing with engaging in TAU in the community. We will use the Treatment Attendance Monitoring Questionnaire (TAM) for this data collection. Patients who chose to participate in the study will go on to be randomized to waitlist or treatment through the Senyo health app (see study design section below).

Intervention

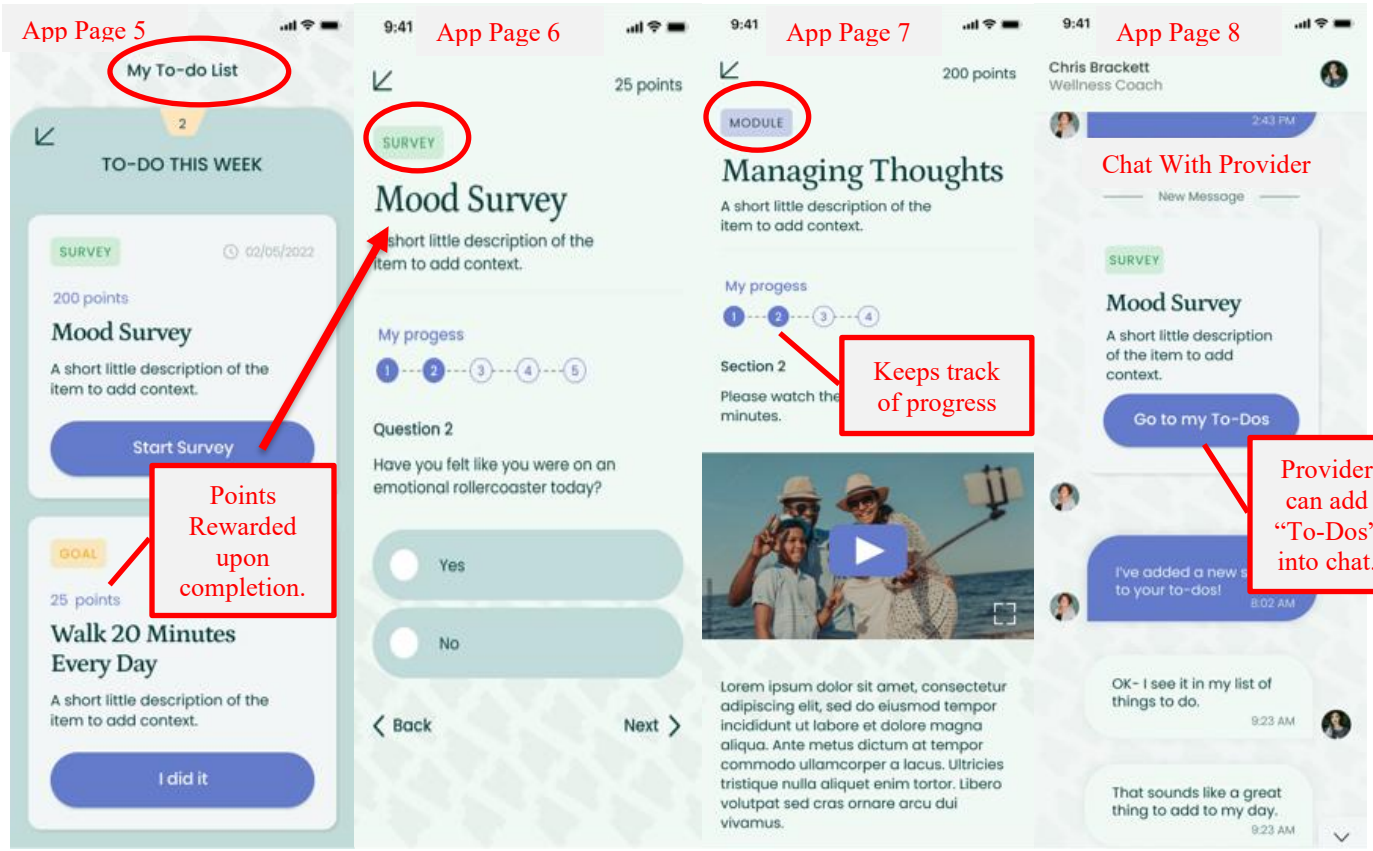
Methods Aim 2:
Senyo Health Information

Senyo Health delivers several well-studied app-based components, including asynchronous cognitive behavioral therapy (CBT) modules, contingency management, behavioral activation, and an interface to interact with the care manager/LADC. The platform also has a coach portal to interact with the patient and track utilization of the app features and SUD-specific outcome measures. A separate admin portal allows for convenient content creation and updating based on stakeholder feedback.

We designed our mobile phone application (MPA, also referred to as app) (see images below) to be simple and user-friendly. App pages 1 and 2 allow for some small customization (protected health information is not contained on the app but stored on the provider interface behind the Mayo Clinic firewall). App page 3 is the “home” screen.


App Page 1
What would you like us to call you?
Name
Jenny
Next
App Page 2
Add a profile photo
Remove photo
Create Account
App Page 3 (Home Screen)
Account created!
MY
To-do List
3
MY MODULES
2
TO-DO THIS WEEK
1
TO-DO TODAY
To-Do List
Chat
Rewards
App Page 4
Sharing your device data helps us help you.
Grant sage permission to your data

App page 5 shows what happens when "Due Today" is pressed on the "home screen." App page 6 provides an example of a survey displayed within the app, which was created via the admin portal. App page 7 displays a module created within the admin portal., and App page 8 shows how a care manager/LADC can directly communicate with a patient through the "chat" functionality.



Application features

Data protection

Data collected by the app system is securely transferred using industry-standard encryption to the "Backend Services" (i.e., Mayo Clinic servers behind HIPAA-compliant firewall). This cloud-based infrastructure serves and communicates with the patient-facing MPA. The Backend Services contain all data and analytics specific to the MPA clients (participants, researchers, and providers). All data the MPA uses follow various internationally recognized security standards such as the National Institute of Standards and Technology SP800-53 and HIPAA. All patient information is automatically encrypted when entered in the system, allowing for secure data transfer (from patient device to provider or researcher computer) and storage. PHI will be included within the Senyo admin Portal which is only accessed by study staff. PHI will include medical record number, date of birth, full name, phone number, and email address. This info and the mailing address will be used for remuneration with PEXCard for mailing their reloadable visa card.

Asynchronous modules: MPAs allow for the "asynchronous" delivery of therapeutic content that participants can use at any time. Current research supports delivering asynchronous content through "modules" or "activities." Psychotherapeutic modules within MPAs contain brief text-based content, videos, and related questions, that patients can experience independently whenever convenient. CBT is the most researched content-type for asynchronous modules.[16-18] "Activities" within apps are usually actions that the patient performs, such as filling out a survey, doing a mindfulness exercise, or being physically active.[22-23] 14 modules currently exist based on Mayo Clinic patient education pamphlets that have been digitized for use within the MPA. Topics include: "Addictive Thought Patterns," "Living with Emotions in Recovery," "Self-Esteem and Relationships," "My Recovery Building Blocks," "Self-Care in Recovery," "Cravings," and "Relapse Prevention." These modules will be adjusted, removed, or expanded based on stakeholder feedback. Participants will be provided with points (positive reward) for completing each module section and for completing a full module. Participants can work through the modules on their own and provide feedback on module content through the MPA.

Contingency management (CM): CM is a behavioral therapeutic intervention where monetary or prize-based rewards are "contingent" on objective evidence of drug abstinence and abstinence-promoting behaviors, such as mutual support meeting attendance and attending counseling sessions.[24] Therefore, CM does not deliver education or concepts for individuals to learn; instead, it is a strategy to encourage positive behaviors. CM has decades of research representing hundreds of controlled trials demonstrating its safety and efficacy in assisting in-person SUD treatment.[24] It is arguably one of the most effective therapeutic strategies available today but can be challenging to implement within conventional in-person treatment programs.[25] "ReSET" and "ReSET-O" are FDA-approved products that utilize CM to encourage the completion of in-app modules.[17-18] CM relies on this reward architecture to encourage engagement with SUD treatment. Virtually delivered CM through an MPA appears to improve engagement at a similar level to CM delivered in-person.[26] Senyo is unique because it incorporates IBH into a CM approach based on a token economy structure.[34] The MPA awards points for doing things in the app, like completing surveys, modules, or activities. The points per action are customizable through the research interface allowing for the adjustment of relative incentives associated with each task. Participants can use points to purchase rewards through a reloadable card (PEX Card; see App page 9). The purchased rewards will be tracked and documented in the research participant remuneration application (RPPA). For this study the point value is $.25 per point with 1 point being earned for each page of a module, minute of a video, and each question in a survey. Other activities may be available to earn additional points outside of the examples listed above.

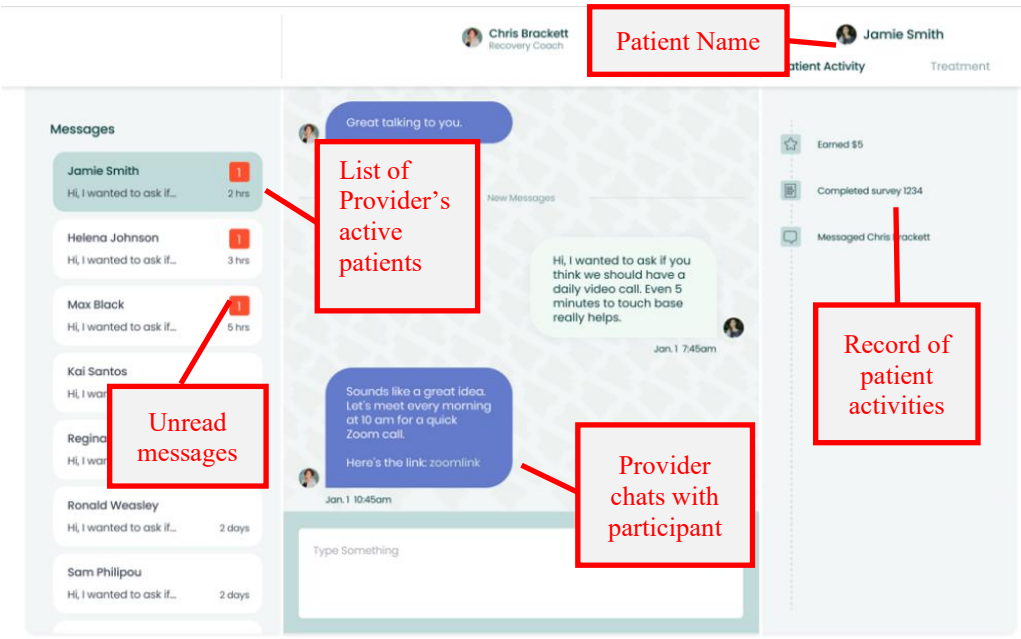
App Page 9

Goal/Activity:

Our MPA was built to work with Apple research kit and Google health kit wearable platforms to gather data from wearable device sensors. If a device is detected and the patient authorizes this, the wearable device sensor will track activity, heart rate, and oxygen saturation to determine how these physical parameters correlate with outcome measures. We will also use this data to encourage physical activity by connecting sensor data to CM rewards. The study will not provide a wearable device. This data will only be collected from those who already have and wear a personal device.

Interface with the care manager/LADC (Coach Portal below): Care managers/LADC use the coach portal to

Coach Portal



communicate through the MPA with their patients. Social rewards through MPAs, such as support from a clinician or peer via messaging or telephone, produce significantly greater user engagement than fully automated apps.[27] Typically, this support aims to maintain patient adherence with the app, monitor user progress through periodic symptom assessments, assist the patient in understanding therapeutic concepts or skills training, and triage patients who do not respond to app-based interventions.[28]

Subject Information

Target accrual: The study plans to have 60 subjects active in Senyo. The study will recruit patients from Mayo Clinic Health System primary care clinics and Mayo Clinic Rochester's non-rural Primary Care Clinic or Integrated Behavior Health (IBH). Once we have solidified our implementation strategy, specific sites will be added upon selection and agreement.

Subject population(s)
Inclusion Criteria:

1. Age>=18 years;
2. Ability to read, write, and understand English;
3. Minimum DAST (1+) or audit-C score (3+)
4. Access and willingness to use a mobile device for asynchronous (text) and synchronous (video) engagement with care;
5. Access to or willingness to obtain a Primary care provider at a participating Mayo Clinic site;
6. Eligibility determined by ASAM Assessment

Exclusion Criteria:

1. Diagnosed personality pathology as the primary presenting concern based on clinical judgment, severe cognitive impairment (e.g., intellectual disability or dementia), or psychosis;

2. Inability to actively participate in and learn from psychotherapeutic interaction based on clinical evaluation and clinical judgment;
3. Needing a higher level of mental health care as demonstrated by ASAM[32] assessment;
4. Decline to answer suicidality questions;
5. Already admitted into or about to initiate treatment in another addiction treatment program.
6. Currently attending High School.

Study Procedures

Study Design

Once primary care patients have selected the study treatment path, they will be asked to complete the following activities: sign an informed consent, complete an interview to collect medical and psychiatric history for comorbidities, and answer a questionnaire about mood and anxiety The active intervention (Senyo) will have patients complete visits through a clinical treatment phase and a follow-up phase (24 weeks: 12 active, 12 follow-up).

Study activities (detailed in table below):

Baseline Visit involves:

- Sign consent
- Interview with study staff
    - American Society of Addiction Medicine (ASAM)[32] diagnostic interview to determine level of outpatient care, (eligibility criteria)
    - Timeline Follow Back (TLFB) - gather history of substance use such as how much you used each day.
- Complete questionnaires
    - Brief Substance Craving Scale (BSCS)
    - Patient Health Questionnaire-9 (PHQ-9)
    - Generalized Anxiety Disorder-7 scale (GAD-7)
    - Brief Version of the Pittsburgh Sleep Quality Index (B-PSQI)
    - Brief Assessment of Recovery Capital (BARC-10)
    - Treatment Attendance Monitoring Questionnaire (TAM)
    - Urine test - check for certain drugs, including alcohol and illegal drugs, (for example, cocaine).

Active intervention phase involves:

- Set-up participants in Senyo Health app (send out invite email)
- A variety of quotes and questions will be delivered daily via the Senyo interface to encourage daily engagement.
- Weekly check-in visits by phone or virtual zoom call to get health and substance use updates, provide encouragement and motivational care management, and offer any counseling to assist with reduction of use or to quit completely.
- Timeline Follow Back (TLFB) - gather history of substance use such as how much you used each day
- Monthly urine test – check for certain drugs, including alcohol or illegal drugs such as cocaine.
- Complete questionnaires
    - Brief Substance Craving Scale (BSCS) - weekly
    - Generalized Anxiety Disorder-7 (GAD-7) - weekly
    - Patient Health Questionnaire-9 (PHQ-9) - weekly

- Brief Version of the Pittsburgh Sleep Quality Index (B-PSQI) - monthly
- Brief Assessment of Recovery Capital (BARC-10) – monthly
- Treatment Attendance Monitoring Questionnaire (TAM) - monthly

- At the final weekly visit, you will be asked to complete questionnaires about how you liked using the app. This will help us make future improvements to fit patient needs.
  - System Usability Scale (SUS)
  - Acceptability of Intervention Measure (AIM)
  - Intervention Appropriateness Measure (IAM)
  - Feasibility of Intervention Measure (FIM)

A semi-structured interview, collecting feedback of the app and LADC process, will be offered to patients once the active phase of the study is completed. This interview is voluntary and will be recorded with oral permission captured.

Follow-up Phase involves:

- Monthly check-in phone or virtual zoom calls to get health and substance use updates
- Timeline Follow Back (TLFB) - gather history of substance use such as how much you used each day
- Monthly urine test – check for certain drugs, including alcohol or illegal drugs such as cocaine.
- Complete questionnaires
  - Brief Substance Craving Scale (BSCS)
  - Generalized Anxiety Disorder-7 (GAD-7)
  - Patient Health Questionnaire-9 (PHQ-9)
  - Brief Version of the Pittsburgh Sleep Quality Index (B-PSQI)
  - Brief Assessment of Recovery Capital (BARC-10)
  - Treatment Attendance Monitoring Questionnaire (TAM)

1-year follow-up visit includes (One year from week 12 intervention)

- Check-in by phone or virtual Zoom call to get health and substance use updates
- Timeline Follow Back (TLFB)
- Urine test - check for certain drugs, including alcohol or illegal drugs such as cocaine
- Complete questionnaires
  - Brief Substance Craving Scale (BSCS)
  - Generalized Anxiety Disorder-7 (GAD-7)
  - Patient Health Questionnaire-9 (PHQ-9)
  - Brief Version of the Pittsburgh Sleep Quality Index (B-PSQI)
  - Brief Assessment of Recovery Capital (BARC-10)
  - Treatment Attendance Monitoring Questionnaire (TAM)

NOTE: The results of the urine drug test will become part of your medical record but not reported to anyone.

Participant events		Active Treatment phase (week)												Follow-up phase (week)											**1yr**
Assessment	Baseline	1	2	3	4	5	6	7	8	9	10	11	**12**	1	2	3	4	5	6	7	8	9	10	11	12	
Consent	X																									
Check-in		X	X	X	X	X	X	X	X	X	X	X	X				X				X				X	X
TLFB	X	X	X	X	X	X	X	X	X	X	X	X	X				X				X				X	X
BSCS	X	X	X	X	X	X	X	X	X	X	X	X	X				X				X				X	X
B-PSQI	X				X				X				X				X				X				X	X
PHQ-9	X	X	X	X	X	X	X	X	X	X	X	X	X				X				X				X	X
GAD7	X	X	X	X	X	X	X	X	X	X	X	X	X				X				X				X	X
TAM	X				X				X				X				X				X				X	X
Urine test	X				X				X				X				X				X				X	X
BARC	X				X				X				X				X				X				X	X
SUS													X													
AIM													X													
IAM													X													
FIM													X													

Safety monitoring

During the study, the care coordinator/LADC will focus on assessing symptoms, addressing clinical concerns, and providing brief encouragement to continue predetermined goals. The care managers/LADC will meet with the consulting psychiatrist and review the history obtained from the patient during their initial evaluation. The care coordinator/LADC will write a formal weekly update note on each patient, and monthly clinical tracking scores will be reviewed and reported to the consulting psychiatrist. Psychiatric recommendations for the management of addiction concerns and related mental health issues (i.e. worsening mood or suicidality) will be reported back to the primary care provider, who will ultimately remain responsible for clinical decision-making and the treatment plan that could involve starting medications as a part of their clinical care (though this plan will be informed by the specialty psychiatric expertise and frequent clinical updates provided to the care coordinator/LADC by the patient). This patient review and consultation system will be managed through the provider portal, which will also serve as the patient population registry for quantitative tracking of clinical concerns with specific and quantitative endpoint treatment goals.

Once a patient is enrolled in the study, the care coordinator/LADC/study staff will utilize the ASAM criteria to determine ongoing appropriateness for the current level of care[32]. To stay in the study, participants must remain eligible for outpatient SUD care. If the participant's ASAM criteria worsens enough that psychiatric recommendation is a higher level of care they will be referred clinically to residential SUD treatment. The participants' active treatment phase will be stopped, and they will be moved into the follow-up phase. Adverse events will be reported to the psychiatrist for evaluation and reviewed for reporting requirements to the IRB. PHI such as medical record number, date of birth, full name, phone number and email will be included within the Senyo Admin Portal.

Remuneration:

The treatment phase of this project uses the contingency management method. Participants earn points for completing treatment tools within the Senyo app. They turn in those points for rewards of specified dollar amounts. These dollar amounts are loaded on a reloadable cash card (PEX Card). The app will notify study staff of the dollar amount, which will be loaded onto the card and documented in the RPPA system. The amount of

points a participant can earn is approximately 1500 (converts to $399), but this amount will vary depending on participation and points received. Follow-up participants will receive $25 for each visit where they complete interviews and questionnaires. Total remuneration will not exceed $599 per patient.

Data Analysis

Power Statement:

Data Analysis Plan:
The intervention will have four core components that will be improved based on feedback. First, each patient will receive digitally native IBH for SUD treatment and be tracked by a care coordinator/LADC with weekly virtual check-ins (video or text-based communication) with monthly reviews of clinical cases by an overseeing psychiatrist. Second, the patient will be offered, initiated, or continued on medications to manage psychiatric and addiction symptoms. Third, the patients will use a digital clinical platform to complete a set of automated but interactive CBT and behavioral activation-based psychotherapeutic modules. Fourth, patients will use a digital contingency management platform through an app on their phones. We will use mixed methods (interviews and questionnaires) to evaluate implementation outcomes.

Clinical Outcomes: We anticipate that patient involvement will positively impact substance use as measured by a statistically significant reduction in one month consumption in the active group compared to the waitlist as measured by TLFB. Secondary outcomes will explore abstinence rates, treatment retention, treatment effects on craving, recovery capital, psychiatric well-being (PHQ9, GAD7, ESS) and use of clinical services throughout the intervention and 12-week follow-up period.

Data Analysis: Clinical treatment outcomes will be analyzed by comparing participant data at baseline, weekly during the intervention, and 12 weeks post-treatment (after completion of care coordinator/LADC visits). We will utilize information from this pilot to inform sample size calculations for a larger controlled efficacy trial. Several exploratory endpoints (e.g., anxiety and depression) will be evaluated to contextualize the primary endpoint effect.

Indicate which of the following methods will be utilized for analysis of the data

☒ Descriptive statistics will be utilized to broadly analyze the sample. No power calculation is needed.
Describe: Outcomes will be summarized descriptively and graphed at each time point. Several exploratory endpoints (e.g., anxiety, depression) will be evaluated to contextualize the primary endpoint effect.

☒ Statistical modeling including multivariable modeling will be utilized and power calculations will be utilized when appropriate.
Describe: Our MPA meta-analysis showed that contingency management app content had a large Hedges' g effect size.[37] The power for reducing substance use-related outcomes relative to the control arm with Hedges g effect size(1.29; 95% CI, 1.088-1.482) and 30 in each arm is approximately 0.8.

☐ Formal modeling with unique data sets within the entire data group will be compared.
Describe:

BIBLIOGRAPHY & REFERENCES CITED

1. SAMHSA. National Survey of Drug Use and Health 2019.
2. Oesterle TS, Kolla B, Risma CJ, Breitinger SA, Rakocevic DB, Loukianova LL, Hall-Flavin DK, Gentry MT, Rummans TA, Chauhan M, Gold MS. Substance Use Disorders and Telehealth in the COVID-19 Pandemic Era: A New Outlook. Mayo Clinic Proceedings. 2020;95(12):2709-18. doi: 10.1016/j.mayocp.2020.10.011.
3. Blanco C, Wall MM, Olfson M. Psychological Aspects of the COVID-19 Pandemic. J Gen Intern Med. 2020;35(9):2757-9. Epub 2020/06/17. doi: 10.1007/s11606-020-05955-3. PubMed PMID: 32542499; PMCID: PMC7295318.
4. Browne T, Priester MA, Clone S, Iachini A, DeHart D, Hock R. Barriers and Facilitators to Substance Use Treatment in the Rural South: A Qualitative Study. J Rural Health. 2016;32(1):92-101. Epub 2015/07/18. doi: 10.1111/jrh.12129. PubMed PMID: 26184098.
5. Ahrnsbrak R BJ, Heeden SL, Lipari RN, Park-Lee E. Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health (Internet). Rockville MD2017.
6. Huskamp HA, Busch AB, Souza J, Uscher-Pines L, Rose S, Wilcock A, Landon BE, Mehrotra A. How Is Telemedicine Being Used In Opioid And Other Substance Use Disorder Treatment? Health Aff (Millwood). 2018;37(12):1940-7. Epub 2019/01/12. doi: 10.1377/hlthaff.2018.05134. PubMed PMID: 30633671; PMCID: PMC6671682.
7. Andrilla CHA, Moore TE, Patterson DG. Overcoming barriers to prescribing buprenorphine for the treatment of opioid use disorder: recommendations from rural physicians. The Journal of Rural Health. 2019;35(1):113-21.
8. Lanham HJ, Papac J, Olmos DI, Heydemann EL, Simonetti N, Schmidt S, Potter JS. Survey of Barriers and Facilitators to Prescribing Buprenorphine and Clinician Perceptions on the Drug Addiction Treatment Act of 2000 Waiver. JAMA Network Open. 2022;5(5):e2212419-e. doi: 10.1001/jamanetworkopen.2022.12419.
9. Peters DJ. Community Susceptibility and Resiliency to COVID-19 Across the Rural-Urban Continuum in the United States. J Rural Health. 2020;36(3):446-56. Epub 2020/06/17. doi: 10.1111/jrh.12477. PubMed PMID: 32543751; PMCID: PMC7323251.
10. Kamath CC, Kelpin SS, Patten CA, Rummans TA, Kremers HM, Oesterle TS, Williams MD, Breitinger SA. Shaping the Screening, Behavioral Intervention, and Referral to Treatment (SBIRT) Model for Treatment of Alcohol Use Disorder in the COVID-19 Era. Mayo Clin Proc. 2022;97(10):1774-9. Epub 2022/10/07. doi: 10.1016/j.mayocp.2022.07.006. PubMed PMID: 36202491; PMCID: PMC9293785.
11. Rahm AK, Boggs JM, Martin C, Price DW, Beck A, Backer TE, Dearing JW. Facilitators and Barriers to Implementing Screening, Brief Intervention, and Referral to Treatment (SBIRT) in Primary Care in Integrated Health Care Settings. Subst Abus. 2015;36(3):281-8. Epub 2014/08/16. doi: 10.1080/08897077.2014.951140. PubMed PMID: 25127073.
12. Williams M, Angstman K, Johnson I, Katzelnick D. Implementation of a care management model for depression at two primary care clinics. The Journal of ambulatory care management. 2011;34(2):163-73.
13. DeJesus R. Utilization of antidepressant medications among elderly patients with depression: Comparison between usual care and collaborative care using care managers. American Journal of Geriatric Psychiatry. 2013;21(3):S130-S. doi: DOI 10.1016/j.jagp.2012.12.173. PubMed PMID: WOS:000330358400143.
14. LaBelle CT, Han SC, Bergeron A, Samet JH. Office-Based Opioid Treatment with Buprenorphine (OBOT-B): Statewide Implementation of the Massachusetts Collaborative Care Model in Community Health Centers. J Subst Abuse Treat. 2016;60:6-13. Epub 2015/08/04. doi: 10.1016/j.jsat.2015.06.010. PubMed PMID: 26233698; PMCID: PMC4682362.
15. Alford DP, LaBelle CT, Kretsch N, Bergeron A, Winter M, Botticelli M, Samet JH. Collaborative care of opioid-addicted patients in primary care using buprenorphine: five-year experience. Arch Intern Med.

2011;171(5):425-31. Epub 2011/03/16. doi: 10.1001/archinternmed.2010.541. PubMed PMID: 21403039; PMCID: PMC3059544.
16. Kiluk BD, Ray LA, Walthers J, Bernstein M, Tonigan JS, Magill M. Technology-Delivered Cognitive-Behavioral Interventions for Alcohol Use: A Meta-Analysis. Alcohol Clin Exp Res. 2019;43(11):2285-95. Epub 2019/09/30. doi: 10.1111/acer.14189. PubMed PMID: 31566787.
17. Campbell AN, Nunes EV, Matthews AG, Stitzer M, Miele GM, Polsky D, Turrigiano E, Walters S, McClure EA, Kyle TL, Wahle A, Van Veldhuisen P, Goldman B, Babcock D, Stabile PQ, Winhusen T, Ghitza UE. Internet-delivered treatment for substance abuse: a multisite randomized controlled trial. Am J Psychiatry. 2014;171(6):683-90. Epub 2014/04/05. doi: 10.1176/appi.ajp.2014.13081055. PubMed PMID: 24700332; PMCID: PMC4079279.
18. Christensen DR, Landes RD, Jackson L, Marsch LA, Mancino MJ, Chopra MP, Bickel WK. Adding an Internet-delivered treatment to an efficacious treatment package for opioid dependence. J Consult Clin Psychol. 2014;82(6):964-72. Epub 2014/08/05. doi: 10.1037/a0037496. PubMed PMID: 25090043; PMCID: PMC4244262.
19. Bangor A, Kortum P, Miller J. Determining what individual SUS scores mean: Adding an adjective rating scale. *Journal of usability studies*. 2009;4(3):114-12326.
20. Bush K, Kivlahan DR, McDonell MB, et al (1998). The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Arch Intern Med. 158:1789-95.
21. Somoza, E., Dyrenforth, S., Goldsmith, J., Mezinskis, J., & Cohen, M., 1995. In search of a universal drug craving scale. Paper presented at the Annual Meeting of the American Psychiatric Association, Miami Florida.
22. Paquette CE, Rubalcava DT, Chen Y, Anand D, Daughters SB. A Mobile App to Enhance Behavioral Activation Treatment for Substance Use Disorder: App Design, Use, and Integration Into Treatment in the Context of a Randomized Controlled Trial. JMIR Form Res. 2021;5(11):e25749. doi: 10.2196/25749.
23. Tison GH, Hsu K, Hsieh JT, Ballinger BM, Pletcher MJ, Marcus GM, Olgin JE. Abstract 21029: Achieving High Retention in Mobile Health Research Using Design Principles Adopted From Widely Popular Consumer Mobile Apps. Circulation. 2017;136(suppl_1):A21029-A. doi: doi:10.1161/circ.136.suppl_1.21029.
24. Higgins ST, Silverman K, Heil SH. Contingency management in substance abuse treatment: Guilford Press; 2007.
25. Dutra L, Stathopoulou G, Basden SL, Leyro TM, Powers MB, Otto MW. A meta-analytic review of psychosocial interventions for substance use disorders. Am J Psychiatry. 2008;165(2):179-87. Epub 2008/01/17. doi: 10.1176/appi.ajp.2007.06111851. PubMed PMID: 18198270.
26. Pratap A, Neto EC, Snyder P, Stepnowsky C, Elhadad N, Grant D, Mohebbi MH, Mooney S, Suver C, Wilbanks J, Mangravite L, Heagerty PJ, Areán P, Omberg L. Indicators of retention in remote digital health studies: a cross-study evaluation of 100,000 participants. npj Digital Medicine. 2020;3(1):21. doi: 10.1038/s41746-020-0224-8.
27. Hackenberg TD. Token reinforcement: a review and analysis. J Exp Anal Behav. 2009;91(2):257-86. doi: 10.1901/jeab.2009.91-257. PubMed PMID: 19794838.
28. Mohr DC, Azocar F, Bertagnolli A, Choudhury T, Chrisp P, Frank R, Harbin H, Histon T, Kaysen D, Nebeker C, Richards D, Schueller SM, Titov N, Torous J, Areán PA. Banbury Forum Consensus Statement on the Path Forward for Digital Mental Health Treatment. Psychiatr Serv. 2021;72(6):677-83. Epub 2021/01/21. doi: 10.1176/appi.ps.202000561. PubMed PMID: 33467872; PMCID: PMC8822332.
29. Skinner HA. The drug abuse screening test. Addict Behav. 1982;7(4):363-71. Epub 1982/01/01. doi: 10.1016/0306-4603(82)90005-3. PubMed PMID: 7183189.

30. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606-13. Epub 2001/09/15. doi: 10.1046/j.1525-1497.2001.016009606.x. PubMed PMID: 11556941; PMCID: PMC1495268.
31. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092-7. Epub 2006/05/24. doi: 10.1001/archinte.166.10.1092. PubMed PMID: 16717171.
32. Mee-Lee D, Shulman GD, Fishman MJ, Gastfriend DR, Miller MM. The ASAM Criteria: Treatment Criteria for Addictive, Substance-Related, and Co-Occurring Conditions. 3rd ed. ed. Carson City, NV: The American Society of Addiction Medicine; 2013.
33. Sobell, L. C., & Sobell, M. B. (1992). Timeline follow-back: A technique for assessing self-reported alcohol consumption. In R. Z. Litten & J. P. Allen (Eds.), Measuring alcohol consumption: Psychosocial and biochemical methods (pp. 41–72). Humana Press/Springer Nature. https://doi.org/10.1007/978-1-4612-0357-5_3
34. Vilsaint CL, Kelly JF, Bergman BG, Groshkova T, Best D, White W. Development and validation of a Brief Assessment of Recovery Capital (BARC-10) for alcohol and drug use disorder. Drug Alcohol Depend. 2017 Aug 1;177:71-76. doi: 10.1016/j.drugalcdep.2017.03.022. Epub 2017 May 19. PMID: 28578224.
35. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14(6):540-5. Epub 1991/12/01. doi: 10.1093/sleep/14.6.540. PubMed PMID: 1798888.
36. Mattoo SK, Prasad S, Ghosh A. Brief intervention in substance use disorders. Indian J Psychiatry. 2018 Feb;60(Suppl 4):S466-S472. doi: 10.4103/0019-5545.224352. PMID: 29540915; PMCID: PMC5844156.
37. Oesterle TS, Hall-Flavin DK, Bormann NL, Loukianova LL, Fipps DC, Breitinger SA, Gilliam WP, Wu T, da Costa SC, Arndt S, Karpyak VM. Therapeutic Content of Mobile Phone Applications for Substance Use Disorders: An Umbrella Review. Mayo Clin Proc Digit Health. 2024 Jun;2(2):192-206. doi: 10.1016/j.mcpdig.2024.03.004. Epub 2024 Apr 11. PMID: 38983444; PMCID: PMC11232654.
38. Cloud W, Granfield R (2008) Conceptualizing recovery capital: expansion of a theoretical construct. Subst Use Misuse 43:1971-1986. DOI: 10.1080/10826080802289762