Woebot for Substance Use Disorders During COVID-19

NCT04460027

April 30, 2022

Title : Woebot for Substance Use Disorders during COVID-19 (SU sIRB)
Approval Period: 04/30/2022 - 04/30/2023

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Continuing Review Form

1. Participant Enrollment

a. Number of participants entered (or number of specimens examined or charts reviewed) since the beginning of study. If this is a combined VA-Stanford study, in addition indicate how many of the participants (or number of VA specimens examined or VA charts reviewed) enrolled with a VA consent. If this is a multi-site study, in addition to the number of participants enrolled locally, include the number of participants enrolled study-wide.

N=180
Study is closed to enrollment and in data analysis in 2021.

b. Number of: males, females, others or individuals whose sex/gender are unknown or not reported.

Male: 63
Female: 117

c. Minority status of participants entered since beginning of study.

American Indian/Alaska Native: 4
Asian: 11
African American: 22
Multiracial: 3
White: 140

d. Number of children (less then 18 years) entered since beginning of study.

0

e. Number of other potentially vulnerable subjects (if applicable) entered since the beginning of study, including prisoners, pregnant women, economically and educationally disadvantaged, decisionally impaired and homeless people.

N/A

2. Study Problems/Complications

a. Number of withdrawals of participants from the research (both participant and investigator initiated) since the beginning of the research study. Provide reasons for the withdrawals.

None

b. Number of participants lost to follow-up since the beginning of the study.

28

c. State if all adverse events have occurred at the expected frequency and level of severity as per study documents or provide a narrative summary of the adverse events since the last continuing review indicating whether the adverse events were expected and/or related to the study.

Below is the information reported in the previous continuing review:

One SAE was reported. The event is unrelated, expected, and resolved.

Participant 014 reported in final follow up survey that they went into the hospital on their own to detox

from alcohol. Participant reported experiencing D.T.'s, severe shaking, visual or auditory hallucinations after heavy drinking on 10/22/20. They put down the reason or cause of the event as attempting to detox on their own before deciding to go to a facility for assistance. 10/29/20: After further inquiry regarding what led to the hospitalization, the participant mentioned they were drinking entirely too much and was on a bad bender. They are on day 8 of sobriety.

d. Have there been any unanticipated problems involving risks to participants or others (UPs) since the beginning of the study? A UP must be unexpected (including in severity or frequency), related, AND harmful. Confirm that all UPs have previously been reported to the IRB (guidance GUI-P13).

N/A

e. Provide a narrative summary of all external (e.g. FDA, OHRP, sponsor) audit reports, monitoring visits, inspections, and multi-center trial reports received in the past year. Include corrective actions taken as a result of any audits, inspections, or monitoring visits.

N/A

f. Complaints about the research in the past year.

N/A

g. Have there been any instances of noncompliance or deviations since the beginning of the study that have not already been addressed in 2e? Provide a summary and indicate if it has been previously reported to the IRB. Provide a corrective action plan that includes how you will ensure the noncompliance does not recur.

No new instances.

Below is the information reported in the previous continuing review:

N=160 was proposed for study enrollment. Final enrollment was N=180. Qualtrics panel recruitment was the main recruitment method and had resulted in n=160; n=20 were from other recruitment sources described in the protocol. For the next study, we'll try Qualtrics recruitment before other sources, as the Qualtrics panel requires a prepaid agreement and results in speedy recruitment.

Below are summaries of responses removed from the study. There's no known effective way of preventing these types of responses. Future studies will involve quality check of responses.

Four surveys were screened as eligible. These surveys completed the baseline assessment and were randomized (1 to treatment, 3 to waitlist). Based on the four surveys having identical IP address, common birth year, and overlap in name/email addresses these surveys were presumed to be a single individual enrolling at four different time points.
Four survey respondents (screened in and randomized: 1 to treatment, 3 to waitlist) did not provide a valid email or phone number for follow ups (eligibility criteria).
One survey respondent (screened in and randomized) is confirmed to be a duplicate of another survey response. The respondent was randomized to the treatment group at both survey completions.

3.Study Assessment

a. Provide a narrative summary of any interim findings from your data in the past year.

Vogel EA, Chieng A, Robinson A, Pajarito S, Prochaska JJ. (2021). Associations between substance use problems and stress during COVID-19. Journal of Studies on Alcohol and Drugs, 82, 776-781.

Experiencing worsened mental health symptoms during COVID-19 was associated with more substance use

problems and symptoms of depression and anxiety. Pandemic disruptions may exacerbate preexisting substance use problems.

Prochaska JJ, Vogel EA, Chieng A, Baiocchi M, Maglalang DD, Pajarito S, Weingardt KR, Darcy A, Robinson A. (2021). A randomized controlled trial of a therapeutic relational agent for reducing substance misuse during the COVID-19 pandemic. Drug & Alcohol Dependence, 227, 108986

W-SUDs was associated with significant reductions in substance use occasions. Reduction in substance use occasions was associated with better outcomes, including improved mental health. W-SUDs satisfaction was high.

b. Provide a narrative summary of any recent relevant literature.

From Phase 1 (Prochaska JJ, Vogel EA, Chieng A, Kendra M, Baiocchi M, Pajarito S, Robinson A. (2021). A therapeutic relational agent for reducing problematic substance use (Woebot): Development and usability study. Journal Medical Internet Research, 23(3): e24850): W-SUDs was feasible to deliver, engaging, and acceptable and was associated with significant improvements in substance use, confidence, cravings, depression, and anxiety. Study attrition was high. Future research will evaluate W-SUDs in a randomized controlled trial with a more diverse sample and with the use of greater study retention strategies.

c. Attach Data Safety Monitoring Reports in section 16 received in the past year which have not previously been submitted to the IRB.

None. June 2021 meeting minutes attached. We are planning another DSMB meeting in April 2022.

d. Provide a narrative summary of benefits experienced by participants in the past year.

None

e. Provide an assessment of whether the relationship of risks to potential benefits has changed.

None

4. Description of remainder of project:

a. N **Is the study open to enrollment?**

b. Y **Is the study permanently closed to enrollment of new participants?**

c. Y **Have all participants completed all research-related interventions?**

d. N **Are you still engaged in research-related intervention(s)? If yes, please describe.**

e. N **Do you wish to renew this study only for long term follow-up?**

f. Y **Are you only doing data analysis?**

5. Potential Conflict of Interest

N **Is there a change in the conflicting interest status of this protocol?**

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6. Protocol Changes

Please note that if these changes involve changes to Radiation Safety or Biosafety, the IRB will hold its approval until Radiation Safety or Biosafety forwards its approval to the IRB. Use track changes IF revising consent, assent or HIPAA.

- **Summarize all of the proposed changes to the protocol application including consent form changes.**

  Erin Vogel and Dale Maglalang have been removed from Personnel.

  Protocol Information section 8m has been updated to extend the time frame of data analyses and dissemination.

- **Indicate Level of Risk**

  No Change

- **Describe any other changes.**

  None

Protocol Director

[redacted]

Admin Contact

[redacted]

Investigator

Name		Degree (Program/year if student)		Position, e.g. Assistant Professor, Resident, etc.
Department		Phone		E-mail
CITI Training current				

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Other Contact

Name		Degree (Program/year if student)		Position, e.g. Assistant Professor, Resident, etc.
Department		**Phone**		**E-mail**
CITI Training current				

Academic Sponsor

Name		Degree (Program/year if student)		Position, e.g. Assistant Professor, Resident, etc.
Department		**Phone**		**E-mail**
CITI Training current				

Other Personnel

[redacted]		[redacted]		[redacted]
Department		**Phone**		[redacted]
[redacted]				

Participant Population(s) Checklist	Yes/No
• Children (under 18)	N
• Pregnant Women and Fetuses	N
• Neonates (0 - 28 days)	N
• Abortuses	N
• Impaired Decision Making Capacity	N
• Cancer Subjects	N
• Laboratory Personnel	N
• Healthy Volunteers	N
• Students	N
• Employees	N
• Prisoners	N
• Other (i.e., any population that is not specified above)	Y
• International Participants	N
Please enter the countries separated by comma	

Study Location(s) Checklist	Yes/No
• Stanford University	Y
• Clinical & Translational Research Unit (CTRU)	

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- Stanford Hospital and Clinics
- Lucile Packard Children's Hospital (LPCH)
- VAPAHCS (Specify PI at VA)
- Other (Click ADD to specify details)

General Checklist

Multi-site	**Yes/No**
• Is this a multi-site study? A multi-site study is generally a study that involves one or more medical or research institutions in which one site takes a lead role.(e.g., multi-site clinical trial)	N

Collaborating Institution(s)	**Yes/No**
• Are there any collaborating institution(s)? A collaborating institution is generally an institution that collaborates equally on a research endeavor with one or more institutions.	Y

Institution Name	Contact Name	Contact Phone	Contact Email	Permission?	Engaged?
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Cancer Institute	**Yes/No**
• Cancer-Related Studies (studies with cancer endpoints), Cancer Subjects (e.g., clinical trials, behavior/prevention) or Cancer Specimens (e.g., blood, tissue, cells, body fluids with a scientific hypothesis stated in the protocol).	N

Clinical Trials	**Yes/No**
• Investigational drugs, biologics, reagents, or chemicals?	N
• Commercially available drugs, reagents, or other chemicals administered to subjects (even if they are not being studied)?	N
• Investigational Device / Commercial Device used off-label?	Y
• IDE Exempt Device (Commercial Device used according to label, Investigational In Vitro Device or Assay, or Consumer Preference/Modifications/Combinations of Approved Devices)	N
• Will this study be registered on# clinicaltrials.gov? (See Stanford decision tree)	Y
• Who will register for ClinicalTrials.gov? NCT#	N

Tissues and Specimens	**Yes/No**

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• Human blood, cells, tissues, or body fluids (tissues)?	N
• Tissues to be stored for future research projects?	N
• Tissues to be sent out of this institution as part of a research agreement? For guidelines, please see https://sites.stanford.edu/ico/mtas	N

Biosafety (APB)	**Yes/No**
• Are you submitting a Human Gene Transfer investigation using a biological agent or recombinant DNA vector? If yes, please complete the Gene Transfer Protocol Application Supplemental Questions and upload in Attachments section.	N
• Are you submitting a Human study using biohazardous/infectious agents? If yes, refer to the Administrative Panel on BioSafety website prior to performing studies.	N
• Are you submitting a Human study using samples from subjects that are known or likely to contain biohazardous/infectious agents? If yes, refer to the Administrative Panel on BioSafety website prior to performing studies.	N

Human Embryos or Stem Cells	**Yes/No**
• Human Embryos or Gametes?	N
• Human Stem Cells (including hESC, iPSC, cancer stem cells, progenitor cells)	N

Veterans Affairs (VA)	**Yes/No**
• The research recruits participants at the Veterans Affairs Palo Alto Health Care System(VAPAHCS).	N
• The research involves the use of VAPAHCS non-public information to identify or contact human research participants or prospective subjects or to use such data for research purposes.	N
• The research is sponsored (i.e., funded) by VAPAHCS.	N
• The research is conducted by or under the direction of any employee or agent of VAPAHCS (full-time, part-time, intermittent, consultant, without compensation (WOC), on-station fee-basis, on-station contract, or on-station sharing agreement basis) in connection with her/his VAPAHCS responsibilities.	N
• The research is conducted using any property or facility of VAPAHCS.	N

Equipment	**Yes/No**
• Use of Patient related equipment? If Yes, equipment must meet the standards established by Hospital Instrumentation and Electrical Safety Committee (650-725-5000)	N
• Medical equipment used for human patients/subjects also used on animals?	N
• Radioisotopes/radiation-producing machines, even if standard of care? http://www.stanford.edu/dept/EHS/prod/researchlab/radlaser/Human_use_guide.pdf More Info	N

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Payment	**Yes/No**
• Subjects will be paid/reimbursed for participation? See payment considerations.	Y

Funding	**Yes/No**
• Training Grant?	N
• Program Project Grant?	N
• Federally Sponsored Project?	Y
• https://doresearch.stanford.edu/policies/research-policy-handbook/definitions-and-types-agreements/specialized-categories-sponsored-p Industry Sponsored Clinical Trial?	N

Funding

Funding - Grants/Contracts

Funding Administered By : STANFORD
SPO # (if available) : 138716
Grant # (if available) :
Funded By (include pending) : NIH Prime Woebot

Principal Investigator : Judith Prochaska

Grant/Contract Title if different from Protocol Title :
RCT of Woebot for Treating Substance Use Disorders

Y For Federal projects, are contents of this protocol consistent with the Federal proposal?
N Is this a Multiple Project Protocol (MPP)?
N Is this protocol under a MPP?

Funding - Fellowships

Gift Funding

Dept. Funding

Other Funding

Resources :

a) Qualified staff.

Please state and justify the number and qualifications of your study staff.

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The staff are well versed in the ethics and rigorous methods of conducting research trials with human subjects. The staff are responsible for recruitment and consenting, assessments, treatment delivery, and follow-up activities.

b) Training.

Describe the training you will provide to ensure that all persons assisting with the research are informed about the protocol and their research-related duties and functions.

All study staff maintain up-to-date CITI certification and current knowledge of the research literature on use of digital health technologies for health behavior change.

c) Facilities.

Please describe and justify.

Dr. Prochaska has a faculty office at Stanford University in the Medical School Office Building with full computing resources needed for the trial.

All study data are gathered on a HIPAA compliant web platform that resides behind Stanford security firewalls and has been tried and tested by the University for several years, thus actual risk from data breach for study data is low.

d) Sufficient time.

Explain whether you will have sufficient time to conduct and complete the research. Include how much time is required.

Dr. Prochaska's faculty time is 100% devoted to research and this is one of her funded projects to which she dedicates her time.

e) Access to target population.

Explain and justify whether you will have access to a population that will allow recruitment of the required number of participants.

This NIDA-funded project (funding pending) is a collaboration with Woebot, a technology start up that is using artificial intelligence (AI) in a bot to deliver tailored messaging to improve mental health.

Participants will be recruited through a wide variety of strategies including but not limited to paid online advertising (e.g., sidebar Gmail and Yahoo advertisements); flyers; social media; free online and email advertising (e.g., Dr Prochaska's laboratory webpage, email listservs of digital health companies and the Stanford University student, faculty, and staff community); participants from previous studies who have interest in other studies; and national outpatient clinics with substance abuse programming including Stanford's Department of Psychiatry and Behavioral Sciences' Dual Diagnosis Clinic.

Dr. Prochaska's team has extensive experience in recruiting research participants who use substances, including for online studies and has published on best practices.

f) Access to resources if needed as a consequence of the research.

State whether you have medical or psychological resources available that participants might require as a consequence of the research when applicable. Please describe these resources.

Study informed consent will state that Woebot (the app being used to deliver the intervention) is not a crisis program designed to address active suicidal ideation or overdose. Woebot also conversationally informs first time users that it is not a crisis service. Our current safety net protocol will be adapted for this study. Woebot detects crisis language and asks to confirm it with the user. If the user confirms, Woebot offers resources (911, suicide crisis hotlines), carefully curated with expert consultation. Our data indicate that users do not use Woebot for crisis management; about 6.3% trigger the safety net protocol, with 27% confirming that it is indeed a crisis when Woebot asks to confirm (i.e., our true positive rate). To make sure that we do not miss any cases, we over detect, rather than under detect. In addition, we periodically check the data for true/false positive rates.

Foreseeable risks to subjects include the possibility that some assessment questions and/or treatment procedures may be upsetting to subjects. Experience at Stanford with similar populations has indicated that the risk of emotional upset during the assessments is low and if it occurred, the upset would likely not be

serious in nature and temporary. Such risks will be minimized by the thoughtful selection of questionnaires. Potential participants will also be informed that they may drop out of the study at any time and if requested, appropriate treatment referrals would then be given.

g) Lead Investigator or Coordinating Institution in Multi-site Study.

Please explain (i) your role in coordinating the studies, (ii) procedures for routine communication with other sites, (iii) documentation of routine communications with other sites, (iv) planned management of communication of adverse outcomes, unexpected problems involving risk to participants or others, protocol modifications or interim findings.

1. Purpose

a) In layperson's language state the purpose of the study in 3-5 sentences.

This study aims to develop a digitally-delivered substance use disorder program through the Woebot app-based platform to inform a study that will test the comparative efficacy of the mobile-app based substance use disorder program to reduce substance use relative to a wait list control condition, and explore between group differences on quality of life indices as well as retention and engagement during COVID-19.

b) State what the Investigator(s) hope to learn from the study. Include an assessment of the importance of this new knowledge.

The COVID-19 pandemic introduced significant, unprecedented, and immediate psychological challenges to all, including individuals with substance use disorders (SUDs). The impact upon individuals with SUDs will be multifaceted and far reaching. In terms of physical health, experts postulate that individuals with SUDs may be at greater risk of mortality from COVID-19 given the variety of pre-existing physical health conditions this group has traditionally faced (i.e., COPD, cardiovascular disease, general poor respiratory health). In addition, the pandemic will beget significant emotional and psychiatric disruption from the multifaceted impact of the illness. Such responses may include large-scale grief, loneliness, fear, loss of life experiences, constrained or frank inability to work, financial instability, risk of contagion, overwhelmed hospitals, limited access to recovery programs and reduced or significantly changed mental health service provision from clinics.

Woebot, the landmark product released by Woebot Labs Inc. in 2017, is an automated conversational agent, available through a smartphone application, that delivers evidence-based psychotherapeutics, empathy, and emotional health psychoeducation. Woebot for Substance Use Disorders (W-SUDs) is a 2 phase SBIR industry-academic partnership between Woebot Labs Inc. and Stanford University that aims to develop and evaluate the evidence of the novel digital therapeutic, delivered by an artificial intelligence (AI)-powered, automated conversational agent named Woebot which is embedded in the therapeutic W-SUDs.
Milestones for Phase I included the development (e.g., content and engineering) of W-SUDs and piloting its preliminary efficacy, feasibility and acceptability among n=100 individuals with SUD. Phase I is well underway presently. At the time of this supplement application,

W-SUDs had been developed and deployed to pilot phase with N=48 individuals already enrolled into the pilot study.
Phase II is multi-pronged and aims to engage the FDA in collaboration regarding W-SUDs, test the comparative efficacy of the W-SUDs relative to a standard control condition (SCC) to reduce substance use, and explore between group differences on quality of life indices as well as retention and engagement.

The current supplement proposes an additional study of W-SUDs to obtain and analyze data on the risks of the COVID-19 pandemic among individuals experiencing SUDs. The study will not disrupt progress or milestones on the parent grant. Rather, it offers an opportunity to expand understanding of W-SUDs' performance among this population whilst contributing to our overall understanding of COVID-19's impact upon this population.

Impact
Immediate access to a digital therapeutic in a resource constrained, social distance healthcare ecosystem amidst growing psychological challenges in this already vulnerable and underserved population. When COVID-19 spread, users from around the world came to Woebot to discuss it and seek help. The company responded by building a Covid-19 specific program for Woebot (W-C19) which is already well underway. Elements of our W-C19 program have already been integrated into W-SUDs because we felt that it was timely and appropriate to address users' concerns about the pandemic and demonstrated that Woebot was 'intelligent' to the current crisis.

c) Explain why human subjects must be used for this project. (i.e. purpose of study is to test efficacy of investigational device in individuals with specific condition; purpose of study is to examine specific behavioral traits in humans in classroom or other environment)

The purpose of this study is to test the efficacy of a mobile-application delivered substance use disorder intervention in adult humans in a pandemic, and assess effects due to COVID-19.

2. Study Procedures

a) Please SUMMARIZE the research procedures, screening through closeout, which the human subject will undergo. Refer to sections in the protocol attached in section 16, BUT do not copy the clinical protocol. Be clear on what is to be done for research and what is part of standard of care.

Updated consent forms and HIPAA authorization will be uploaded before the start of recruitment. Ads, questionnaires, etc. will be uploaded for review before recruitment begins.

Recruitment will be a joint effort by Stanford University and Woebot Labs. Woebot will communicate the research opportunity through social media channels. The Stanford team will recruit through listservs and contact participants from previous research studies who are interested in future studies. Working with Dr. Prochaska's research team at Stanford, the Woebot team will take part in mapping out message development for the intervention and Woebot's IT team will lead the app programming (including build and quality control/de-bugging). Woebot will collect user data via the Woebot app (automatic process), which

will be provided to the Stanford team. The Woebot team will participate in disseminating the study findings via publications and presentations. Participants from recruitment channels will go through and eligibility screener and if eligible, will be asked to use the W-SUDS for 8 weeks and answer a couple of questionnaires administered at the beginning and end of the 8 week period. The data from the questionnaires and app usage during the 8-week period will be analyzed to inform the next study. Woebot will rely on Stanford University IRB for review of this study.

The Stanford team will lead the study evaluations including the study measures, data collection (baseline and follow-ups at the 4- and 8- week marks), data analyses, and writing up of study findings for dissemination. Participants will be randomized to condition after completion via the online assessment platform, which has the functionality to allow randomization to one of two webpages. Those randomized to W-SUDs or WL will see a private, study-only Woebot website or the WL website, respectively. Only then will participants randomized to W-SUDs be informed of Woebot in order to avoid contamination. The WL group has no intervention during the 8-week period and the team will monitor for any intervention usage.

In order to better understand what specific W-SUDs content the participants like, Lesson Completion Rates and Content Rating Metrics will be analyzed. Descriptive statistics will be used for the following scales: Usage Rating Profile Intervention (UPRI)-Acceptability, Usage Rating Profile Intervention (UPRI)--Feasibility, and Client Satisfaction Questionnaire (CSQ-8). Such descriptive statistics will provide a summary index of how likable the content and program was overall. Due to the small sample size of this study, effect sizes, rather than tests involving statistical significance, will be used to assess the intervention's impact from baseline to EOT.

Utilizing study results as described above, the research team will learn the efficacy of a digital substance use therapeutic during a pandemic. The intent is to utilize and leverage what was learned in this study to provide an intervention in a time where in person services are discouraged.

b) Explain how the above research procedures are the least risky that can be performed consistent with sound research design.

Given that the research aims to enroll a low-treatment seeking population, we do not envisage that participation in the study will be associated with elevated risk.
However, some risk is always present in studies that involve human participants.
Such risk may include the following:
Risk from breach of protected health information.
Possibly the greatest risk is from a leak of health information. All study data are gathered on a HIPAA compliant web platform that resides behind Stanford security firewalls and has been tried and tested by the University for several years, thus actual risk from data breach for study data is low. In addition, the Woebot

application encrypts all message data exchanged between service users and Woebot, and collects minimal protected health information. Emails are hashed and not kept along side message data so that they are not easily associated with each other. In addition, the product recently became compliant with General Data Protection Regulations (GDPR) in the European Union which entails a user-ownership model of data protections.
Risk from answering questions that may be emotionally upsetting. Experience at Stanford with similar populations has indicated that the risk of emotional upset during the assessments is low and if it occurred, the upset would likely not be serious in nature and temporary. Such risks will be minimized by the thoughtful selection of questionnaires. Potential participants will also be informed that they may drop out of the study at any time and if requested, appropriate treatment referrals would then be given.
Risk of treatment avoidance due to engagement with either of the randomized interventions. In both interventions it is explicitly stated that the service should not be used in place of traditional treatment. In the case of the W-SUDs intervention, Woebot is designed to hold individuals accountable for pursuing additional options in conditions of unchanged symptoms for a prolonged amount of time (4 weeks). In addition, Woebot will invite the user to consider what seeking additional services would look like.

c) State if deception will be used. If so, provide the rationale and describe debriefing procedures. Since you will not be fully informing the participant in your consent process and form, complete an alteration of consent (in section 13). Submit a debriefing script (in section 16).

No deception will be used.

d) State if audio or video recording will occur. Describe what will become of the recording after use, e.g., shown at scientific meetings, erased. Describe the final disposition of the recordings.

No audio or video recordings will occur.

e) Describe alternative procedures or courses of treatment, if any, that might be advantageous to the participant. Describe potential risks and benefits associated with these. Any standard treatment that is being withheld must be disclosed in the consent process and form. (i.e. standard-of-care drug, different interventional procedure, no procedure or treatment, palliative care, other research studies).

Alternative Treatments for SUDSs include in-person individual and group forms of psychotherapy as well as Alcoholics Anonymous and Narcotics Anonymous.

All alternative options will be provided if she/he/they wishes to engage in an alternative treatment rather than the proposed study. However, given that previous Woebot study results are promising, the proposed line of treatments would appear to be appropriate and acceptable interventions for SUDs.

No standard treatment is being withheld.

f) Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

Yes

g) Study Endpoint. What are the guidelines or end points by which you can evaluate the different treatments (i.e. study drug, device, procedure) during the study? If one proves to be clearly more effective than another (or others) during the course of a study, will the study be terminated before the

projected total participant population has been enrolled? When will the study end if no important differences are detected?

The endpoint will be the 2-month end-of-treatment survey. This will end the study and study staff will do analysis.

3. Background

a) Describe past experimental and/or clinical findings leading to the formulation of the study.

Woebot's app-based platform and user-centered design philosophy makes it an optimal modality for SUDs treatment delivery; it offers immediate, evidence-based tailored support in the patient's peak moment of craving. An RCT demonstrated that Woebot had statistically and clinically significant reductions in depression compared to a control group, along with best in class app-engagement rates (mean=12 interactions in 14 days). Woebot does not currently offer a SUDs program, although 63% of current users expressed interest in said content. Woebot's current, substantial reach as a consumer app, preliminary data indicating its high user engagement plus efficacy to treat a psychological condition, posies it as an ideal platform for a SUDs-focused, tailored, and immediately scalable digital therapeutic.

In the Woebot-SUDs phase 1 (pilot) study, there are 2,450+ screening attempts, indicating interest in a digital therapeutic CA on substance use both nationally and internationally. 260 were screened out solely for not residing in the U.S.

COVID-19 offers a unique opportunity for research to consider outbreak levels and policies in our analyses, and the potential for differential effects of a treatment for reducing substance use problems during an infectious disease outbreak.

b) Describe any animal experimentation and findings leading to the formulation of the study.

N/A

4. Radioisotopes or Radiation Machines

a) List all standard of care procedures using ionizing radiation (radiation dose received by a subject that is considered part of their normal medical care). List all research procedures using ionizing radiation (procedures performed due to participation in this study that is not considered part of their normal medical care). List each potential procedure in the sequence that it would normally occur during the entire study. More Info

Identify Week/Month of study	Name of Exam	Identify if SOC or Research

b) For research radioisotope projects, provide the following radiation-related information:

Identify the radionuclide(s) and chemical form(s).

For the typical subject, provide the total number of times the radioisotope and activity will be administered (mCi) and the route of administration.

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If not FDA approved provide dosimetry information and reference the source documents (package insert, MIRD calculation, peer reviewed literature).

c) For research radiation machine projects, provide the following diagnostic procedures:

For well-established radiographic procedures describe the exam.

For the typical subject, identify the total number of times each will be performed on a single research subject.

For each radiographic procedure, provide the setup and technique sufficient to permit research subject dose modeling. The chief technologist can usually provide this information.

For radiographic procedures not well-established, provide FDA status of the machine, and information sufficient to permit research subject dose modeling.

d) For research radiation machine projects, provide the following therapeutic procedures:

For a well-established therapeutic procedure, identify the area treated, dose per fraction and number of fractions. State whether the therapeutic procedure is being performed as a normal part of clinical management for the research participants's medical condition or whether it is being performed because the research participant is participating in this project.

For a therapeutic procedure that is not well-established, provide FDA status of the machine, basis for dosimetry, area treated, dose per fraction and number of fractions.

5. Devices

a) Please list in the table below all Investigational Devices (including Commercial Devices used off-label) to be used on participants.

5. 1 Device Name : Woebot

Describe the device to be used.

Woebot, a Conversational Agent (CA) instantaneously available 24 hours per day, 7 days per week, 'checks in' with users. Using conversational tones, it encourages mood tracking and delivers general psychoeducation as well as tailored empathy, cognitive behavior therapy (CBT)-based behavior change tools, and behavioral pattern insight. Woebot's app-based platform and user-centered design philosophy makes it an optimal modality for Substance Use Disorders (SUD) treatment delivery; it offers immediate, evidence-based tailored support in the patient's peak moment of craving.

Manufacturer : **Woebot Labs**

Risk : **Non-significant**

Y I confirm the above are true.

Rationale for the device being non-significant risk:

Title : Woebot for Substance Use Disorders during COVID-19 (SU sIRB)
Approval Period: 04/30/2022 - 04/30/2023

The research aims to enroll a low-treatment seeking population, and employ randomization to two low-risk interventions, we do not envisage that participation in the study will be associated with elevated risk.

Sponsor of Project

Indicate who is responsible for submitting safety reports to the FDA:

Y The sponsor is the device manufacturer.

Ordering, Storage and Control

To prevent the device being used by a person other than the investigator, and in someone other than a research participant: Confirm that the device will be handled according to the SHC/LPCH policy for Investigational New Devices or as appropriate. If no, please provide an explanation. :

Y Confirm?

b) Please list in the table below all IDE Exempt Devices (Commercial Device used according to label, Investigational In Vitro Device or Assay, or Consumer Preference/Modifications/Combinations of Approved Devices) to be used on participants.

6. Drugs, Reagents, or Chemicals and Devices

a) Please list in the table below all investigational drugs, reagents or chemicals to be administered to participants.

b) Please list in the table below all commercial drugs, reagents or chemicals to be administered to participants.

7. Medical Equipment for Human Subjects and Laboratory Animals

If medical equipment used for human patients/participants is also used on animals, describe such equipment and disinfection procedures.

N/A

8. Participant Population

a) State the following: (i) the number of participants expected to be enrolled at Stanford-affiliated site(s); (ii)the total number of participants expected to enroll at all sites; (iii) the type of participants (i.e. students, patients with certain cancer, patients with certain cardiac condition) and the reasons for using such participants.

May 2021: N=160 was proposed for study enrollment. Final enrollment was N=180. Qualtrics panel recruitment was the main recruitment method and had resulted in n=160; n=20 were from other recruitment sources described in the protocol. For the next study, we'll try Qualtrics recruitment before other sources, as the Qualtrics panel requires a prepaid agreement and results in speedy recruitment.

N=160 (nationally) will be invited to participate in this study and entered into the study on a rolling basis.

Recruitment will be a joint effort by Stanford University and Woebot Labs. Neither election or declining to participate in the study will impact Woebot users ability to continue using the product as they wish. Inclusion criteria include: all genders aged 18-65 years, access to Woebot on smartphone, be available and committed to engage with app and complete assessments, be willing to provide email address (to distribute incentives), and be literate in English (as W-SUDs conversational and video materials will be in English). Exclusion criteria include: pregnancy (as W-SUDs will not be specifically developed to address the unique needs of this population), history of severe drug/alcohol use, opioid misuse without medication-assisted treatment, and suicide attempt or opioid overdose within the past year. Randomization will occur through the survey program by the time the participant finishes the baseline survey.

Participants and Recruitment: N=160 (nationally) will be invited to participate in this study. Recruitment channels may include Woebot Labs' social media avenues (e.g., Facebook, Twitter, LinkedIn, Woebot.io, Nextdoor), Craigslist, Reddit, physical flyers, emailing clinics (with their permission), posting to Stanford Staffers listserv, and advertising to the WELL cohort. Stanford staff may post in other listservs with permission, and contact participants from other studies if those participants have interest in other studies. The team may use Qualtrics panels to recruit. Participants will be entered into the study on a rolling basis. Neither election or declining to participate in the study will impact Woebot users ability to continue using the product as they wish. Inclusion criteria include: all genders aged 18-65 years, access to Woebot on smartphone, be available and committed to engage with app and complete assessments, be willing to provide email address (as this is how assessment incentives will be distributed), and be literate in English (as W-SUDs conversational and video materials will be in English).

Exclusion criteria include: pregnancy (as W-SUDs will not be specifically developed to address the unique needs of this population), history of severe drug/alcohol use, opioid misuse without medication-assisted treatment, and suicide attempt or opioid overdose within the past year. Participants residing outside the U.S. will not be included. Participants who have ever used Woebot will also not be recruited. Use of Woebot (without SUDs program) post randomization, regardless of group assignment, is allowed. Those who elect to participate will be provided with a specific code to enter into Woebot to cue the SUDs specific content.

Randomization: Randomized controlled trial of W-SUDs vs a wait-list control condition (will get access to the SUD program at the end of the study; no intervention during the 8 week period)
This supplemental study proposes to randomize individuals to two conditions (estimating n=80 in each group), W-SUDs or a wait-list control condition, in order to:
(i) compare between group substance use outcomes at end-of-treatment;
(ii) assess and analyze comparative impact of Covid-19 in each group;
(iii) conduct a moderation analysis. Do putative moderators moderate treatment impact upon substance use outcomes?

Primary aim / outcome: Compare between group treatment outcomes.
Hypothesis: W-SUDs will have significantly improved outcomes compared to the wait-list control group.
Variable of interest: AUDIT/DAST scores across the two groups.

Secondary aim / outcome: Investigate the differential impact of Covid-19 upon psychological functioning across the two groups (one in W-SUDs, the other without intervention).
Purpose: to understand the impact of Covid-19 under a no intervention vs W-SUDs intervention.
Variables of interest: see list below. These variables will be measured at BL, week 4, and end-of-treatment at week 8. Total of 3 surveys.

Exploratory aim / outcome: To investigate putative moderators of treatment on outcome (and/or of treatment engagement).
Variables of interest include:
Mood: depression (PHQ), anxiety (GAD), loneliness, grief
Covid-19 related situational triggers: financial worry, ability to work, essential worker status, safety at home, children at home, degree of closeness to the illness (know someone who is ill, died),

Current treatment engagement: level of engagement in other recovery support systems, alliance to Woebot.

Intervention Delivery: W-SUDs will be administered over the course of 8-weeks. Woebot may follow up by email to encourage participants to open the app and check in. The control group will not have access to the W-SUDs program till after completion of their EOT survey at the 8-week mark. Additionally, while the wait-listed group won't have additional surveys (i.e., post app use), we will gather/analyze the info we get from their use of Woebot.

Survey Administration Plan: Qualtrics or REDCap, HIPAA compliant online data center survey administration tools (commonly used by Stanford University), will be utilized to administer the assessment batteries including BL, 4-week, and the EOT questionnaires. During the consent form section, participants will be asked for their email in order to receive study communications including 1) Their signed consent form, 2) Instructions for downloading the Woebot app and using the referral code for the Woebot-SUDs program, and 3) A survey link for follow up assessments. After the baseline is completed, participants will be emailed their signed consent form and instructions. After the 4-week and 8-week phase, participants will receive their survey links via email.

Data Analysis: In order to analyze feasibility and acceptability data, descriptive statistics will be used for the following scales: Usage Rating Profile Intervention (UPRI)-Acceptability, Usage Rating Profile Intervention (UPRI)--Feasibility, and Client Satisfaction Questionnaire (CSQ-8). Such descriptive statistics will provide a summary index of how likable the content and program was overall.
In order to better understand what specific W-SUDs content the participants like, Lesson Completion Rates, and Content Rating Metrics will be analyzed.

Lesson Completion Rates will indicate which of the specific W-SUDs lessons were completed. Content Rating Metrics are how participants rate each lesson; they are self-reported by the participant, via Woebot, and are provided on a binary scale: either a thumbs up or thumbs down emoticon. If a lesson receives a thumbs down, Woebot offers the user a chance to give additional free-text feedback. Thus, both the binary answers (thumbs up or thumbs down) plus the free-text feedback will be used to pinpoint which lessons are performing well and which need editing. Effect sizes will surmise mean changes from baseline to post-treatment on drug use psychopathology. Due to the small sample size of this pilot study, effect sizes, rather than tests involving statistical significance, will be used to assess the intervention's impact from baseline to EOT.

Additionally, pain and craving questions will be asked in the Woebot app to monitor change over time. Subtle changes to wording in these questions may be made for organic conversation.

Refining W-SUDs: Utilizing study results as described above, the research team will learn the efficacy of a digital substance use therapeutic during a pandemic. The intent is to utilize and leverage what was learned in this study to provide an intervention in a time where in person services are discouraged.

b) State the age range, gender, and ethnic background of the participant population being recruited.

Inclusion Criteria:
Eligible participants for this trial must:
1. Have a smartphone
2. Endorse a substance use concern
3. Be between 18 and 65 years of age
4. Be available and committed to engage with the Woebot app
5. Be literate in English.(This is required for inclusion because all materials for app and website will be in English).

Exclusion Criteria:
1. Pregnancy (as W-SUDs will not be specifically developed to address the unique needs of this population)
2. Suicide attempt within the past year

3. Symptoms of severe drug/alcohol history: History of delirium tremens; Experiencing seizures or confusion after stopping alcohol or drugs; Liver trouble (cirrhosis or hepatitis); Convulsions or GI bleeding due to drug/alcohol use
4. Opioid overdose within the past 12 months
5. Opioid misuse without medication-assisted treatment
6. Ever used Woebot (To avoid sample contamination)

Recruitment efforts will seek to enroll a demographically diverse sample. Substance disorders are prevalent in individuals of all genders, therefore all genders will be recruited as participants in the proposed study.

c) State the number and rationale for involvement of potentially vulnerable subjects in the study (including children, pregnant women, economically and educationally disadvantaged, decisionally impaired, homeless people, employees and students). Specify the measures being taken to minimize the risks and the chance of harm to the potentially vulnerable subjects and the additional safeguards that have been included in the protocol to protect their rights and welfare.

N/A

d) If women, minorities, or children are not included, a clear compelling rationale must be provided (e.g., disease does not occur in children, drug or device would interfere with normal growth and development, etc.).

Exclusion of Pregnant Women: Pregnancy (as W-SUDs will not be specifically developed to address the unique needs of this population). Exclusion of Children. The proposed study will include individuals between 18-65 years of age. Persons younger than 18 will not be included in the study, as the proposed substance disorder treatments were not designed for nor tested among youth and the characterization of SUD in youth differs in meaningful ways from that in adults. Given the small sample sizes for this pilot and that Woebot has not yet been tested among youth, the proposed research is focused on those aged 18 and older.

e) State the number, if any, of participants who are laboratory personnel, employees, and/or students. They should render the same written informed consent. If payment is allowed, they should also receive it. Please see Stanford University policy.

0

f) State the number, if any, of participants who are healthy volunteers. Provide rationale for the inclusion of healthy volunteers in this study. Specify any risks to which participants may possibly be exposed. Specify the measures being taken to minimize the risks and the chance of harm to the volunteers and the additional safeguards that have been included in the protocol to protect their rights and welfare.

0 healthy volunteers. 160 volunteers will have endorsed a substance use concern for problematic use and screened out if pregnant during recruitment. Other than these health implications, participants will otherwise be healthy volunteers and will not be exposed to health risks through their participation.

g) How will you identify and recruit potential participants about the research study? (E.g., by: Honest Broker or other https://researchcompliance.stanford.edu/participantengagement Research Participation services; chart review; treating physician; ads). All final or revised recruitment materials, flyers, etc. must be submitted to the IRB for review and approval before use. You may not contact potential participants prior to IRB approval. See Advertisements: Appropriate Language for Recruitment Material.

Recruitment: For this study, Woebot Labs' will post study advertisements and recruit via their already active internet channels including Twitter (over 2,000 followers), LinkedIn (over 400 followers), and Facebook (over 16,500 followers). To supplement recruiment, Woebot Labs' may post on Craigslist, Nextdoor, and on Reddit through relevant subreddits with written permission from the subreddits' moderators. Woebot may email clinics. Woebot may also post physical flyers and the Stanford team may post on the Stanford Staffers listserv. The Stanford team may recruit from the WELL cohort, with permission. Stanford staff may post in other listservs with permission. The Stanford team may recruit participants from other studies who have

indicated interest in other studies. The team may use Qualtrics panels to recruit. Woebot exchanges an average of 1-2 million messages per week with its users. Woebot users have indicated interest in substance use content. Specifically, 63% of current users (surveyed in July 2018) reported interest in content related to substance use. In regards to their specific substance use behaviors over the previous month, 22% of users reported having 5 or more alcoholic drinks in a row within a couple of hours (i.e., binge use), and 5% endorsed using non-prescription drugs. Woebot Labs has used these channels for previous research participation invitations with success.
Minor editing changes may be made to recruitment materials to enhance clarity.
Participants will be asked for their age during the screener. If ineligible, they will be not be able to participate in the Woebot for Substance Use Disorders study. We will ask for date of birth in the questionnaire after the signed consent to confirm that the participant is not underage. This is standard best practice for use of the program and for other online research studies.

h) Inclusion and Exclusion Criteria.

Identify inclusion criteria.

Inclusion Criteria:
Eligible participants for this trial must:
1. Have a smartphone
2. Endorse a substance use concern
3. Be between 18 and 65 years of age
4. Be available and committed to engage with the Woebot app
5. Be literate in English.(This is required for inclusion because all materials for app and website will be in English).

Identify exclusion criteria.

Exclusion Criteria:
1. Pregnancy (as W-SUDs will not be specifically developed to address the unique needs of this population)
2. Suicide attempt within the past year (12 months)
3. Symptoms of severe drug/alcohol history: History of delirium tremens; Experiencing hypertension, drenching sweats, seizures or confusion after stopping alcohol or drugs; Liver trouble (cirrhosis or hepatitis); Convulsions or GI bleeding due to drug/alcohol use
4. Opioid overdose within the past year (12 months)
5. Opioid misuse without medication-assisted treatment
6. Not residing in the U.S.
7. Ever used Woebot

i) Describe your screening procedures, including how qualifying laboratory values will be obtained. If you are collecting personal health information prior to enrollment (e.g., telephone screening), please request a waiver of authorization for recruitment (in section 15).

Screening
There will be a brief internet delivered (via Qualtrics or REDCap) screener that will ascertain if individuals who express interest in participating in the study meet inclusion criteria. The screener-battery will include the Drug Abuse Screening Test (DAST-10), CAGE Questions Adapted to Include Drug Use (CAGE-AID), Michigan Alcohol Screening Test (MAST), Psychosis Screening Questionnaire (PSQ), and a few relevant demographic questions (i.e., age, pregnancy status, suicide or overdose within the past year). Those who do not meet criteria will be welcomed to begin using the generic (non-SUD focused) Woebot and the website without restriction but will not be enrolled into the study. In addition, additional substance treatment resources will be provided.

j) Describe how you will be cognizant of other protocols in which participants might be enrolled. Please explain if participants will be enrolled in more than one study.

Consent form will ask whether the participant is currently enrolled in any additional studies.

k) Payment/reimbursement. Explain the amount and schedule of payment or reimbursement, if any, that will be paid for participation in the study. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of participants and that they do not constitute undue

pressure on participants to volunteer for the research study. Include provisions for prorating payment. See payment considerations

Supplemental funding pending approval. $25 for an Amazon gift card per assessment (baseline, 4 week, and 8 week) completed for each of the 160 participants. Total potential amount possible per participant: $75

l) Costs. Please explain any costs that will be charged to the participant.

There will be no cost to participants.

m) Estimate the probable duration of the entire study. Also estimate the total time per participant for: (i) screening of participant; (ii) active participation in study; (iii) analysis of participant data.

Total duration estimated to be 3.5 years. Content development is ready. Recruitment for about 2 months. Participation in the study is estimated to be 2 months. Estimated time for screening is 3 minutes or less; Each survey estimated to be 15-30min. Active participation is 2 months with a follow up surveys at the 4-week and 8- week mark. Data analysis and dissemination estimated to be 3 years.

9. Risks

a) For the following categories include a scientific estimate of the frequency, severity, and reversibility of potential risks. Wherever possible, include statistical incidence of complications and the mortality rate of proposed procedures. Where there has been insufficient time to accumulate significant data on risk, a statement to this effect should be included. (In describing these risks in the consent form to the participant it is helpful to use comparisons which are meaningful to persons unfamiliar with medical terminology.)

The risks of the Investigational devices.

N/A

The risks of the Investigational drugs. Information about risks can often be found in the Investigator's brochure.

N/A

The risks of the Commercially available drugs, reagents or chemicals. Information about risks can often be found in the package insert.

N/A

The risks of the Procedures to be performed. Include all investigational, non-investigational and non-invasive procedures (e.g., surgery, blood draws, treadmill tests).

N/A

The risks of the Radioisotopes/radiation-producing machines (e.g., X-rays, CT scans, fluoroscopy) and associated risks.

N/A

The risks of the Physical well-being.

N/A

The risks of the Psychological well-being.

Potential Upset due to Survey Questions: Foreseeable risks to subjects include the possibility that some assessment questions and/or treatment procedures may be upsetting to subjects. Experience at Stanford with similar populations has indicated that the risk of emotional upset during the assessments is low and if it occurred, the upset would likely not be serious in nature and temporary. Such risks will be minimized by the thoughtful selection of questionnaires. Potential participants will also be informed that they may drop out of the study at any time and if requested, appropriate treatment referrals would then be given.

The risks of the Economic well-being.

N/A

The risks of the Social well-being.

Potential loss of confidentiality.

Overall evaluation of Risk.

Low - innocuous procedures such as phlebotomy, urine or stool collection, no therapeutic agent, or safe therapeutic agent such as the use of an FDA approved drug or device.

b) If you are conducting international research, describe the qualifications/preparations that enable you to both estimate and minimize risks to participants. Provide an explanation as to why the research must be completed at this location and complete the [LINKFORINTERNATIONALREASEARCHFORM] International Research Form. If not applicable, enter N/A.

N/A

c) Describe the planned procedures for protecting against and minimizing all potential risks. Include the means for monitoring to detect hazards to the participant (and/or to a potential fetus if applicable). Include steps to minimize risks to the confidentiality of identifiable information.

Given that the research aims to enroll a low-treatment seeking population, we do not envisage that participation in the study will be associated with elevated risk. We are not assessing suicidal ideation in our questionnaires. During the eligibility screener, those who have had a suicide attempt within the past year will be excluded from the study. It is not feasible to confirm the responses by participants to the questionnaires in real time. However, some risk is always present in studies that involve human participants. Such risk may include the following:

1. Data Protection and Privacy: All study data are gathered on a HIPAA compliant web platform that resides behind Stanford security firewalls and has been tried and tested by the University for several years, thus actual risk from data breach for study data is low. All assessments, including the screening, four assessment batteries, and mediator assessment will be administered via a HIPAA compliant survey administration tool commonly used by Stanford University in its clinical trials (Qualtrics or REDCap). Given the high data protection safeguards embedded within Qualtrics or REDCap, there is little risk to the subject associated in regards to their privacy and/or confidentiality.
Research material obtained from human subjects will involve behavioral and psychological assessments including self-report questionnaires. All data will be obtained specifically for purposes of this research project. Data that is obtained from the Qualtrics or REDCap assessments will be stored and protected within Qualtrics or REDCap. Data that is obtained via Woebot will be encrypted and stored on Amazon Web Services (AWS); Woebot Labs data gathering and storage procedures are compliant with both the Health Insurance Portability and Accountability Act (HIPAA) and the European Union's General Data Protection Regulation (GDPR) compliant. Only members of the research team (PI, Co-PIs, biostatistician, research assistant) will have access to the data.

2. Potential Upset due to Survey Questions: Foreseeable risks to subjects include the possibility that some assessment questions and/or treatment procedures may be upsetting to subjects. Experience at Stanford with similar populations has indicated that the risk of emotional upset during the assessments is low and if it occurred, the upset would likely not be serious in nature and temporary. Such risks will be minimized by the thoughtful selection of questionnaires. Potential participants will also be informed that they may drop out of the study at any time and if requested, appropriate treatment referrals would then be given.

3. Risk of treatment avoidance due to engagement with either of the randomized interventions. In both interventions it is explicitly stated that the service should not be used in place of traditional treatment. In the case of the W-SUDs intervention, Woebot is designed to hold individuals accountable for pursuing additional options in conditions of unchanged symptoms for a prolonged amount of time (4 weeks). In addition, Woebot will invite the user to consider what seeking additional services would look like.

4. Risk of suicide: Woebot informs the participant that it is not designed for crisis service. Additionally, Woebot detects crisis language (e.g. "want to kill") and asks to confirm it with the user. If the user confirms,

Woebot automatically, in real-time offers resources (9-1-1, suicide crisis hotlines, referral to ER). Woebot's crisis detectors flags around 200 possible harm to self phrases, including about 10 misspellings and 5 slang phrases. Woebot's data indicate that users do not use Woebot for crisis management; about 6.3% trigger the safety net protocol, of which 27% confirm that it is indeed a crisis (i.e., for a true crisis rate of 1.7%). Woebot's algorithm is over-sensitive, designed to over-detect, rather than under-detect to make sure that cases are not missed. Woebot staff periodically check the data for true/false positive rates. Additionally, if anyone is developing or indicating serious thoughts about suicide or harming themselves, it is best practice to call 9-1-1 and/or go to the nearest ER.

d) Explain the point at which the experiment will terminate. If appropriate, include the standards for the termination of the participation of the individual participant Also discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the participants.

The study will terminate once the 2-month period with all 150 participants has been completed and the analyses run and submitted for publication.

Participants can refuse to participate at any time.

When we learn of a participant's adverse event, the team will report the adverse event and may follow up with the participant for additional information. Resources will be offered. The EOT survey includes questions that assess for SAEs. More details about adverse events are in section e.

e) Data Safety and Monitoring Plan (DSMP). See guidance on Data Safety and Monitoring.

A Data and Safety Monitoring Plan (DSMP) is required for studies that present Medium or High risk to participants. (See Overall Evaluation of Risk above). If Low Risk, a DSMP may not be necessary. Multi-site Phase III clinical trials funded by NIH require the DSM Plan to have a Data Safety Monitoring Board or Committee (DSMC or DSMB). The FDA recommends that all multi-site clinical trials that involve interventions that have potential for greater than minimal risk to study participants also have a DSMB or DSMC.

The role of the DSMC or DSMB is to ensure the safety of participants by analyzing pooled data from all sites, and to oversee the validity and integrity of the data. Depending on the degree of risk and the complexity of the protocol, monitoring may be performed by an independent committee, a board (DSMC/DSMB), a sponsor's Data Safety Committee (DSC), a Medical Monitor, a sponsor's safety officer, or by the Protocol Director (PD).

Describe the following:

What type of data and/or events will be reviewed under the monitoring plan, e.g. adverse events, protocol deviations, aggregate data?

The Data Safety and Monitoring Plan will include Woebot's standard safety net protocol as well as a Data Safety and Monitoring Board overseen by Stanford University. Woebot's Safety Net Procedures Study informed consent will state that Woebot is not a crisis program designed to address active suicidal ideation or overdose. Woebot also conversationally informs first time users that it is not a crisis service. Our current safety net protocol will be adapted for the proposed study. Woebot's crisis detectors flags around 200 possible harm to self phrases, including about 10 misspellings and 5 slang phrases. Woebot detects crisis language (e.g. "want to kill") and asks to confirm it with the user. If the user confirms, Woebot offers resources (9-1-1, suicide crisis hotlines), carefully curated with expert consultation. Our data indicate that users do not use Woebot for crisis management; about 6.3% trigger the safety net protocol, with 27% confirming that it is indeed a crisis when Woebot asks to confirm (i.e., our true positive rate). To make sure that we do not miss any cases, we over detect, rather than under detect. In addition, we periodically check the data for true/false positive rates. Adverse Events We do not anticipate that the use of the interventions will increase risk as outlined above. In addition, there is a limited capacity to detect adverse events (such as overdose, suicide attempt or hospitalization related to substance use or other) unless explicitly voluntarily reported by the participant. In the case Stanford

University and / or Woebot Labs becomes aware of an adverse event, the appropriate protocol, approved by the DSMB and Stanford University's Institutional Review Board, will be immediately implemented. This includes immediate notification of the IRB, DSMB, and NIH, and an immediate convening of the DSMB to discuss requisite follow-up steps.

Identify who will be responsible for Data and Safety Monitoring for this study, e.g. Stanford Cancer Institute DSMC, an independent monitoring committee, the sponsor, Stanford investigators independent of the study, the PD, or other person(s).

To ensure the data protection and safety of research participants, Stanford University will serve as the Data Coordinating Center for the study under the coordination of Drs. Biaocchi and Prochaska. They will convene a group of three to serve as an oversight board with professional expertise in the area of the study. Dr. Prochaska is an expert in the field of addiction and substance use, and Dr. Biaocchi has experience in managing data protections in the context of randomized clinical trials.

Provide the scope and composition of the monitoring board, committee, or safety monitor, e.g., information about each member's relevant experience or area of expertise. If the Monitor is the Stanford Cancer Center DSMC or the PD, enter N/A.

DSMB's specific goals: • Review new or modifications to existing risk management protocols • Review procedures for maintaining confidentiality, data collection, management, and analyses • Review progress towards meeting enrollment goals • Recommend continuation, discontinuation, modification, or termination of a study based on emerging data (from the study and from the literature) and evaluation of risk/benefit ratios • Conduct annual reviews to determine whether patient safety has been adequately safeguarded • Review progress reports

Confirm that you will report Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reactions (SUSARs), or Unanticipated Problems (UPs) to the person or committee monitoring the study in accordance with Sponsor requirements and FDA regulations.

Yes.

If applicable, how frequently will the Monitoring Committee meet? Will the Monitoring Committee provide written recommendations about continuing the study to the Sponsor and IRB?

Dr Prochaska will coordinate the meetings by assisting in setting the agenda and ensuring that the necessary materials are provided for each meeting. The initial meeting of the Board will take place during the first three months of the study, i.e., before entry into the second Phase of the research, to allow for the consideration of the protocol from the viewpoint of data safety and participant confidentiality. Subsequent meetings will be held at 6-month intervals, with the possibility for either an interim meeting or telephone conversation conference call should the necessity arise. At the first meeting, Dr Prochaska will brief the board on the study design and procedures. The Board will then provide feedback on the data that they will wish to review at their subsequent meetings.

Specify triggers or stopping rules that will dictate when the study will end, or when some action is required. If you specified this in Section 2g [Study Endpoints], earlier in this application enter 'See 2g'.

Endpoints will be indicated by the cessation of W-SUDs intervention delivery at 8-weeks, data analysis and interpretation, refinement of W-SUDs, and the end of the 4 month period (ending mark of the study).

Indicate to whom the data and safety monitoring person, board, or committee will disseminate the outcome of the review(s), e.g., to the IRB, the study sponsor, the investigator, or other officials, as appropriate.

The proposed study has a dissemination plan that encapsulates two important arenas: 1) ClinicalTrials.gov compliance and 2) Dissemination. ClinicalTrials.gov Compliance If the proposal is successfully awarded, the applicant will ensure that the the trial's registration and results reporting procedures are thoroughly managed. The trial will be registered promptly upon receipt of the award and before the recruitment of human subjects. All informed consent documents will include specific and thorough statements referring to the posting on ClinicalTrials.gov. At the conclusion of the study and

following analysis of the results, results will be reported as well, in compliance with the ClinicalTrials.gov procedures. Woebot Labs has a protocol in place outlining the importance and details of ensuring the ClinicalTrials.gov procedures are up to date. Dissemination of Research Both Stanford University and Woebot Labs will facilitate with the dissemination of research. They will collaborate on manuscript preparation and submission, as well as abstract submission and presentations at national and international scientific and technology-oriented conferences.

Select One:

The Protocol Director will be the only monitoring entity for this study.

Y This protocol will utilize a board, committee, or safety monitor as identified in question #2 above.

10. Benefits

a) Describe the potential benefit(s) to be gained by the participants or by the acquisition of important knowledge which may benefit future participants, etc.

When evaluating the risks and benefits of the proposed study, it is believed that risks are relatively minimal when compared to the potential therapeutic benefits that subjects are likely to receive. The benefits of receiving W-SUDs include potentially reducing substance abuse, acquiring practical psychotherapeutic skills (from cognitive behavioral therapy, motivational interviewing, dialectical behavior therapy, and mindfulness), and receiving psychoeducation about substance abuse. Participants who reduce substance abuse may derive additional benefits should reduction in substance abuse be associated with other psychological improvements such as interpersonal or occupational functioning. Study of the effectiveness of this intervention will also benefit society more generally by providing data on the efficacy, utility, and cost-benefits of a W-SUDs, the first SUDs-focused digital therapeutic delivered by an artificial intelligence (AI)-powered conversational agent.

The study allows the opportunity to expand understanding of W-SUDs' performance among this population whilst contributing to our overall understanding of Covid-19's impact upon this population. When Covid-19 spread, users from around the world came to Woebot to discuss the pandemic and seek help. The company responded by building a Covid-19 specific program for Woebot (W-C19) which was initially deployed in March 2020. Elements of our W-C19 program have already been integrated into W-SUDs because we felt that it was timely and appropriate to address users' concerns about the pandemic and demonstrated that Woebot was 'intelligent' to the current crisis.

The proposed supplement will offer immediate access to a digital therapeutic in a resource constrained, socially distanced healthcare ecosystem to an already vulnerable and underserved population, who are likely faced with readily growing psychological challenges.

11. Privacy and Confidentiality

Title : Woebot for Substance Use Disorders during COVID-19 (SU sIRB)
Approval Period: 04/30/2022 - 04/30/2023

Privacy Protections

a) Describe how the conditions under which interactions will occur are adequate to protect the privacy interests of participants (e.g., privacy of physical setting for interviews or data collection, protections for follow-up interactions such as telephone, email and mail communications).

All assessments, including the screening and the two assessment batteries, will be administered via a HIPAA compliant survey administration tool commonly used by Stanford University in its clinical trials (Qualtrics or REDCap). Given the high data protection safeguards embedded within Qualtrics and REDCap, there is little risk to the subject associated in regards to their privacy and/or confidentiality.
Research material obtained from human subjects will involve behavioral and psychological assessments including self-report questionnaires. All data will be obtained specifically for purposes of this research project. Data that is obtained from the Qualtrics or REDCap assessments will be stored and protected within Qualtrics or REDCap. Data that is obtained via Woebot will be encrypted and stored on Amazon Web Services (AWS); Woebot Labs data gathering and storage procedures are compliant with both the Health Insurance Portability and Accountability Act (HIPAA) and the European Union's General Data Protection Regulation (GDPR) compliant. Only members of the research team (PI, Co-PIs, biostatistician, research assistant) will have access to the data.

Confidentiality Protections

b) Specify PHI (Protected Health Information). PHI is health information linked to HIPAA identifiers (see above). List BOTH health information AND HIPAA identifiers. If you are using STARR, use the Data Privacy Attestation to ensure that your request will match your IRB-approved protocol. Be consistent with information entered in section 15a.

Individual names, email addresses, phone numbers, dates of birth, gender/biological sex, IP addresses (automatically collected through Qualtrics), geo location (automatically collected through Qualtrics), and zip codes.

Drug Use Psychopathology
1. The Drug Abuse Screening Test 10 (DAST-10), a brief, 10-item self-report measure adapted from the 28-item DAST, assesses consequences related to drug abuse, excluding alcohol and tobacco. A score of 3 or higher indicates significant problems related to drug abuse. The DAST-10 demonstrated discriminate validity between individuals (i) with lifetime drug use disorders and those without and (ii) who are current abusers and those who are former abusers. It also has moderate level of test-retest and reliability as well as sensitivity and specificity.
2. The Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) is a widely used 3-item self-report screen for hazardous or harmful alcohol consumption that is based off of the 10-item original AUDIT. Developed by the World Health Organization, the AUDIT has been tested extensively in primary-care settings and various outpatient substance abuse treatment population, supporting the application of this screener tool. The AUDIT-C has been tested and validated across racial groups.
6. The Drug Abstinence Self-Efficacy Scale (DASE) is a 12-item self-report scale, reflecting Bandura's (1986) cognitive-behavioral

self-efficacy theory, and is a shortened version of the original 20-item scale. The 20-item scale has shown to be a reliable and valid measure of self-efficacy for drug use. The scale will be adapted to refer to use of both drugs and alcohol, by including that language in the item stem.
General Psychopathology
3. The Patient Health Questionnaire (PHQ-9) is a brief 9-item scale used to determine the severity of depression in medical populations. The PHQ-9 has high reliability across populations. We will not include item #9 that assesses suicidal ideation.
4. The Generalized Anxiety Disorder (GAD-7) is a brief self-report scale that identifies the degree to which an individual may have generalized anxiety disorder. This scale has good internal consistency, convergent validity with depression, stress, and anxiety, and is a valid and efficient tool for GAD screening in clinical and general populations.
Employee Health
5. The CAGE Adapted to Include Drug USE (CAGE-AID) was developed by the John Hopkins Dept of Medicine. It's a brief instrument to measure problematic drug use. The CAGE-AID is designed to be an easy yet effective way for primary care providers to determine if substance abuse exists and needs to be addressed.
7. The Michigan Alcohol Screening Test (MAST), revised is a 22 question instrument to measure problematic alcohol use. One of the most widely used measures for assessing alcohol abuse, the MAST is a questionnaire designed to provide a rapid and effective screening for lifetime alcohol-related problems and alcoholism. The MAST has been productively used in a variety of settings with varied populations.
8. The Short Inventory of Problems- Alcohol and Drugs (SIP-AD) is a clinically tested 15-item measure developed by NIH funded research that assesses severity of problematic drinking and drug usage.

c) You are required to comply with University Policy that states that ALL electronic devices: computers (laptops and desktops; OFFICE or HOME); smart phones; tablets; external hard disks, USB drives, etc. that may hold identifiable participant data will be password protected, backed up, and encrypted. See http://med.stanford.edu/datasecurity/ for more information on the Data Security Policy and links to encrypt your devices.

Provide any additional information on ALL data security measures you are taking. You must use secure databases such as https://researchcompliance.stanford.edu/panels/hs/redcap RedCap. If you are unsure of the security of the system, check with your Department IT representative. Please see http://med.stanford.edu/irt/security/ for more information on IRT Information Security Services and http://www.stanford.edu/group/security/securecomputing/mobile_devices.html for more information for securing mobile computing devices. Additionally,any PHI data on paper must be secured in an locked environment.

By checking this box, You affirm the aforementioned. Y

All assessments, including the screening and two assessment batteries, will be administered via a HIPAA compliant survey administration tool commonly used by Stanford University in its clinical trials (Qualtrics or REDCap). Given the high data protection safeguards embedded within Qualtrics, there is little risk to the subject associated in regards to their privacy and/or confidentiality.

Research material obtained from human subjects will involve behavioral and psychological assessments including self-report questionnaires. All data will be obtained specifically for purposes of this research project. Data that is obtained from the Qualtrics or REDCap assessments

will be stored and protected within Qualtrics or REDCap, and on Stanford Medicine Box. Data that is obtained via Woebot will be encrypted and stored on Amazon Web Services (AWS); Woebot Labs data gathering and storage procedures are compliant with both the Health Insurance Portability and Accountability Act (HIPAA) and the European Union's General Data Protection Regulation (GDPR) compliant. Only members of the research team (PI, Co-PIs, biostatistician, research assistant) will have access to the data.

The Stanford research team will use Stanford encrypted, password protected, and backed up electronic devices (laptops, mobile devices) for this project.

d) Describe how data or specimens will be labeled (e.g. name, medical record number, study number, linked coding system) or de-identified. If you are de-identifying data or specimens, who will be responsible for the de-identification? If x-rays or other digital images are used, explain how and by whom the images will be de-identified.

Each participant will be assigned a unique study ID number that will take the place of any identifying information. Surveys will be done online with individual survey URLs matched to study ID provided to participants. All data therefore will be coded for the large dataset.

No names will be attached to surveys. Study staff is responsible for the coding.

Woebot user data provided to Stanford will be de-identified and linked via study ID to the study assessments we collect via RedCap or Qualtrics and the data will not be shared outside of the Woebot and Stanford teams.

e) Indicate who will have access to the data or specimens (e.g., research team, sponsors, consultants) and describe levels of access control (e.g., restricted access for certain persons or groups, access to linked data or specimens).

The PD and co-investigator and the research team will have access to the study data. All data will be locked or password-protected or both.

f) If data or specimens will be coded, describe the method in which they will be coded so that study participants' identities cannot be readily ascertained from the code.

Each participant will be assigned a unique participant ID number, starting with 001 through 1000, to code data.

g) If data or specimens will be coded, indicate who will maintain the key to the code and describe how it will be protected against unauthorized access.

The codes of names and ID numbers will be accessed by the research team only, stored securely in Qualtrics or REDCap, and/or a password protected file.

h) If you will be sharing data with others, describe how data will be transferred (e.g., courier, mail) or transmitted (e.g., file transfer software, file sharing, email). If transmitted via electronic networks, describe how you will secure the data while in transit.See http://www.stanford.edu/group/security/securecomputing/ http://www.stanford.edu/group/security/securecomputing/. Additionally, if you will be using or sharing PHI see https://uit.stanford.edu/security/hipaa https://uit.stanford.edu/security/hipaa.

Coded data may be sent by secure email settings provided by Stanford.

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Woebot user data provided to Stanford will be coded and linked via study ID to the study assessments we collect via RedCap or Qualtrics and the data will not be shared outside of the Woebot and Stanford teams.

i) How will you educate research staff to ensure they take appropriate measures to protect the privacy of participants and the confidentiality of data or specimens collected (e.g. conscious of oral and written communications, conducting insurance billing, and maintaining paper and electronic data)?

The research staff will all be HIPAA and CITI trained and compliant and supervised by Dr. Prochaska.

12. Potential Conflict of Interest

Investigators are required to disclose any financial interests that " https://researchcompliance.stanford.edu/eprotocol-coi" target="_blank" reasonably appear to be related/li to this protocol.

Financial Interest Tasks

Investigators	Role	Potential COI?	Date Financial Interest Answered	Date OPACS Disclosure Submitted	COI Review Determination
[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
[redacted]	[redacted]	[redacted]	[redacted]		[redacted]

13. Consent Background

13. 1 Consent W-C19 Consent Form

Check if VA related

a) Describe the informed consent process. Include the following.

i) Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)

ii) When and where will consent be obtained?

iii) How much time will be devoted to consent discussion?

iv) Will these periods provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent?

v) What steps are you taking to minimize the possibility of coercion and undue influence?

vi) If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.

Consent will be received via the mobile application wherever and whenever the participants choose and will

take approximately 5 minutes. This will provide sufficient opportunity for the participant to consider whether or not to participate and sign the online consent by mouse, finger, or stylus since there will be no time limit. The online survey platform can obtain electronic signatures. Study staff will not be with the potential participant and there will be no possibility of coercion or undue influence. No children will be recruited.

b) What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See HRPP Chapter12.2 for guidance.

Only English speaking participants will be recruited. The consent form will be readable so those with a hearing impairment will still be able to access it.

c) What steps are you taking to determine that potential participants are competent to participate in the decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent,(iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.

The consent form will only be accessible to those using a mobile application since that is the investigational device. Participants will only include those competent to consent in the very low risk study.

13. 2 Consent — W-C19 Screener Consent Form

Check if VA related

a) Describe the informed consent process. Include the following.

i) Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)

ii) When and where will consent be obtained?

iii) How much time will be devoted to consent discussion?

iv) Will these periods provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent?

v) What steps are you taking to minimize the possibility of coercion and undue influence?

vi) If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.

(i)Study staff will be obtaining the consent via online questionnnaire (Qualtrics or REDCap). (ii)This consent will be at the beginning of the screening questionnaire (Qualtrics or REDCap). Since consent is obtained online, it can be obtained at any location of the participants choosing. (ii)There is no time limit- each respondent can take much time as they want to read through the consent. Reading consent is anticipated to not take more than five minutes. (iv)Since consent is obtained online, the participant may take as much time as they wish to consider whether or not to participate and proceed with the screener. The online survey platform can obtain electronic signatures, and participants can sign the online consent by mouse, finger, or stylus. (v)No incentive for form of coercion is present for the screening process. The study is voluntary; Participants are informed that they can withdraw or choose not to participate at any time. There is no payment for going through the screener. (vi)N/A.

b) What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See HRPP Chapter12.2 for guidance.

We are not recruiting participants who cannot understand English.

c) What steps are you taking to determine that potential participants are competent to participate in the decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent,(iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.

Participants will be reading the consent form before beginning the screener. Participants must be English literate to participate as the questionnaires, consent forms, and Woebot app are only available in English. The participant will have to select "Agree" to participate in the study. Contact information is also provided during consent for the participant to use if they have questions about the study.

14. Assent Background (less than 18 years of age)

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15. HIPAA Background

15. 1 Waiver of Authorization for Recruitment

waiver of authorization for recruitment

a) **Describe the protected health information (PHI) needed to conduct screening or recruitment. PHI is health information linked to HIPAA identifiers. List BOTH health information AND HIPAA identifiers. If you are using STARR, use the Data Privacy Attestation to ensure that your request will match your IRB-approved protocol.**

The following PHI will be collected via online screening through REDCap or Qualtrics. PHI collected: name, phone number, email address, date of birth, gender/biological sex, substance use, health, demographic information, zipcode, IP address (auto collected by Qualtrics), geographic location (auto collected by Qualtrics).

b) Please Answer:

Y **Do you certify that the use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals?**

Y **Do you certify that the research could not practically be conducted with out the waiver?**

Y **Do you certify that you have adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted?**

Y **Do you certify that the research could not practically be conducted with out access to and use of the protected health information?**

c) **Please describe an adequate plan to protect any identifiers from improper use and disclosure.**

Data that is obtained from the Qualtrics or REDCap assessments will be stored and protected within Qualtrics or REDcap. Data that is obtained via Woebot will be encrypted and stored on Amazon Web Services (AWS); Woebot Labs data gathering and storage procedures are compliant with both the Health Insurance Portability and Accountability Act (HIPAA) and the European Union's General Data Protection Regulation (GDPR) compliant. Only members of the research team (PI, Co-PIs, biostatistician, research assistant) will have access to the data. Each participant will be assigned a unique study ID number that will take the place of any identifying information. Surveys will be done online with individual survey URLs matched to study ID provided to participants. All data therefore will be coded for the large dataset. No names will be attached to surveys. Study staff is responsible for the coding. De-identified data may be sent by secure email settings provided by Stanford. Woebot user data provided to Stanford will be de-identified and linked via study ID to the study assessments we collect via REDCap or Qualtrics and the data will not be shared outside of the Woebot and Stanford teams. The PD and co-investigator and the research team will have access to the study data. All data will be locked or password-protected or both. The codes of names and ID numbers will be accessed by the research team only, stored securely in Qualtrics or REDCap. The research staff will all be HIPAA and CITI trained and compliant and supervised by Dr. Prochaska.

d) **Please describe an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.**

The identifiers in the research will be destroyed following publication of the main manuscript.

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16. Attachments

Attachment Name	Attached Date	Attached By	Submitted Date
Woebot Recruitment Flyer	04/27/2020	achieng	
Woebot for Substance Use Disorders - Possible Subreddits	04/27/2020	achieng	
Woebot Branching Logic	04/27/2020	achieng	
Referrals for Substance Use Treatment 12.9.19	04/27/2020	achieng	
Directions installing registering Woebot App	04/27/2020	achieng	
Woebot Crisis Language Response	04/27/2020	achieng	
Erin Vogel's CITI Completion Report	04/27/2020	achieng	
Woebot Security Risk Management Plan	04/27/2020	achieng	
Athena Robinson PHRP Certificate	04/27/2020	achieng	
Pain and Craving Questions to be asked in the bot	04/27/2020	achieng	
Stanford Staffers Listserv Permission	04/27/2020	achieng	
DRAFT NIDA Covid 19 Suppl - New Items - April27_2pm	04/27/2020	achieng	
Reddit Posting for NIDA SUD Phase 1 Study Covid Supplement for IRB Review 5.14.20	05/14/2020	achieng	
Student Wellness Listserv Permission	05/14/2020	achieng	
Covid19 NIDA Application PHS 398_5.05.20	05/14/2020	achieng	
Woebot Listerv Recruitment	05/14/2020	achieng	
Screenshots of Woebot Conversational Pieces	05/14/2020	achieng	
Timeline Flow and Woebot Modules	05/14/2020	achieng	

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Woebot EOT Survey Email Template and Instructions	05/14/2020	achieng	
Woebot Terms of Service	05/14/2020	achieng	
Woebot Privacy Policy	05/15/2020	achieng	
WC19 Scientific Protocol	05/15/2020	achieng	
NIDA DSMB Meeting Welcome Packet- 01.15.20	05/15/2020	achieng	
NIDA DSMB Meeting Agenda 01.15.20	05/15/2020	achieng	
NIDA SUD DSMB Meeting Minutes_01.15.20	05/15/2020	achieng	
Woebot Data Protection	05/15/2020	achieng	
NIDA SUD Phase I DSMB Meeting Agenda - 5.6.2020	05/15/2020	achieng	
DRA #731 Status	05/15/2020	achieng	
WSUDs COVID Screener Questions	05/15/2020	achieng	
Assessment Timeline	05/18/2020	achieng	
NIDA SUD DSMB Meeting Minutes 5.6.20	05/18/2020	achieng	
COVID 19 Clinical Research Review Panel Response	05/18/2020	achieng	
Emailing previous participants	05/19/2020	sfelice	
SUsIRB_IAA_Prochaska_56439_SU signed	05/26/2020	srayate	
Email template for Amazon gift code	05/27/2020	achieng	
NIH_NOA_3R44DA048712-01S1	06/16/2020	achieng	
NIDA_SUD_Flyer_COVID	06/16/2020	sfelice	
Qualtrics Auto Email Templates	06/22/2020	achieng	
thumbnail_woebot-header-01	06/22/2020	achieng	
thumbnail_woebot	06/22/2020	achieng	
thumbnail_woebot-header-02	06/22/2020	achieng	
thumbnail_woebot-header-04	06/22/2020	achieng	
Woebot Phone Script	06/24/2020	achieng	

WC19 Baseline Questions 6.24.20	06/24/2020	achieng	
Woebot Reminder email	06/24/2020	achieng	
WC19 EOT Questions 7.20.20	07/20/2020	achieng	
WC19 4Week Questions 8.12.20	08/12/2020	achieng	
NIDA SUD DSMB Meeting 1.27.21_FINAL	03/25/2021	achieng	
NIDA SUD DSMB Meeting Minutes 1.27.21	03/25/2021	achieng	
AshleyLee CITI Certifications	06/30/2021	achieng	
NIDA SUD DSMB Meeting 6.16.21_FINAL	04/19/2022	gkmurphy	
NIDA SUD DSMB Meeting Minutes_06.16.21	04/19/2022	gkmurphy	

Obligations

The Protocol Director agrees to:

- Adhere to principles of sound scientific research designed to yield valid results
- Conduct the study according to the protocol approved by the IRB
- Be appropriately qualified to conduct the research and be trained in Human Research protection, ethical principles, regulations, policies and procedures
- Ensure all Stanford research personnel are adequately trained and supervised
- Ensure that the rights and welfare of participants are protected including privacy and confidentiality of data
- Ensure that, when de-identified materials are obtained for research purposes, no attempt will be made to re-identify them.
- Disclose to the appropriate entities any potential conflict of interest
- Report promptly any new information, modification, or unanticipated problems that raise risks to participants or others
- Apply relevant professional standards.

Any change in the research protocol must be submitted to the IRB for review prior to the implementation of such change. Any complications in participants or evidence of increase in the original estimate of risk should be reported at once to the IRB before continuing with the project. Inasmuch as the Institutional Review Board (IRB) includes faculty, staff, legal counsel, public members, and students, protocols should be written in language that can be understood by all Panel members. The investigators must inform the participants of any significant new knowledge obtained during the course of the research.

IRB approval of any project is for a maximum period of one year. For continuing projects and activities, it is the responsibility of the investigator(s) to resubmit the project to the IRB for review and re-approval prior to the end of the approval period. A Notice to Renew Protocol is sent to the Protocol Director 7 weeks prior to

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the expiration date of the protocol.

https://stanfordmedicine.box.com/shared/static/qbsi8u8h47qsotxhdpuzz50xlrqa0sgo.pdf Report promptly any new information, complaints, possibly serious and/or continuing noncompliance, or unanticipated problems involving risks to participants or others.

All data including signed consent form documents must be retained for a minimum of three years past the completion of the research. Additional requirements may be imposed by your funding agency, your department, or other entities. (Policy on Retention of and Access to Research Data, Research Policy Handbook, http://doresearch.stanford.edu/policies/research-policy-handbook/conduct-research/retention-and-access-research-data)

APPROVAL LETTER/NOTICE NOTE: List all items (verbatim) that you want to be included in your approval letter (e.g., Amendment date, Investigator's Brochure version, consent form(s) version(s), advertisement name, etc.) in the box below.

Y By checking this box, I verify that I, as the Protocol Director (PD) responsible for this research protocol, have read and agree to abide by the above obligations, or that I have been delegated authority by the PD to certify that the PD has read and agrees to abide by the above obligations.