Study Title: Mobile Technology for Reducing and Preventing Adolescent Suicide

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SPECIFIC AIMS

Suicide is the second leading cause of mortality among children (ages 10 - 14) and adolescents (ages 15 - 24) in the United States (US), and the rates of suicides in these age groups continue to rise (Miron, et al., 2019). Among youth aged 15 to 24, the suicide rate has reached its highest levels in nearly two decades, rising from 8 per 100,000 in 2000 to 11.8 per 100,000 in 2017 (CDC, 2020). From 2007 to 2018, death by suicide of people aged 10 to 19 increased by 56 percent in the US, despite significant national initiatives to reverse this trend (CDC, 2020). The year following a hospital visit for a suicide attempt is an especially vulnerable time period for teens. Death by suicide in this cohort is 50 times more likely when compared to the general population (Hawton, et al. 2015). More specifically, nearly half of all suicide deaths in the year following psychiatric hospitalization occur within the first month after discharge (Deisenhammer, et al 2007). This suggests teens hospitalized for suicide attempts are at great risk for making a second attempt to end their life.

Fortunately, unlike other top ten causes of death among youth (e.g., congenital anomalies, heart disease), suicide is preventable when timely intervention is available (WHO, 2019). However, only a relatively limited number of treatment interventions have been developed for these youth. Rudd et al. (1996) studied the effects of a time-limited intervention targeting suicidal young adults and found that the experimental treatment was more effective than treatment as usual at preventing suicide among the highest risk participants. Rudd and colleagues went on to develop the intervention for adults. Rudd et al. (2015) demonstrated that their intervention, brief cognitive behavioral therapy (BCBT), was effective in reducing suicide attempts by active duty soldiers. In this randomized controlled trial (RCT), which followed soldiers for two years after treatment, patients in the CBT group were 60% less likely to make a suicide attempt than soldiers in the treatment as usual group.

Based on this research, and other similar findings, our company, Oui Therapeutics, LLC, built a product for adults called [redacted] is a suicide prevention app to reduce the risk of suicide among adults. Recently, Drs. David Tolin and Gretchen Diefenbach conducted a feasibility open trial of BCBT in adult inpatients. Their findings suggest that BCBT may be a helpful intervention for adults hospitalized following a suicide attempt. Also recently, Sinyor et al. (2020) examined BCBT in youth hospitalized after an episode of suicidal behavior and despite small numbers, found a significant reduction in suicide behavior in the BCBT group. It is essential to examine whether this approach yields similar reductions in suicide re-attempt risk among adolescents, as well as whether this intervention can be delivered effectively via a smartphone app. We aim to build on their promising findings and extend this line of research to adolescent inpatients by developing a youth adapted version of our smartphone app product [redacted] We will collect pilot feasibility data on [redacted] from this new population.

Specific Aim 1 – Create a beta version o[redacted] for youth (ages 13 - 17). Drawing on our experience in developing and implementing digital applications (i.e. "mobile apps" for Apple/Android devices) that have been shown to increase access to effective care for a variety of conditions (e.g. insomnia, anxiety, substance use) and are now available in benefit packages for over 50 million covered lives nationally, we will prepare the release of a beta version of [redacted] Creation of this beta version will constitute the bulk of the work to be accomplished in our proposed twelve-month Phase I project. [redacted]

Specific Aim 2 – To test the feasibility and acceptability of the beta version of [redacted] in a single-group, open-label trial. Following its creation, we will test the feasibility and acceptability of the Beta Version of [redacted] in a clinical sample of 20 adolescents (ages 13 - 17) who were recently admitted for suicidal ideation with a suicidal plan or report a lifetime suicide attempt. This will be done in a single-site, 16-week, single-group clinical trial. Feasibility and acceptability will be measured with logs and questionnaires.

Anticipated Outcome and Future Directions: [redacted]

BACKGROUND AND SIGNIFICANCE

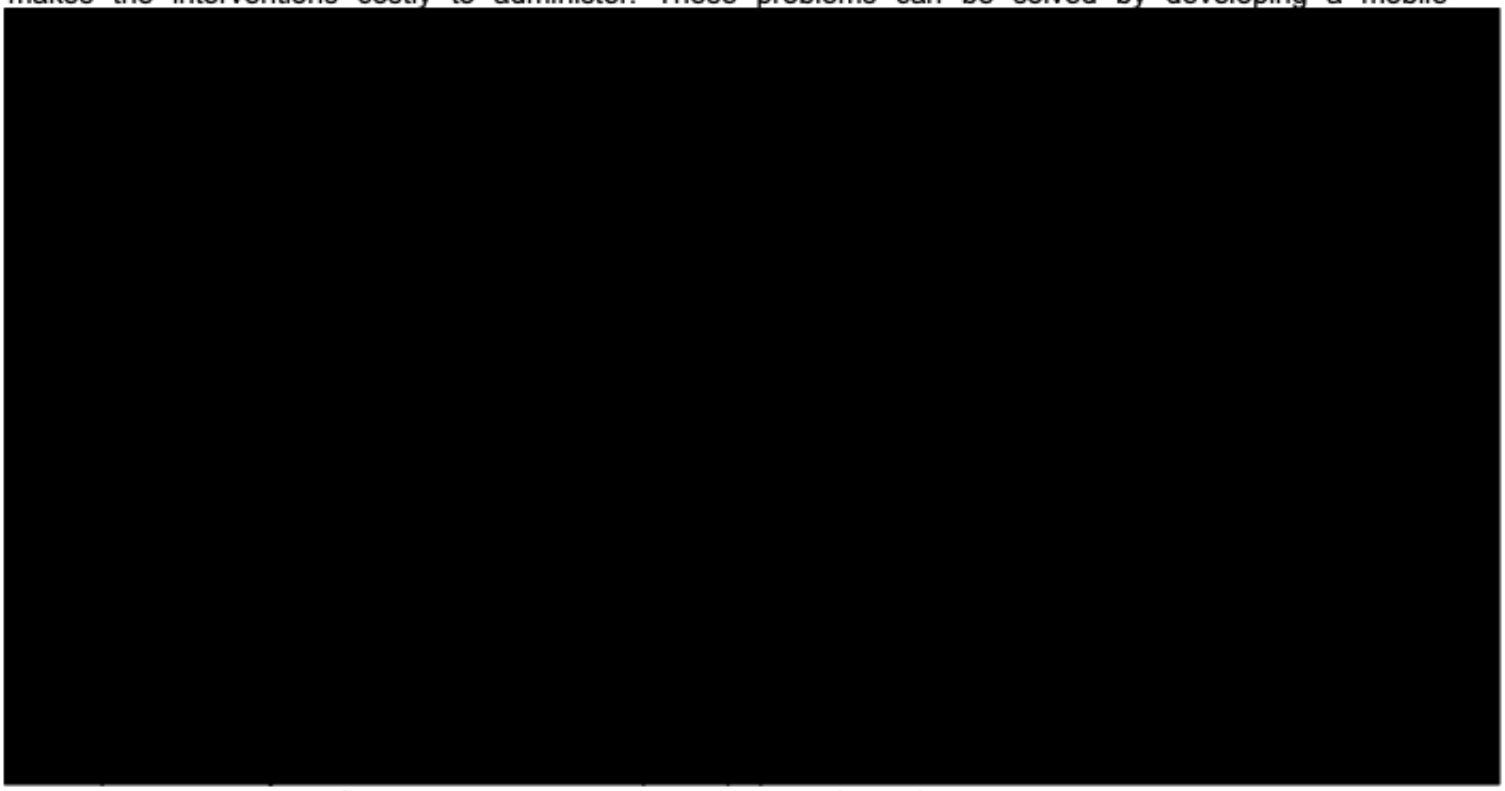
A.1. Suicide is a public health crisis. Suicide is one of the top 10 causes of death in the United States (US). More than 48,000 people died by suicide in 2018 and nearly 500,000 people stayed at a hospital overnight (or longer) due to a suicide attempt (CDC, 2020). There is especially cause for concern among youth: Suicide is the second leading cause of mortality among young people age 10 to 24 in the US, and the rates of suicides in this age group continues to rise (Miron et al 2019). From 2007 to 2018, death by suicide of people age 10 to 19 increased by 56 percent, despite significant national initiatives to reverse this trend (CDC, 2020). Furthermore, chronic or intermittent thoughts of suicide cause significant distress (Nock et al 2013). In addition to the tremendous human toll from suicidal ideation (SI) and suicide attempts, the economic impact of this public health crisis is estimated at more than $93.5 billion per year (Shepard et al 2016).

A.2. The period following hospitalization is one of great risk for suicide. Nearly half of all suicide deaths in the year following psychiatric hospitalization occur within the first month after discharge (Deisenhammer et al 2007). The year following a hospital visit for a suicide attempt is an especially vulnerable time period for teens. Death by suicide in this cohort is 50 times more likely when compared to the general population (Hawton et al 2015). Therefore, teens hospitalized for suicide attempts are at great risk for making a second attempt. Several factors likely contribute to suicide risk after discharge from the hospital. Chief among these is the fragmented and poor transition of care from inpatient to outpatient care.

A.3. The transition from inpatient to outpatient care is poor. Following discharge from inpatient or emergency units, patients often have to wait days, weeks, or months to access mental health services due to limited availability of resources (Hester 2017). For some youth, the hospital is the only setting where they receive care, but the majority of youth are likely to engage in outpatient treatment after discharge (Yen et al 2014). Despite engagement in outpatient treatment, previous research has indicated that suicide attempts are frequent and rates of readmission to more intensive levels of care (from outpatient care) are high. A major reason for this is that when youth are finally able to access care, the quality of care received varies and almost never includes care directed specifically at suicide prevention which was developed by experts in that field. Thus, there is a need to improve outpatient treatment to reduce rates of suicide attempts and decrease the high rates of use of intensive care among youth. Moreover, given the high volume of patients presenting to hospitals and the heightened risk of suicide shortly after discharge, the hospital is an opportune location to initiate suicide prevention interventions that can be implemented with high fidelity.

A.4 CBT has been adapted for the treatment of individuals at risk for suicide, with good results. Given the variable nature of symptomatology associated with suicide risk, particularly SI, a reasonable marker of lower suicide risk following treatment is a reduction in suicide attempts during the follow-up period (Stanley et al 2018). Two CBT interventions have been proven to be efficacious in helping prevent reattempts at suicide: Brief CBT (BCBT; Rudd et al 2015) and Cognitive Therapy for Suicide Prevention (CT-SP, Brown et al 2005). **BCBT** is 12- sessions and is also implemented in three phases. Phase 1 consists of assessment, cognitive behavioral conceptualization, crisis response planning (CRP), and basic emotion-regulation skills. Phase 2 emphasizes cognitive strategies to reduce vulnerability to suicidal behaviors. Phase 3 focuses on relapse prevention. Rudd et al.'s (2015) RCT recruited individuals with a suicide attempt or clear SI and showed a 60% reduction in suicide attempts relative to controls at 18-months. **CT-SP** has been developed using a 10-session protocol consisting of three phases: early (engagement, risk assessment, safety planning, means restriction), intermediate (cognitive restructuring and coping skills training) and later (relapse prevention). Brown et al.'s (2005) RCT recruited individuals following a suicide attempt and showed a 50% reduction in suicide attempts relative to controls at 18 months. Two recent trials testing elements of BCBT and CT-SP, the Attempted Suicide Short Intervention Protocol (Gysin-Maillart et al 2016), and CRP (Bryan et al 2017) provided even more support for psychological treatments that directly target two key mechanisms contributing to suicidality: emotion regulation and cognitive flexibility. Additionally, CRP was associated with significantly faster decline in SI as measured by the Beck Scale for Suicide Ideation (BSS; Beck et al 1991). Recently, Sinyor et al. (2020) examined BCBT in youth hospitalized after an episode of suicidal behavior and despite small numbers, found a significant reduction in suicide behavior in the BCBT group. In light of these collective findings, several procedures pulled from BCBT and CT-SP have been recommended for standard care with suicidal patients by the National Alliance for Suicide Prevention (2018). However, despite existence of these interventions, some shown to be efficacious nearly 15 years ago (Brown et al 2005), and recommendations by experts, neither are widely integrated into standard care for suicidal patients (Ghahramanlou-Holloway et al 2014).

A.5. CBT is poorly implemented with high fidelity in community settings. Several factors limit the rapid, system-wide uptake of existing CBT interventions: First, to deliver these interventions face-to-face, substantial training and ongoing supervision is required. Second, these interventions require substantial time commitment from patients; sessions last approximately 60 minutes and often necessitate a patient taking time off from work in addition to travel time. Third, the high level of education of therapists (masters or above) makes the interventions costly to administer. These problems can be solved by developing a mobile



A.7. **Adolescent Suicide Prevention Treatment.** The field of adolescent suicide prevention research has changed substantially in the past five years. Up until recently, it could be stated that there were no well-established treatments (i.e., studies that have shown positive results in two independent randomized controlled trials) for suicide ideation or suicide attempts (King et al., 2018). However, strong support has emerged for interventions guided by the cognitive behavioral model, with the strongest evidence for Dialectical Behavior Therapy (DBT).

In two independent studies with adolescents, DBT (vs. active control condition) significantly reduced self harm (suicide attempts and non-suicidal self-injurious behavior) (McCauley et al., 2018; Mehlum et al., 2014). Additional interventions that are guided by a cognitive behavioral model have been shown to be effective for suicide prevention among youth. Compared with treatment as usual (TAU), Integrated Cognitive–Behavioral Therapy (I-CBT, Esposito-Smythers, Spirito, Kahler, Hunt, & Monti, 2011) for adolescents with comorbid suicidality and substance abuse significantly reduced suicide attempt rate. SAFETY, a DBT-informed cognitive–behavioral family treatment, has also been shown to reduce suicide attempt risk over time and lower rates of suicide attempts, compared with TAU (Asarnow, Hughes, Babeva, & Sugar, 2017). Notably, Dr. Cheryl King's psychosocial intervention, youth nominated support team, demonstrated that 11 to 14 years after participating in the intervention, suicide attempt rates were significantly reduced (King et al., 2019).

While the interventions reviewed are remarkable in that they have significantly impacted suicide ideation and/or attempts, their uptake has been slow and scaling has been challenging. This is because of the more intensive involvement required on the part of the family, therapist and the patient. For example, both I-CBT and SAFETY use a two-therapist model, with one therapist working with youth and the other with parent/family. Asarnow & Mehlum (2019) note that these effective interventions may be costly and time intensive. Also, the level of intensity required for these interventions may not be required for all adolescents. Thus, Iyengar et al. (2018) advocate for a stepped care approach.

Effective digital interventions may be a key component of a stepped care approach for adolescents as both stand-alone programs and as adjunctive components to more comprehensive interventions for youth who

need it. Kennard et al. (2018) published results of an RCT testing a face-to-face intervention supplemented by follow up tools delivered digitally. The intervention, ASAP, is initiated on an adolescent inpatient unit to reduce suicide attempts following hospital discharge. In the study, there was a 3-hour, face-to-face intervention implemented on the inpatient unit. The session consisted of four therapist-delivered modules—chain analysis and safety planning; distress tolerance and emotion regulation; increasing positive affect through savoring and switching; and review of the skills, safety plan, and app. The 3-hour session was followed by use of the BITE app, which prompted youth to use skills taught in the initial training. This study did not observe significant treatment effects for suicide attempts or suicide ideation, likely because it was underpowered. The observational data were encouraging, as attempts in the ASAP condition were half those of the control condition. These findings provide support for the development of [redacted] because ASAP's preliminary data suggests that youth will use an app that is designed for suicide prevention. Additionally, similar to ASAP, [redacted] is guided by a cognitive behavioral approach and uses an app to prompt youth to practice skills.

[redacted]

INVESTIGATIVE TEAM

Our team is comprised of experts who have built clinically, and financially successful digital interventions and our consultants include several NIH funded researchers in the field of suicide prevention. **Seth Feuerstein, MD, JD**, will be the principal investigator. Dr. Feuerstein has 5 years of experience working as the Chief Innovation Officer at Magellan Health. Here he oversaw the development of effective business and clinical programs that leverage technology in several areas. Specifically, Dr. Feuerstein led the development of a mobile technology program to address 90 percent of behavioral health disorders, this digital care platform was designed to help Magellan and its customers, and their collective members achieve better health, better care, and lower costs. With its acquisition of Cobalt Therapeutics (a company founded and led by Dr. Feuerstein), Magellan delivered digital CBT programs to address conditions such as anxiety, insomnia, depression, OCD and substance use. Given this experience, Dr. Feuerstein brings critical experience and understanding from the perspective of third-party payers with respect to the emerging field of digital therapeutics. As the Principal Investigator, Dr. Feuerstein will assume primary responsibility for all aspects of the research project and will assure that milestones are met in a timely manner. **Dr. Patricia Simon**: Dr. Simon is an adolescent substance use treatment and prevention expert. Because of the high rate of co-occurrence between suicidal ideation/attempts and substance use problems, Dr. Simon has been collaborating with suicide prevention experts and has sought and received extensive training in suicide prevention. From 2004-2007, while working as a Substance Abuse Undergraduate Research Fellow on the Drug Abuse Treatment for Adolescents (DATA) study at Duke University Child and Family Study Center, Dr. Simon gained early exposure to suicide prevention principles, treatment development, and suicide prevention study start up activities when the Treatment of Adolescent Suicide Attempters (TASA) study (which was referenced by the reviewers as a key study) was launched at the Center. Her mentors at the time were Drs. John F. Curry, Ph.D., Sara J. Becker, PhD, and Alfiee Breland-Noble, PhD. Based on these early experiences with adolescent suicide prevention protocols, Dr. Simon was hired from 2008 to 2010 to work for Dr. John R.Z. Abela, Ph.D. on a study of child and adolescent depression (that also involved assessing their parents). Dr. Simon's role was to assess depression and suicide risk and implement suicide prevention protocols among high-risk participants. From 2012 to 2013, Dr. Simon built upon her experiences with suicide risk assessment and prevention by training with Drs. Courtney Bagge, Ph.D. and Matt Tull, Ph.D. at the University of Mississippi Medical Center. She received specific training in the implementation of depression treatment and suicide prevention protocols in inpatient and outpatient settings and delivered those interventions in the referenced settings. Based on these experiences, Dr. Simon was hired as Vice President for Clinical Affairs at Oui Therapeutics, LLC, a company formed to prevent suicide. From 2018 to 2020, Dr. Simon has worked at Oui Therapeutics, LLC to develop digital applications for proven face-to-face suicide prevention protocols, this includes working closely with Dr. Cheryl King to develop the initial mock-ups for translating her youth nominated support team into a digital application. Thus, Dr. Simon has nearly 10 years of adolescent and young adult suicide prevention

experience. Dr. Simon has also published more than 30 peer-reviewed papers focused on adolescent mental health and has previously served as PI on 2 NIH grants conducting research on adolescents (F31DA030040, R03CA245991). **Multiple PI Leadership Plan**: Drs. Feuerstein and Simon will provide oversight of the entire program and development and implementation of all policies, procedures and processes. In these roles, Drs. Feuerstein and Simon will be responsible for the implementation of the Scientific Agenda, the Leadership Plan and the specific aims and ensure that systems are in place to guarantee institutional compliance with US laws, DHHS and NIH policies including human research, data and facilities. Dr. Feuerstein will be responsible for the technical requirements of executing Aims 1 and 2. Dr. Simon will oversee Aims 1 and 2 to ensure that study procedures are developmentally appropriate. Dr. Feuerstein will serve as contact PI and will assume fiscal and administrative management including maintaining communication among PI s and key personnel through monthly meetings. Dr. Feuerstein will be responsible for communication with NIH and submission of annual reports. Publication authorship will be based on the relative scientific contributions of the PIs and key personnel. Conflicts between the PIs will be resolved by Oui's Senior Scientific Advisor (Benjamin "Steve" Bunney, MD). **Brian Keenaghan** is also a cofounder at Oui Therapeutics and Vice President of Operations. For this project, Mr. Keenaghan will serve as a research coordinator. Mr. Keenaghan has worked productively on previous projects with Drs. Feuerstein and Bunney in developing CBT-based mobile apps at Cobalt and Magellan, including RESTORE for sleep problems and insomnia, which is currently available from both the Apple iOS and Google Play mobile app stores. This app has been translated into 3 languages and has been used commercially by several different health insurance companies, and pharmacy benefit management companies, including Magellan Health. Mr. Keenaghan is well trained in coordinating large scale projects as well as CBT; before Cobalt he worked at the world-renowned Beck Institute CBT training center. **Benjamin S. Bunney, MD** is the former chair of psychiatry at Yale School of Medicine and cofounder of Cobalt and Oui Therapeutics. Dr. Bunney will serve as a co-investigator on the proposed project; given his extensive experience as an administrator of the clinical services at a large academic medical center, Dr._Bunney is ideally situated to provide input on the perspectives of administration in the tremendous challenges of caring for patients at risk of suicide. Dr. Bunney's role will hence be to advise on ways that the product might interface with healthcare systems in order to facilitate its potential adoption into clinical practice. **Dr. Cheryl King**: Dr. King is a clinical scientist and Director of the Youth and Young Adult Depression and Suicide Prevention Research Program in the Department of Psychiatry at the University of Michigan. She has a longstanding research focus on improving screening, risk assessment, and intervention strategies for adolescents and young adults at elevated risk for suicide. She also has a strong history of collaborative interdisciplinary research and received a NIMH Mid-career award for focused research on the development of interventions for youth and young adults that are guided by health behavior models. This award also supported her expanded involvement in the mentorship of intervention researchers. Dr. King has conducted NIMH- and CDC-funded studies focused on screening and intervention, including multiple randomized intervention trials, which have resulted in a number of significant contributions pertaining to intervention effectiveness. These include a study of long-term mortality outcomes associated with the Youth-Nominated Support Team (YST) intervention for adolescents. She is currently a PI of several NIMH-funded collaborative studies: Emergency Department Screen for Teens at Risk for Suicide (ED- STARS), 24-Hour Risk for Suicide in a National Cohort of Adolescents (Warning Signs), and Electronic Bridge to Mental Health for College Students (eBridge). Dr. King's substantial experience with intervention science and, more specifically, with the development and implementation of YST and a web-based intervention make her highly qualified for being a consultant on this project. **David Tolin, PhD** is Director of the Anxiety Disorders Center at Institute of Living (IOL) at Hartford Hospital (HH) and Adjunct Professor of Psychiatry at Yale School of Medicine. He is President of the Association for Behavioral and Cognitive Therapies, and Past-President of the Clinical Psychology Division of the American Psychological Association. Dr. Tolin will serve as co-investigator on the proposed project and site PI for the feasibility open trial. Given his expertise in cognitive behavioral intervention and experience with previous trials of BCBT in an inpatient setting, he is well-suited to be responsible for provision of scientific input and project management oversight of the clinical team at the Hartford Hospital sites. **Gretchen Diefenbach, PhD** is Senior Scientist at the Anxiety Disorders Center at IOL at HH and Adjunct Assistant Professor of Psychiatry at Yale School of Medicine. Dr. Diefenbach will serve as co-investigator on the proposed project. She has been principal investigator and co-investigator on several NIH-funded clinical trials. She is thus, well-suited to be responsible for the overall supervision and administration of the feasibility study, coordinating interactions with patients and the clinical team at the IOL site. She will also be responsible for research

summary reports, overseeing recruitment and enrollment and the execution of other research related tasks at IOL. Since this IRB approval will only cover the feasibility open trial, Drs. Tolin and Diefenbach are the only investigative team members listed as study personnel on the IRB application. For the feasibility open trial, Oui will not have direct contact with participants. Oui will provide technical support if needed, communicated by way of IRB-approved study staff at the ADC. Coded data from the feasibility open trial will be shared with Oui through a secure data transfer system (e.g., REDCap or password protected file sent via secure e-mail). In order to download the app, the participant will need to register directly with Oui. No PHI is required for app registration and download. The only data collected directly through the app is number of log ins and number of treatment modules completed. Oui's data and security for user information is detailed in the Data Security and Resource Sharing Plan section below. Oui has also signed a Business Associate Agreement with HHC (see attached).

INNOVATION

Several aspects of this application are novel. First, in the wake of the FDA's new guidance (2017) on mobile applications, this project attempts to capitalize on this guidance to address a great unmet need (reduction of youth suicide attempts). We are not aware of any other mobile technology attempting to address this issue in this way for youth. Second, the proposed project will lay the groundwork for a large, randomized clinical trial (RCT) powered to detect differences in rates of suicide attempts among youth recently discharged from a psychiatric hospital. Whereas most clinical trials in depression and related disorders are powered to detect differences in symptom severity or SI as measured by clinical rating scales, the next line of research following the successful completion of this project would use suicide attempts as a primary outcome. Third, the current project will involve feedback from multiple stakeholders, including patients, providers, administrators, and third-party payers. By considering the needs and perspectives of these various stakeholders, such an approach greatly enhances the likelihood that a clinically successful intervention will be adopted into clinical practice. Some additional innovative aspects of this project are outlined below. Shifting Clinical Practice with a Novel Digital Approach to Suicide Interventions: To date, there has only been one published study examining the effects of digital tools for suicide prevention, ASAP. It examined suicide attempts and suicide ideation among adolescents (Kennard et al., 2018). In this intervention, the therapist provides all the training live, on an inpatient unit, and an app is used to prompt patients to use the learned skills while they are off the unit. The study observed small treatment effects that were not statistically significant. [redacted]

[redacted]

APPROACH

The goal of this Phase I application is for Oui Therapeutics, LLC to collect feedback and further develop mobile health technology for mental health research and practice. Specifically, this project will focus on refining and further developing mobile technology – [redacted] designed to help reduce the risk of suicide. We will work with a panel of experts (see Section B.1.1.) to review the Alpha Version of [redacted] for adults and to adapt the existing content for youth. We will then build a Beta Version, conduct feedback sessions, and iteratively refine a novel delivery system for CBT principles for SI. Specifically, the content of [redacted] which are well tested and published face-to-face delivered treatments that have never previously been developed as an app for adolescents. Successful execution of this Phase I will generate and refine a new (beta) version of [redacted] that is ready to be tested for efficacy with discharging adolescent patients who were admitted for SI or suicide attempts in a RCT. Our approach to developing [redacted] as a novel digital intervention for youth is based on the Stage Model of Behavioral Therapy Research developed at Yale in collaboration with NIDA (Rounsaville, Carrol & Onken, 2001). Dr. Simon learned about this model while working on an adolescent treatment study at Dr. Kathleen Carrol's Psychotherapy Development Center (Simon et al, 2015). In this model, stage 1 development of a novel treatment requires a strong theoretical framework. Consistent with this model, [redacted] is strongly influenced by a cognitive behavioral framework (Beck, 1979). The theoretical basis for cognitive behavioral therapy (CBT), generally, is well-established and CBT has been used to treat a number of conditions among adolescents including anxiety, depression, and substance use (Charmaine et al., 2016, Fadus et al., 2019, and Klein et al., 2007). Accordingly, in a recent systematic review of randomized controlled trials targeting suicide attempts and self-harm among adolescents, Iyengar et al. (2018), noted that after collapsing across different variations of CBT, CBT is the only intervention with replicated positive impact on reducing self-harm in adolescents. BCBT's specific cognitive behavioral framework is guided (in part) by the understanding of the suicide mode. This framework supports targeting risk and protective factors (e.g., emotion regulation, patterns of problematic thinking) that have been identified in the empirical literature to prospectively predict suicide attempts among adolescents (Yen et al., 2013, Wichstrøm et al., 2000). Thus, [redacted] builds on a strong theoretical framework. The potential utility of that framework is supported by prospective observational studies (Yen et al., 2013, Wichstrøm et al., 2000) and the preliminary findings [redacted] We believe this is a strong foundation for building a novel intervention.

We do not report preliminary data for the adult version of [redacted] because we have only recently launched the trial. Nevertheless, the early data we have suggests it is feasible to deploy [redacted] on an inpatient unit with adults and that users like the app. We have enrolled five out of fifteen patients at Yale New Haven Hospital. We present some information about patient progress and participant (patient/clinician) feedback below. Note, the five patients started treatment at different times and are therefore at different points in treatment progression. To date, no participants have dropped out.

- All five adult participants have completed two or more sessions.
- [redacted]
- Four participants have reached the point where it is time to participate in follow-up calls with research team to report on progress and complete ongoing screening. Of those four, three of them have reported improvements on the Patient Health Questionnaire (PHQ-9), a screening tool for depressive symptoms including one question related to suicidality.
- Patients have given the following qualitative feedback: "the process of downloading the app and setting up the account was easy", "the module was easy to follow", "liked how the lessons get (progressively) longer, more in-depth, and more interactive. "

- Clinicians have given the following qualitative feedback: "the platform has a beautiful interface that is easy to navigate"

[redacted] Patients will complete [redacted] onboarding, during their inpatient stay with an aim to schedule the session within two business days before their discharge. In the event that an onboarding session could not feasibly take place while the participant is on the inpatient unit, the participant may complete the onboarding session with study staff on an outpatient basis within 2 business days after their discharge. We expect the remaining [redacted] sessions to be completed in an outpatient context. Each session covers therapy components and includes a variety of digital features. Videos can be an effective tool in teaching what can seem like complicated or complex concepts. [redacted] incorporates videos into sessions. The videos are designed to 1) prompt the working memory of patients (i.e. users) to accept, process, and send to long- term memory the most crucial information; 2) impact engagement; and 3) promote active learning. The videos are embedded within the Chat Thread in a context of active learning by using guiding questions, interactive elements, and associated homework assignments. Other features are designed to reinforce skills and increase adherence to the digitally delivered therapy. [redacted] *Sessions*. The patient completes onboarding with assistance from their clinician who instructs the patient to complete one session to two sessions each week on their own. After each session is completed, the patient will be encouraged to practice what they've learned before the next session unlocks. [redacted] designed this way to enable the patient to put into practice what they have learned from each session. [redacted] keeps track of which sessions have been completed and, once a session has been completed, patients can go back and repeat it as often as they wish, but the focus is on moving the patient forward. The sessions vary in length from 10 to 45 minutes. Each digital session contains similar patient-facing features. The Main Navigation Icons are accessible throughout the [redacted] patient user experience. The primary content delivery feature is a chatbot which is driven by an ongoing Chat Thread and delivers various elements (i.e. support features and tools) to guide the patient through activities progressively introduced and practiced throughout the twelve sessions. Involvement of Parents in [redacted]: During the development process, our experts will discuss which adaptations are required of the software platform to better serve adolescents. Given that our participants are minors, one developmental consideration will be the role of parents (and other caring adults). While there is evidence from face-to-face interventions that suggests it is helpful to include parents in the suicide prevention process, it is unclear that parents in the inpatient setting will engage with these interventions. Specifically, Kennard et al. (2018) noted that it was difficult to get family participation in the inpatient context. Thus, our approach to adding parent-facing features will be based on careful consideration of the stressors facing parents (and families). We will have several whiteboard sessions with all applicable stakeholders to map out a realistic workflow for parent involvement. Some examples of adaptations that can be explored in consultation with our experts and with feedback from parents and adolescents include: Inclusion of a space in the digital crisis response plan (aka safety plan) to include a parent/caring adult as a contact, creating a parent version of our clinician dashboard that will allow parents to track participant progress, creation of parent specific video content to support the family's onboarding to the treatment and other evidence-based approaches. In selecting features, we aim to strike a balance between parental support and adolescent autonomy. We will have discussions regarding which parent features will be the default for all participants and which parent features can be turned off based on adolescent preferences. Please note that our team includes Dr. Cheryl King whose work includes adults in the care of at-risk teens. She is widely published and her consultation is incorporated into our plans. Use of Measures: *Qualitative User Experience Measures*. We will use the qualitative data to develop a better understanding of the key themes we want to follow up with in the product development process. The leads of Oui's product, engineering, and clinical teams will each read the qualitative feedback and organize the feedback based on recurring themes. Their reports will be combined and sorted by themes that are consistent across most readers versus those that are infrequent. Next, we will have a meeting to develop a prioritized list of themes. Decisions on which themes to pursue will be based on their relative importance and the feasibility of addressing them. In the past, we have

found that it is most productive to address no more than 3 themes during each product cycle. Thus, we will begin the product iteration process with the top 3 themes identified. In addressing these three themes, we will conduct more user research (e.g., user interviews), diving more deeply into those themes to better understand what problems users are facing, or what opportunities there are to improve our app. In these interviews, we will try to mirror the language used by respondents from the original qualitative feedback. The goal is to confirm or modify what was expressed in the original qualitative feedback. Through this process, we will develop a better understanding of the themes, and start developing product features that address each of the themes, prioritizing on what would best optimize our organizational metrics. After a round of sharing the prioritized feature list with both internal and external stakeholders, we will then add the features into the product queue for engineering to build.

B.1. Specific Aim 1 – Create a beta version of [redacted]

B.1.1. Alpha [redacted] Review. We assembled an expert panel of suicide prevention, adolescent mental health, inpatient site, digital health, and software development experts to deliver evaluation reports on Alpha [redacted] and recommend adaptations of the Alpha [redacted] for adolescents. Given that the targets of [redacted] are minors, our exerts will also consider features that may be needed to support involvement of parents/guardians. Our assembled team includes **Micheal David Rudd, PhD, ABPP, Craig Brian, PsyD, David Tolin, PhD, Gretchen Diefenbach, PhD, Patricia Simon, PhD, Seth Feuerstein, MD, JD, Benjamin "Steve" Bunney, MD, Leng Lee, DPhil and Brian Keenaghan, MS** (see biosketch and letters of support for review members). **Drs. Rudd and Bryan** (consultants) will contribute suicide prevention expertise. They will dedicate 40 hours to independently evaluating Alpha [redacted] fidelity to the BCBT, and CRP interventions they developed and tested with suicidal patients (Rudd et al 2015; Bryan et al 2017). They will also advise the team at Oui on ways to enhance the usability and patient-user experience. **Dr. Simon** (11% effort) will leverage her adolescent mental health expertise to evaluate the Alpha [redacted] appropriateness for adolescent users by examining language, activities, and methods to address safety. **Drs. Tolin** (5% effort) **and Diefenbach** (10% effort) will leverage their inpatient unit expertise to evaluate the Alpha [redacted] for workflow issues that would need to be addressed before and after the feasibility study. Note, their ongoing review of the resulting beta version [redacted] during the feasibility trial will assist with preparation of a future larger trial. **Drs. Feuerstein** (11% effort)**, Bunney** (11% effort)**, Simon, and Mr. Keenaghan** (11% effort) will leverage digital health expertise to independently evaluate how to integrate the feedback from all experts. The goal is to produce a product that not only provides a scientifically accurate experience, but also an enjoyable user experience. More clearly, we expect our experts to provide feedback on the clinical principles that need to be integrated, and it will be up to the digital health experts to determine the best digital approaches to realize the clinical principles. **Drs. Bunney and Simon** will be responsible for reviewing all the video content included in Alpha [redacted] drafting comparable scripts for adolescent actors and coordinating the filming of those scripts. **Dr. Lee** (software development expert; 8% effort) will work with Oui's engineering team to evaluate the technical feasibility of the updates requested by the digital health experts and recommend modifications. **Mr. Keenaghan** will coordinate the request and gathering of evaluation reports from the suicide prevention experts, adolescent health expert, and digital health experts to share with the software development expert. This process of review will be iterative, with the software development expert and digital health experts sending back their recommendations to all experts for feedback.

MILESTONE 1. *Completion of Alpha [redacted] Review within 30 days.*

B.1.2. Beta Version Development. Beta Version Development for this project will be orchestrated by the Oui development team (including four team members identified as Other Personnel in the Budget Justification) who operate in 30-day development cycles (also called sprints). The Oui development team is a collection of individuals working together to deliver the requested and committed product increments (or iterations). Within the sprint, our development team (see Other Personnel in Budget Justification) will build the Beta [redacted]

MILESTONE 2. *Completion of Beta [redacted] within 30 days.*

B.2. Specific Aim 2 – To test the feasibility and acceptability of the beta version of [redacted] in a single-group, open-label trial.

B.2.1. Primary Objective. The primary objective of the feasibility portion of the project is to assess the feasibility, and usability of [redacted] to deliver targeted CBT to adolescent patients recently hospitalized for SI or suicide attempts. The secondary objectives of this study are to assess the effects on SI and behavior in a

pre/post design of [redacted] with adolescent patients being discharged from a hospital.

B.2.2. Endpoints. Consistent with the primary objectives of assessing feasibility, and usability of the intervention, the primary endpoints of this study will be to measure rates and descriptions of recruitment, attrition, data collection, study resources, intervention delivery and acceptability. Hence, our data for this Aim will be descriptive in nature. Formal statistical comparisons will not be performed. Our study will hence focus on process, consistent with a feasibility study. Semi-structured interviews will be conducted by a mental health professional with patients via telephone (according to the Timeline in the Human Subjects and Clinical Trials Information section). Interviews will be recorded digitally for internal use by ADC staff only (e.g., rater training and interrater reliability reviews) and will not be shared with Oui, Therapeutics. Study data will be entered into REDCap. We will use the System Usability Scale (SUS), the Utility of Techniques (UT) questionnaire and also conduct a semi- structured user feedback interview to systematically capture usability and accessibility.

B.2.3. Usability and Acceptability. The SUS is a valid and reliable, 10-item measure that can be used to effectively differentiate between usable and unusable systems among adolescents and adults (Dexheimer, et al., 2017; Brooke, 1996). Sample items are "I think that I would like to use this app frequently" and "I felt very confident using the system." Responses are rated using a 5-point (strongly disagree to strongly agree) Likert scale. Scores range from 0 to 100. A score of 68 is the minimal indicator of usability.

B.2.4. User Feedback Interview Questions. Participants and parent/guardians will be asked to give their feedback about experiences using the app and any suggestions for improving the app. The Utility of Techniques (UT) questionnaire will determine perceived helpfulness of the strategies taught in [redacted] The questionnaire will ask about each component of [redacted] separately. For each [redacted] session, participants will be asked: Did you use the skills presented in this session? Which ones? Were they helpful?

B.2.5. Secondary Endpoints. Diagnostic interviews will be conducted with each participant with the **Mini International Neuropsychiatric Interview Neurocognitive for Children and Adolescents (MINI-KID),** a widely used, structured diagnostic interview that will be used to verify diagnosis at the screening visit (Sheehan et al 2010). Secondary endpoints will consist of the following measures, assessed using a within-group comparison, over time: **1) Suicidal ideation.** The Suicide Ideation Questionnaire (SIQ) is a 30 – item self or clinician administered instrument used to measure the current intensity of patients' specific distress and suicidal intent, which has been validated for use with adolescents (Pinto et al 1997). Score range is 0-180, with higher score indicating higher intensity. **2) Suicide attempts and other behaviors.** This outcome will be assessed via the Columbia Suicide Severity Rating Scale (CSSRS), which was designed to classify suicide attempts, aborted suicide attempts, and other suicidal behaviors and has been validated for use with adolescents (Gipson et al 2015). 3) Depressive symptoms. The Patient Health Questionnaire (PHQ-9) is a 9-item self-report form to assess the severity of depressive symptoms that has been widely used in practice and research and validated for use with adolescents. This will be used throughout the study to assess severity of any depressive symptoms each subject is experiencing (Richardson et al 2010).

B.2.6. Participant Remuneration for follow-up sessions. All participants will be paid $20 for completing each post-discharge assessment (weeks 1, 4, 8, 12, and 16; $100 total) and a $25 bonus for completing all assessments. Adolescents and parents/guardians will be paid separately, with separate ClinCards, for their participation (maximum $125 each). Data from parent/guardians will continue to be collected in cases where participants reach age of maturity during study participation so long as the child continues participation in the study as an adult (i.e., signs adult informed consent form). Parent/guardian date of birth is required in order to register the ClinCards to the parent/guardian. This information will be collected during the consenting process. Payments will not be prorated for partial completion of assessments. Sufficient funding has been budgeted for this portion of the project (see Budget Justification).

B.2.7. Inclusion Criteria. Qualified subjects will meet all of the following criteria:

Patients of any gender, age 13-17 years
Inpatient psychiatric patients who have attempted suicide (lifetime) or have documented SI and a plan to harm themselves at admission
Understand written and spoken English
Own an iPhone with iOS 11 or higher, or Android with OS 8.1 or higher
Willing and able to complete enrollment procedures
Parent/guardian (and youth) able to understand the nature of the study and provide written informed consent (assent for youth)
Willing to agree to release of information to their parent/guardian and providers when clinically indicated.

B.2.8. Exclusion Criteria. Subjects who meet any of the following criteria are disqualified from this study:

Patients with active psychosis
Patients experiencing substance withdrawal

Currently enrolled in other treatment studies for the symptoms and behaviors targeted
Patient unwilling or unable to wear mask during in-person study procedures
Patients who, in the judgment of the investigator, would have an unfavorable risk/benefit profile with respect to [redacted]
Any other psychiatric or medical condition (e.g., intellectual disability) or custody arrangement that in the investigator's opinion would preclude informed consent/assent or participation in the trial.

B.2.9. Safety Evaluations. Adverse events (AEs) will be assessed at each study visit and will be reported according to Policy 910. AEs will be assessed with the questions "Have there been any changes to your physical health since the last study visit (or "start of the visit" if it is the first study visit)" and "Have there been any changes to your mental health since the last study visit (or "start of the visit" if it is the first study visit)". Assessments will be carried out throughout the study to help participants in need of more extensive support know when to contact their usual care provider and be guided to crisis contact services.

MILESTONE 3. *Completion of the feasibility study within 6 months.*

B.2.10. Data Processing and Analysis Plan. Data processing and analyses will be completed within 60 days and will be primarily descriptive. Data analyses will address the outcomes relating to the feasibility of [redacted] and study procedures. Data collected will be used to determine whether revisions should be considered before proceeding to a controlled trial.

MILESTONE 4. *Completion of Data Processing and Data Analysis within 2 months.*

B.2.11. Rationale for Number of Subjects. We will recruit 20 youth age 13-17 years who complete enrollment in the [redacted] app. Expecting 10% attrition rate before completing enrollment in the [redacted] app we will consent 22 youths to reach our target enrollment number of 20. Means, medians, ranges, and standard deviations for the length of time taken for patients to work through the intervention and for patients to complete the eligibility interview, baseline, post-treatment (8 weeks) and follow-up (12 and 16 weeks) assessments will be reported. In addition, means and SDs will be reported for the length of time it takes project personnel to administer the data collection procedures from invitation through treatment. These data will be used to assess the feasibility of the intervention and study procedures. They will also be used for formal power calculations to design an adequately powered RCT in a subsequent project.

TIMELINE

	Screening Period [a, f]	App Testing Period					Follow-Up Period	
Week(W)	W0	W1 [b]	W1-3	W4 [b]	W5-7	W8 [b]	W12 [b]	W16 [b]
Informed Consent	X							
Participant Information Sheet [c]	X							
Medications at Discharge (from medical record)	X							
Medication history form (parent report)		X		X		X	X	X
Research team phone call with outpatient provider		X						
Enrollment i[redacted]	X							
Mini-international neuropsychiatric interview (MINI-KID)	X							

Health Screen Interview	X							
Suicide Ideation Questionnaire (SIQ)	X	X		X		X	X	X
AE Assessment)	X	X		X		X	X	X
Patient Health Questionnaire (PHQ-9)	X	X		X		X	X	X
Columbia Suicide Severity Rating Scale (C-SSRS) - lifetime	X							
Columbia Suicide Severity Rating Scale (C-SSRS) – since last contact		X		X		X	X	X
Frequency of Use of App [d]		X	X	X	X	X	X	X
Interviews for feedback [redacted]		X		X		X	X	X
Utility of Techniques		X		X		X	X	X
Usability and Acceptability [e]		X		X		X	X	X
Assessment of healthcare resource utilization (parent report)		X		X		X	X	X

a Screening will be conducted while adolescent patients are at an inpatient psychiatric facility.
b Over the phone with member of the research team
c Sheet to collect demographic and contact information
d Unique logins and duration of each login
e System Usability Scale
f Visit 0 may take place over multiple sessions

RECRUITMENT AND RETENTION PLAN

Enrollment Procedures. Eligible participants will be identified through medical record review. Consultations will be completed with participant's attending psychiatrists to confirm eligibility. Attending psychiatrists will be asked to inform the parent and patient that they will be contacted by staff about a research study; however, only IRB-approved study staff (without a treatment relationship with the patient) will recruit participants. When possible, parents and participants will be invited to participate in the study together. However, given that participants are inpatients and housed separately from parents, in most cases parents and patients will be invited to participate separately. When parents are not on site, IRB staff will call parents to invite them to participate. If parents agree, a remote consenting procedure will occur. Patients will all provide assent in person. Behavioral observations will be used as an additional indicator of assent. If patient's behavior does not indicate assent (e.g., avoiding eye contact, withdrawn) the participant will not be enrolled. Participants will not be recruited on the patient's first day of admission.

Retention Methods. We recognize that obtaining follow-up data is critical. Therefore, we will take several steps to optimize our ability to collect such data. During the informed consent process, participants (parents/guardians) will be asked to provide multiple forms of contact including a direct telephone contact and e-mail as well as the back-up numbers of at least two family members or friends in case study staff are unable to reach the participant at the direct number. If study staff is unable to reach the participant for follow-up at all contact numbers provided following no less than three call attempts, then a letter will be sent to the participant requesting that they contact the study staff. If no reply is received from 1 week of mailing the first letter, then a second letter will be sent requesting that the participant contact the study staff and also indicating a date by which study staff will no longer contact them to schedule follow-up calls. If no reply is received by the indicated date, then the participant will be considered lost to follow-up and will be withdrawn from the study.

Early Withdrawal of Participants. Participants may voluntarily withdraw from the feasibility study at any time. They may contact the site PI at the phone number(s) listed on the informed consent document. Participants may be withdrawn from the feasibility study by the site PI if they no longer meet eligibility criteria, are unable to be contacted (lost to follow-up) or are otherwise unable to complete study procedures, or are determined to be adversely affected by content in [redacted] Participants who attempt suicide while an active participant in the study will continue to be enrolled in the study so long as no criterion for withdrawal (e.g., no longer meet study criteria, adversely affect by content in [redacted] is met. Participants will have access to the app for the duration of their participation in the study. Participants who withdraw or are withdrawn early from the feasibility study will no longer have access to the app.

PROTECTION OF HUMAN SUBJECTS

RISKS TO HUMAN SUBJECTS.

Human Subjects Involvement, Characteristics, and Design. The Institute of Living (IOL) leadership has consented to permit recruitment of patients to volunteer to participate in the feasibility study (see e-mail from Michael Dewberry, MD, Medical Director). The proposed feasibility study will include 22 (of which 20 are expected are complete enrollment in the [redacted] app) adolescent patients from the IOL's CARES and Adolescent Psychiatry Units at Hartford HealthCare, who have attempted suicide (lifetime) or have clinically significant suicidal ideation and a plan to harm themselves.

Study Procedures, Materials, and Potential Risks. All participants will receive access to the Beta Version of [redacted] for the feasibility study. There are risks of emotional discomfort and distress from talking about suicide and other sensitive topics. There is also the risk that confidentiality may be broken.

ADEQUACY OF PROTECTIONS AGAINST RISKS.

Informed Consent. Using procedures approved by Hartford HealthCare's IRB, participants' parent/guardian will be able to provide informed consent and participants will provide assent. IRB-approved study staff will inform potential participants about the voluntary nature of their participation and that their data will remain confidential. We will inform participants that we have an NIH certificate of confidentiality. We will communicate the limits of confidentiality, which include reports of imminent suicide risk, homicide risk, abuse of vulnerable individuals (e.g., minors, elderly, and individuals with intellectual disability), and compliance with federal, state or local laws. In these instances, we will report to the appropriate authorities and/or provide participants with referrals for immediate treatment. Patients will also be informed that they have the right to not participate, or to stop participating in the feasibility study at any time.

Protections Against Risk. Participants will be given an identification number, which will be matched to participant names in a password-protected electronic document, which will only be accessible to IRB-approved study staff. Participant data will be entered into REDCap or stored on HHC's HIPAA compliant servers. Only

coded data will be shared with Oui through REDCap or other secure data transfer system. We recognize that our population will include patients who may have arrived to the hospital in crisis, and our procedures have the potential to cause emotional distress. For these reasons, participants will not be recruited for the study on the first day of admission.

Potential Benefits of the Proposed Research to Research Participants and Others. The benefits of crisis response planning and follow-up after a hospital visit for suicidal ideation have been well-documented in the research of Drs. Rudd and Bryan. A digital approach will provide these resources and evidence-based support systems to individuals who otherwise might go without them.

Importance of the Knowledge to be Gained. The proposed research offers a way to expand access to crisis response planning and aftercare for adolescent patients at high risk of suicide. A mobile technology approach to this type of intervention would allow adolescent patients to access care faster, less expensively, and more reliably than they do today.

Risk Management. Suicidal ideation/behaviors will be assessed during each study interview (Week 0, Week 1, Week 4, Week 8, Week 16). Week 0 is the study baseline assessment, which occurs while the participant is housed in an inpatient treatment facility. For purposes of risk management, results of the study assessment at Week 0 will be shared with the inpatient treatment team in order to provide information relevant to their treatment/discharge planning. Remaining assessments are conducted by phone. In order to facilitate risk management during these calls we will do the following: 1) only enroll participants who provide assent/consent for the study to release information to their parent/guardian (note a parent/guardian interview is also routinely completed at this time), 2) only enroll participants who provide assent/consent for the study to release information to their outpatient provider (note that provider information may not be known at the time of consent in which case authorization will be obtained at the earliest possible time after provider information is known prior to making the initial outpatient provider call), 3) obtain location information at the start of each phone assessment, and 4) schedule phone assessments at a time when the parent/guardian is present at the same location as the participant. In addition to the routine outpatient provider call at week 1, increases in suicide risk will be communicated to the parent/guardian and outpatient provider. Details of study assessments indicating changes (i.e., increases) in risk since the previous assessment will be shared with the parent/guardian and outpatient provider. In addition, interviewers will engage in risk management interventions as clinically indicated following the guidelines outlined in the Risk Management Documentation Form. For patients scoring in the moderate or high-risk categories, a follow-up contact will be made with the parent/guardian and/or outpatient provider within 48 hours of the study call to assess follow-through with risk management recommendations provided by the study clinician. Participants will be informed that information they input to the app is not monitored for purposes of risk assessment.

AE Reporting. Adverse events (AEs) will be monitored and documented at each study visit. Reporting of AEs will follow the Hartford HealthCare Institutional Review Board Policy 910 and NIMH policy. Given that all enrolled participants will have a history of suicidal ideation with plan, AEs related to suicidal thoughts/behaviors, including death by suicide, will be categorized as "expected". Further, AEs meeting any of the following criteria will be categorized as "Serious": results in death; is life-threatening (places the subject at immediate risk of death from the event as it occurred); requires inpatient hospitalization or prolongation of existing hospitalization; results in a persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; an important medical event, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition; or results in a severely debilitating situation for the subject, such as psychological distress, financial hardship or damaging impact on social standing or employability. AEs which are unexpected, related, and serious will be reported to the HHC IRB within 7 calendar days and to the NIMH PO within 10 business days. Death related to the study will be reported to the NIMH PO within 5 business days. All other AEs will be documented and reported to HHC IRB and NIMH PO at the time of the respective annual progress reports.

OUI's DATA SECURITY AND RESOURCE SHARING PLAN

The PI, Dr. Seth Feuerstein, and the Research Coordinator, Mr. Brian Keenaghan, both have extensive experience in digital health and privacy protection through previous projects at Cobalt and Magellan Health where they developed and implemented eight patient facing apps (now accessible in the Google Play and Apple App Store), and other digital health products that required data protection for more than 50 million covered lives. They have undergone annual HIPAA compliance trainings over the last five years and have overseen the data compartmentalization for tens of thousands of users. They both have more than a decade of experience delivering programs with personalized user experience in safe, secure environments designed to mitigate risk. As Research Coordinator, Mr. Keenaghan will serve as the Privacy and Security Officer and his responsibilities will include ensuring that: (1) Oui and affiliated partners are adequately trained and are following HIPAA guidelines; (2) Oui HIPAA Compliant servers are generating de-identified datasets to offer increased protection for patient privacy through masking of direct and some indirect identifiers; and (3) appropriate levels of security will be used for transferring data or providing access with a secure system to provide additional safeguards.

The dataset available for resource sharing by Oui will not have personal identifiers. Before data will be shared to prospective users, they must agree to the conditions of use governing access to the public release data, including restrictions against attempting to identify study participants, destruction of the data after analyses are completed, reporting responsibilities, restrictions on redistribution of the data to third parties, and proper acknowledgement of the data resource. The information provided by users (i.e. feedback session participants) will not be used for commercial purposes. During their participation in feedback sessions, participants will download and use [redacted]. Data collected through [redacted] may be shared with the app development team according to its Terms of Service with users. These data will be used internally to conduct data analytics aimed at improving [redacted] and customizing user experience, and their disclosure would compromise Oui's intellectual property and competitive advantage. All data supporting published scientific results will be de-identified and added to the shared data products described above.

Cybersecurity and Data Collection. The team at Oui has developed and implemented certain measures to ensure cybersecurity and data protection on previous digital platforms. [redacted] is built on the fundamental principle of anonymity with security and privacy engineered into the core design. This includes (1) applying a security framework, and (2) ensuring data segregation of Protected Health Information (PHI). The data will not retain participant names when entered into our system and will only be accessible by authorized users. Our measures to ensure cybersecurity and data protection include:

1. Unique password-protected user accounts.
2. Strong password requirements. User passwords will be required to be 8 or more characters in length.
3. Security and penetration testing.
    a. Security culture. The technology group's primary tool to ensure security for the users will be by starting with a security culture. All server-side processes run in docker containers with minimal privileges. Access to non-development environments will be restricted to few employees and policy requires it to be used only in emergency measures and with oversight.
    b. Communication. Connectivity to and within [redacted] will be severely restricted, and all communication will be encrypted.
    c. Role-based production access. Access across all deployment tiers (development, beta, production) leverages a role-based entitlement system that associates privileges with a certain role, which will be then associated with appropriate users to ensure comprehensive access management.
    d. Data encryption. All data will be decrypted only in-memory and encryption keys provide a second check on access controls.
    e. Auditing. All activity within, access of, and attempted access of [redacted] will be monitored, logged, and stored for anomaly detection and auditing.

f. Testing. A[redacted] will be declaratively provisioned and will have an extensive testing process run with automated scripts.

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