STU00219136

STUDY TITLE:
Developing a Digital Intervention for Adolescent Nonsuicidal Self-injury

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STUDY SUMMARY:
Check any **applicable** boxes in the table below – you will be asked for further detail on these topics later in the protocol form:

Indicate Vulnerable Populations to be enrolled: ☒ Children ☐ Cognitively Impaired Adults ☐ Pregnant Women (IF the research activities will affect the pregnancy or the fetus) ☐ Prisoners (or other detained/paroled individuals)
☐ International Research (check this box if you will collect data from individuals located outside the United States)
☐ Research involving external collaborators (some research activities will be carried out by individuals not employed by Northwestern or NU affiliates will carry out some research activities)
☒ Research has U.S. Federal government funding via one or more direct awards or a sub-award (e.g., NIH, NSF, other federal agencies or departments) NIMH K01MH131898 PI Kaylee Kruzan; Sponsored Research ID: CERES AWD00000328 Human Subjects Research: YES

Sample size: Longitudinal field usability trial: 10; **Clinical trial:** 80
DSMB: Yes

1.0 Purpose and rationale of the study:

Purpose:
The primary purpose of this study is to design and evaluate a DMHI (digital mental health interventions) attuned to the needs and preferences of non-treatment engaged adolescents (14-18 years) who engage in nonsuicidal self-injury (NSSI). NSSI is the intentional damage of body

tissue without suicidal intent[1] and affects an estimated 17% of adolescents worldwide.[2–4] NSSI is associated with considerable distress, increases risk of hospitalization and developing a mental health condition, and contributes significantly to risk for suicide attempts and death.[5] Commonly beginning around age 14 years, earlier onset is linked to more severe trajectories of NSSI, suicide plans,[6] and poorer quality of life.[7] *Early intervention for NSSI is critical.*

However, most adolescents who engage in NSSI do not seek professional help.[8–11] Between 1/3 and 1/2 of young people who engage in NSSI do not self-disclose their behaviors to anyone in person, limiting their access to informal and formal supports and *preventing pathways to treatment*.[12,13] Though several psychological interventions have been effective in reducing NSSI,[14,15] structural (e.g., time, cost),[16–21] attitudinal barriers (e.g., stigma, mental health literacy), and non-disclosure constrain accessibility and reach among adolescents.[10,12,22,23]

DMHIs present an opportunity to increase access to evidence-based psychological strategies, while also reducing common barriers to treatment. Although young people are hesitant to disclose NSSI in person, they engage in NSSI help-seeking online at high rates.[12,24–26] Sociotechnical affordances of online interactions (e.g., anonymity, asynchrony)[27–29] can attenuate concerns around disclosure of stigmatized conditions, making them an opportune point of first contact.[28,30,31] Yet, most spaces where people access NSSI information online do not contain high-quality, evidence-based resources.[32] Growing rates of NSSI among adolescents[3] and low rates of traditional help-seeking and treatment engagement,[8–11] demand alternative approaches to intervention. DMHIs designed for implementation within online spaces where adolescents already seek mental health information can capitalize on unique moments of disclosure to identify and provide resources. Though DMHIs show promise for reducing NSSI and are acceptable;[33–38] there are no rigorously-tested, publicly-available DMHIs for adolescent NSSI.

We will develop a DMHI in collaboration with Mental Health America (MHA), the nation's largest mental health advocacy organization which hosts online self-assessment tools. Partnering with MHA to design and deliver the DMHI provides a clear dissemination pathway and access to a diverse group of adolescents not in treatment.[39] Additionally, the DMHI will be designed in collaboration with adolescents with lived experience of NSSI, through rigorous user-centered design (UCD) research activities. The DMHI will require low intensity engagement and utilize a conversational agent to guide adolescents through module content and skills training using dialogue tailored to the user's unique goals. Conversational agents produce stronger motivation and engagement than standard app interfaces,[40,41] and tailoring improves app acceptance.[42–44] Informed by models of behavior change and help-seeking, the DMHI will incorporate evidence-based cognitive and behavioral strategies to reduce NSSI frequency and severity, and increase help-seeking activities.

The project has the following overarching aims:

Aim 1. Design and develop a fully automated DMHI for adolescents who engage in NSSI.

To complement Aim 1, we will form a **stakeholder advisory board (SAB)**. The SAB will be comprised of 4 members of MHA leadership and staff and 4-5 adolescents recruited through MHA. The SAB will meet at least twice prior to the initiation of the trial. Members will have varying perspectives to oversee and provide feedback on the digital intervention design, delivery, and implementation of the digital intervention within MHA. The goals of the SAB are for members to provide input on what can be done to develop and deliver the digital intervention in a way that meets their both adolescent and MHA's needs. The study team has determined this

activity to be non-human subjects research as there is no research intent for the SAB and data will only be kept in de-identified formats.

Aim 2. Pilot a randomized controlled trial (RCT) of the DMHI with 80 adolescents. I will examine the feasibility of conducting a fully powered type 1 hybrid implementation-effectiveness RCT. Participants will be randomized to receive the DMHI (n=40) or an active psychoeducational control (n=40) for 8 weeks.

Aim 2a: Evaluate the feasibility of an RCT using the following markers: Recruit 80 adolescents with current NSSI, achieve 80% assessment completion, and <30% loss to follow-up across follow-up period.

Aim 2b. Evaluate the implementation potential for the intervention by assessing the implementation cascade (flow of participants from initial engagement through follow-up) and participant-reported intervention acceptability and appropriateness.

Aim 2c. Explore treatment effects, testing the hypothesis that: the DMHI will result in greater improvements in the primary outcomes (NSSI frequency, severity, help-seeking actions), secondary outcomes (depression, anxiety, intentions to seek help), and treatment targets (mental health stigma, literacy, cognitive, behavioral, and emotional self-regulation), relative to the control.

Aim 2d. Explore mediational effects of the treatment targets and engagement targets (app use and subjective engagement) on primary outcomes and moderation effects of psychiatric comorbidity (e.g., depression, anxiety) and demographics (gender, race, ethnicity).

Study endpoints:

This protocol describes procedures for two separate, but related, studies:

1. Design Studies (Specific Aim 1)
    a. Elicitation Interviews and Workshops **Completed**
    b. SAB meetings **Ongoing**
2. **[we removed remote usability testing due to time constraints]**Clinical Trial (Specific Aim 2)

    Participants will receive the treatment app (Coping Compass for teens) or a control app. Participants will complete study within 16 weeks, this includes 8 weeks of intervention and follow up at weeks 12 and 16.

This work will be carried out over 5 years.

Year 1. Milestones are: 1) Begin early user-centered design activities; 2) Develop intervention content. **[Complete]**

Year 2. (Adjusted Timeline) Milestones are: 1) Complete user-centered design activities; 2) Begin

Year 3. Milestones are: 1) Complete usability testing (longitudinal field usability test) ; 3) Complete refinements to intervention; 4) Begin participant recruitment for trial. 5) Begin and provide study treatments, 6) Collect clinical trial data.

Year 4. Milestones are: 1) Continue and complete clinical trial data collection; 2) Complete treatments; 3) Begin analysis.

Year 5. Milestones are: 1) Complete analysis, 2) Write the primary outcomes papers; 3) Write and submit NIH R01 grant.

STUDY INTERVENTION(S) / INVESTIGATIONAL AGENT(S):

- **Coping Compass for Teens:** Coping Compass is a web-app intervention designed for young adults (18-24) that engage in NSSI (See STU00215892). In this study we are adapting Coping Compass to meet the specific needs and preferences of adolescents (14-18). Coping Compass for teens consists of 16 modules (8 focused on internal skills and 8 focused on external sources of support) to be delivered twice weekly for 8 weeks. Modules contain psychoeducation and skill-based practice, and brief assessments. All content is delivered by a highly interactive conversational agent that guides users through the app content via a text-like interface. Psychoeducational content and strategies center on cognitive behavioral principles and support increased knowledge of external sources of support. Brief assessments examine NSSI and use of skills.
- **Control app:** The control app uses the same interface as above but contains only modules with psychoeducation on healthy living (e.g., Water Intake, Sleep Hygiene, Active Lifestyle, Safe Skin Protection, Social Connections, Healthy Media Consumption, Stress Management, Green Spaces)

Device handling: Purple Workshops, the application developer, has made an administrative account that allows study team members to create new accounts for users. An account and login credentials will be required in order to access Coping Compass for Teens. Those login credentials will only be provided to enrolled participants (i.e., those who have consented and been randomized).

NSR (Abbreviated IDE) Device rationale: Under 21 CFR 812.3(m) Coping Compass for teens is not believed to be a Significant Risk (SR) device. It is not intended as an implant, purported to be for use supporting or sustaining human life, for a use of substantial importance in diagnosing, curing, mitigating, or treating a disease, or otherwise represent a potential for serious risk to the health, safety, or welfare of a subject. Coping Compass for Teens is an adaptation of an application recently developed through NIH R34 funding (R34MH128410 / STU00215892]). As a result, limited information about the potential negative effects of using the application are available. However, the application showed no negative effects or increases in risk during the above noted clinical trial. Additionally, the concepts underlying the app (derived from cognitive-behavioral treatments) have been well studied (Andover et al., 2017; Washburn et al., 2012; Labelle et al., 2015) and shown to be low-risk and not cause harm to users.

DATA AND SPECIMEN BANKING
Deidentified data will be stored indefinitely for secondary analyses.

SHARING RESULTS WITH PARTICIPANTS
Study results will be made available to the public through publications. Interested participants can opt into receiving an email from the study team when results are published in the consent process by answering “Yes” to an optional element.

STUDY TIMELINES
Enrollment timeline: The anticipated start date for the trial is October 2025. All participants will be recruited through Mental Health America as described in the recruitment section below. Consent, randomization and assessment will be handled through REDCap. We feel confident in our recruitment strategy, which is based on our prior work using similar methods (STU00215892). We expect to enroll approximately 10 participants per month during the trial, which is very achievable given our experience with online recruitment and our virtual clinical trials platform. The lost-to-follow-up rate will be minimized by 1) paying participants $20 for

each assessment and 2) encouraging participants to continue completing paid outcomes assessments even if they drop out of treatment.

Timeline of participant activities: Participants will be enrolled in the study for a total of 4 months (the 2-month intervention period and follow ups at 1 and 2 months post intervention). Accounting for recruitment and follow–up we expect the trial to run for 2 years with 1 year allotted to analysis.

2.0 Enrollment Criteria (who can be in your study and who would not be eligible to participate in your study):

Inclusion criteria include:

1. Current NSSI, defined as NSSI on 2 or more days in the past month
2. English language skills sufficient to engage in the consent and intervention procedures. The intervention content will only be available in English at this time.
3. Age 14 to 18
4. Access to smartphone.
5. U.S. resident OR U.S. citizen.

Exclusion criteria include:

- Severe mental health diagnoses for which this intervention would be inappropriate (e.g., autism spectrum, intellectual disability, psychotic disorders, active manic episodes).
- Severe suicide risk, including suicidal ideation with a plan and intent to act (score >= 4), or history of suicide attempt in the past 3 months

3.0 Sample Size:

1. **Design Studies (Specific Aim 1)**:
    a. Elicitation Workshops -- Interviews will be conducted with adolescents until thematic saturation is reached. This is usually around 15 interviews[46] which is our aim.
    b. [Note. We removed design feedback sessions,usability testing and longitudinal field usability testing due to time constraints]
2. **Trial (Specific Aim 2):**80 adolescents will be recruited from MHA and randomly assigned to receive the DMHI (n=40) or an active control (n=40). The primary goal of this pilot is to trial procedures for a larger, fully-powered trial.[47] The sample size (n=80) provides adequate experience to develop procedures and assess feasibility. Using an independent t-test at a type I error rate of 5%, this sample size achieves 80% power to detect an effect size from baseline to end of treatment of .63. This equates to an actual difference of 2.3 on the ABASI scale or the PHQ-A (assuming both have a SD=6) (PASS 2021, Kaysville, UT).[48]

4.0 Recruitment and Screening Methods:

The below methods will be used to recruit for: elicitation activities **[complete]** (1c); Longitudinal field usability testing (1d); Stakeholder advisory board (adolescent participants only; note this is a non-research activity) (1e); Trial (2):

Recruitment: Recruitment will primarily be through Mental Health America, although we will

use these two additional venues if we are not reaching recruitment targets: 1) Online web forums related to self-injury (e.g., self-injury subreddit on Reddit) after securing approval from moderators, 2) Researchmatch.com

Participants will be recruited through the Mental Health America (MHA) website. MHA will support recruitment by displaying an IRB approved clickable teaser advertisement (See advertisement text uploaded to eIRB+) for the current study to individuals who (a) complete any of MHA's screeners except for screeners for bipolar disorder or psychosis. MHA will not be engaged in the research or have access to any identifiable information gathered through this study. Individuals can elect to click the advertisement if they are interested in learning more about the study. This ad will direct interested individuals to read an IRB approved description of the study that will be hosted on the Center for Behavioral Intervention Technologies (CBITs) website (website text uploaded to eIRB+). The study description will contain a link to a screener consent document. Participants will be able to provide assent (eConsent via REDCap) **The RA will be available to address any questions and facilitate this consent process.** After providing informed eConsent for the screening procedures (which includes the collection of an individuals' first and last name as well as the date of signature), individuals will complete a screening questionnaire on REDCap (screening questionnaire in eIRB+), which assesses demographic information and participant characteristics, mental health symptoms and history, and smartphone ownership information.

Individuals that meet inclusion and exclusion criteria, will be contacted by the study's research assistant, and emailed or texted a link to the consent document for actual study, which will give them an option to provide consent through an eConsent procedure to participate in the study. **The RA will be available to address any questions and facilitate this consent process.**

We will be using the REDCap e-Consent process. Participants will view a digital copy of the consent document to read through REDCap (Research Electronic Data Capture) a secure, web-based application. Participants will be able to click "yes" to consent and "sign" their name either by typing in their name or by utilizing REDCap's 'Signature' field type on the survey. Upon completion of the survey, a static copy of their responses in the form of a consent-specific PDF will be stored in the project's File Repository. Values including name are automatically added to the PDF as extra documentation of the identity of the person who is consenting. As additional identity verification, the e-Consent Framework also records the IP address of each participant and displays this information in the file repository in order to help regulate potential duplicate forms from a single IP address. Immediately following adolescent e-Consent, participants will complete a brief baseline survey and be contacted via email, phone, or text message within 1 – 3 days for scheduling.

Individuals **not** meeting eligibility criteria will be informed and will be offered a link to learn more about our CBITs Research Registry and will be provided with a list of nationally available mental health resources, including the Substance Abuse and Mental Health Services Administration's (SAMHSA) treatment referral hotline, the National Suicide Prevention Lifeline, the Crisis Text Line, as well as a list of nationally available mental health warmlines.

Online web forums related to self-injury: We will post a clickable teaser advertisement in online forums related to self-injury after securing approval from forum moderators. We will follow 3-step process to ensure that our research activities are perceived as credible and that we are respectful of the forum members and forum norms in recruitment: 1) A research team member

will join forums, 2) Upon entry, we will ask forum moderator (if applicable) for permission/approval to post recruitment ad, 3) If approval is secured, we will post a clickable ad in general forum and monitor direct messaging for interest. Once the advertisement is clicked the procedure will unfold exactly as above.

Research Match : An email explaining the study will be sent to potential participants identified in the ResearchMatch. Once the advertisement is clicked the procedure will unfold exactly as above.

Stakeholder Advisory Board:

Adolescents will be recruited in two ways. First, participants who meet inclusion criteria for, and participate in, an elicitation interview and are deemed by the research staff to provide substantive responses to the interview, and are sufficiently diverse so as to reflect the makeup of the user-base of online resources such as MHA's website will be invited to serve on a stakeholder advisory board. Participants can indicate on the consent form that they are interested in being contacted for future related research.

Participants will be invited via the email address used for coordinating study activities. Participants who are invited to serve on the stakeholder advisory board will be emailed a link (see Stakeholder Advisory Board recruitment email) to an additional informed consent document hosted by NU REDCap which will outline stakeholder advisory board responsibilities. The recruitment email states that the decision of whether to join the stakeholder advisory board will have no bearing on their ability to participate in the other study activities.

Secondly, we may also recruit stakeholder advisory board members from Mental Health America's peer support group. In this case, we've included an ad as well as a brief description that can be posted on MHAs website or distributed to members of the peer support group via email.

Determining Eligibility: The REDCap screening survey will be used to 1) determine eligibility and 2) securely gather and store potential participant contact information. See attachment for the REDCap Eligibility Survey for more detail. For participants that are ineligible to participate, researchers will notify the potential participant via email, thanking them for their interest (See eligibility survey).

5.0 Research Locations:

All research activities will occur remotely through zoom.

6.0 Multi-Site or Collaborative Research:

N/A

7.0 International Research (where data collection will occur outside the United States and U.S. territories, including online activities)

N/A

8.0 Procedures Involved:

Please check the boxes for all applicable data collection procedures you plan to use:

☒One-on-one interviews

☐Focus Groups

☒Questionnaires/surveys

☐Secondary Data Analysis (medical record data, educational records, government or private sector datasets, etc.)

☐Ethnographic observation

☐Physiological measurements (e.g., EEG, EKG, MRI)

☐Biospecimen collection (saliva samples, blood draws, hair samples, etc.)

☐Mobile applications/data collection devices (e.g., Fitbits, actigraphs, etc.)

☐Behavioral decision making tasks (e.g., puzzles, interactive games, etc.)

☐Physical activities such as walking and other forms of exercise

☐Other procedures (briefly list types of procedures here if not covered by the check-boxes above):

Design studies:

Elicitation activities. [COMPLETED] Remote interviews will be conducted to understand how adolescents use technologies to access NSSI support or information, to identify the types of content and resources they would be receptive to, and to explore potential barriers and facilitators to use and implementation through MHA. All interviews will be under 1 hour and will occur via zoom. Audio will be recorded.

1. Following consent which includes participant contact information so they can be reached to set up the interview, the RA will reach out to the participant to secure a date and time for the interview.
2. Participants will be sent a link to a baseline questionnaire, asking questions about, as well as a link to zoom.
3. The participant and research will log into zoom at the mutually agreed upon interview time and the interview will be conducted.
4. At the start of the interview the researcher will ask if the adolescent has any questions or concerns on the consent document or study. The interviewer will answer any questions or concerns and provide a brief overview of what the adolescent can expect to happen.
5. The researcher will reiterate that participation is voluntary and that they can discontinue the interview or skip over questions at any point. The reviewer will ask for permission to record.
6. The researcher will begin recording and will ask questions about the adolescents' experience of NSSI and their goals and coping strategies, and their existing and desired use of technologies to self-manage NSSI. The researcher may also share features of a prior version of coping compass (developed through STU00214610 and currently being tested in STU00215892) as well as mock-ups of potential novel designs with participants via screen share to elicit feedback on the design (See examples in attached documents).
7. The researcher will stop recording, explain that they will be compensated with a amazon gift card sent to their email in the next 2-3 days, and the interview will conclude.
8. The audio recording will be uploaded to fsmresfiles and immediately deleted from the

researcher's computer.

(We originally planned to do design feedback sessions,remote usability testing, and a longitudinal field usability test, but have removed these from the protocol (below) due to time constraints.)

Stakeholder advisory board (non-research activity):
If participants from the elicitation interviews are selected to serve on the stakeholder advisory board (and have consented to be contacted for future research) or peer supporters are interested in the study, the research staff will email a link to the stakeholder advisory board information (see Stakeholder Advisory Board recruitment email). The link will be to a NU-hosted REDCap consent form where the participant can read more about the stakeholder advisory board. Those that consent will be invited to participate in a number of meetings leading up to the trial. In these meetings, they will be asked to provide feedback on early versions of the digital intervention design, comment on implementation of the intervention within MHA, and their preferences for accessing the digital intervention. They may also be invited to provide feedback through brief surveys or prompts through asynchronous focus groups. All surveys will be hosted through REDCap.

Clinical trial:

I will use a 2-arm RCT to measure treatment effects and maintenance of gains at follow-up period. Participants will be randomized to receive the DMHI (n=40) or an active control (n=40), upon consent I will pilot and evaluate RCT methods for a subsequent trial and obtain pilot data on clinical outcomes, implementation potential, mediating mechanisms and moderators. Participants will be 1:1 randomized to arms in varying block sizes of 4 and 6 prior to any study procedures to protect against allocation bias. Assessments will be administered online vie REDCap. Outcomes will be assessed for the duration of the trial (at 4, 8 weeks) with two follow-up timepoints (at 12 and 16 weeks). Participants not responding to follow-up assessments will be contacted by the RA and, if necessary, primary measures will be administered over the phone.

PROCEDURES INVOLVED:

This study is a 2-arm RCT designed to measure treatment effects and maintenance of gains at follow-up period. Participants will be randomized to receive the DMHI (n=40) or an active control (n=40). I will pilot and evaluate RCT methods for a subsequent trial and obtain pilot data on clinical outcomes, implementation potential, mediating mechanisms and moderators. Participants will be 1:1 randomized to arms in varying block sizes of 4 and 6 prior to any study procedures to protect against allocation bias. Assessments will be administered online via REDCap. Outcomes will be assessed for the duration of the trial (at, 4, 8 weeks) with two follow-up timepoints (at 12 and 16 weeks).

Participants will be permitted to keep the app on their phone and continue using it after their 8-week intervention period ends. This is consistent with how digital interventions are used, and has been a standard feature of DMHI trials.[53,66–68]

When a participant concludes the intervention, they may be asked to engage in a 30-45-minute user feedback interview, to identify problems and deficiencies with the aim of improving the intervention. We will select a subset of participants reflecting different use patterns (high and low) to gather feedback on their experience using the app. Participants who discontinue the

intervention prior to the study end will be contacted and invited for an interview at the time their discontinuation is confirmed.

The three components/data types of this study are:

App use data: This will include participant use data (e.g., log data on use, frequency and time of app use, questions answered, and answers to questions).

Interview data: Participants may be invited to a telephone or videoconference interview at the end of the intervention period. Interviews will last no more than 45 minutes and will be audio recorded and transcribed. Interviews are semi-structured, such that we touch on certain high priority topics and questions, but also may deviate from the script to ask follow-up questions based on users' responses. Interviews will elicit qualitative feedback about the acceptability and usefulness of the app, allowing us to understand the nature of problems encountered.

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Assessment data. Data will be gathered from study participants as outlined in the table below. The primary outcome, frequency of NSSI behaviors, will be measured using the Alexian Brothers Assessment of Self-Injury Scale (ABASI)[69] which will be adapted to measure monthly NSSI frequency through a checklist of the most common methods of self-injury. All measures of primary and secondary outcomes, and targets will be administered at baseline, and weeks 4, 8 , 12, and 16 except for measures of usability and subjective engagement which will not be administered at baseline, as participants will not have been exposed to the treatment. Moderators are administered at baseline only. All self-report assessments will be conducted online using REDCap.[71]

All measures are self-report. For follow-up assessments, participants who do not respond will be contacted by research staff and, if necessary, the primary measures will be administered over the phone. We will ensure that participants understand that they are free to terminate the treatment at any time, and that compensation is for assessment completion only.

Name	Type	Time Frame	Brief Description
Alexian Brothers Assessment of Self-Injury (ABASI checklist)	Primary	Baseline, weeks 4, 8, 12, 16	Checklist that assesses frequency of 21 forms of NSSI (α=0.75)
Actual Help-Seeking Questionnaire (AHSQ)	Primary	Baseline, weeks 4, 8, 12, 16	10-item measure assessing recent help-seeking from a variety of formal and informal sources
Patient Health Questionnaire-A (PHQ-A)	Secondary	Baseline, weeks 4, 8, 12, 16	9-item measure assessing depression symptom severity (α=.86-.89)
Generalized Anxiety Disorder-7 (GAD-7)	Secondary	Baseline, weeks 4, 8, 12, 16	8-item measure assessing GAD symptom severity (α=.92)

General Help-Seeking Questionnaire (GHSQ)	Secondary	Baseline, weeks 4, 8, 12, 16	10-item questionnaire assessing intentions to seek help from informal and informal sources (α=.83)
Internalized Stigma of Mental Illness scale	Target	Baseline, weeks 4, 8, 12, 16	9-item measure of mental health stigma (omega=.91)
Mental health literacy scale	Target	Baseline, weeks 4, 8, 12, 16	35 item measure of mental health literacy (α=.87)
Self-regulation Difficulties in Emotion Regulation Scale (DERS)	Target	Baseline and weeks 4, 8, 12, 16	36-item measure assessing six facts of emotion regulation (α=.93)
Self-regulation Cognitive Behavioral Response to Stress Scale (CB-RSS)	Target	Baseline and weeks 4, 8, 12, 16	9-item measure of behavioral and cognitive coping related skills (αs=.77-.83).
Acceptability of Intervention Measure (AIM)	Secondary	Weeks 4, 8, 12, 16	4-item measure of intervention acceptability (α=.85).
Intervention Appropriateness Measure (IAM)	Secondary	Weeks 4, 8, 12, 16	4-item measure of intervention appropriateness (α=.91).
Objective engagement markers	Target	Continuous	App use (number of app launches, time from first to last use)
Usefulness, Satisfaction, and Ease of Use Questionnaire (USE)	Quality metric	Weeks 4, 8, 12, 16	21-item measure of 3 core dimensions of usability: Usability, usefulness, and ease of use (α=.98).
Demographics	Moderator	Baseline	Age, sex, gender, sexual orientation, race, ethnicity,
DSM-5 Cross Cutting Symptom Questionnaire – Adolescent	Moderator	Baseline	23-item self-report measure assessing mental health domains across psychiatric diagnoses

9.0 Research with Vulnerable Populations

Children (Adolescents, 14-17 years old).

Care will be taken to ensure that appropriate mechanisms are in place to protect adolescents. The safeguards below are consistent with other research studies that involve adolescents under a waiver of parental consent.

1. The assent process will include developmentally appropriate materials including individual assessments of capacity to consent to ensure (1) understanding of things they will be expected to do during the study; (2) what they would do if they no longer wished to participate in the study; (3) the potential risks for participating in the study.
2. All participants will be provided with access to resources (e.g., National Suicide Hotlines, mental health resources, safety planning tools) at multiple timepoints throughout the study (Screening, Baseline, End of Study, and anytime they trigger the risk management protocol).
3. Participants can ask questions about the study throughout the process (during the interview for example) and before providing consent to the study if they have concerns or questions. They may also discontinue participation at any point if they feel uncomfortable. This will be made clear in the assent documents and at the beginning of each research activity (e.g., interviews, design feedback sessions, trial).
4. A detailed risk management protocol is in place if suicide risk is detected in communication with the study team, in the survey responses, or in interviews.

Data Collection

Data will be collected from REDCap surveys and through audio recording remote interview sessions. We provide details on what will be collected, as well as risks associated with these types of data, in the consent document as well as contact information in case the adolescent would like to ask follow-up questions. All data will be stored independent from personal identifiers.

Participants will engage with the intervention alone since it is meant to provide psychoeducation and practice on individual coping skills and enhance self-efficacy. We hope to foster an experience of autonomy and agency.

Additional safeguards for risk

In this study we will be working with adolescents with a history of NSSI, which can be a high risk behavior. Although NSSI is by definition "without suicidal intent," many adolescents with NSSI do report suicidal ideation. We have built in additional safeguards at all phases of research, but describe those most relevant for the stage we are seeking approval for now (elicitation) and will seek and obtain approval via a modification submitted to the IRB before proceeding with any other phase of research.

Risk can be detected in several ways: through (1) one-on-one communication with the research team via email, (2) during the interview, or (3) in assessments. In any of these cases we will follow the CBITs Suicidality Protocol.

If risk is detected via email, the study research assistant, trained to administer the Columbia-Suicide Severity Rating Scale (CSSRS), will contact the participant by phone within 1 business day for further assessment using the interview-based CSSRS. On weekends all participants that reach out to the study team email will receive an immediate email response that states that CBITs health is not a crisis or emergency service and lists resources for crisis mental health services including the Suicide and Crisis Lifeline (9-8-8); the Crisis Text Line.

If risk is detected in the interview itself, the researcher will enact the CBITs protocol and begin the CSSRS while on the zoom call.

Suicide risk could be detected in the baseline assessment, if participants score >=1 on the PHQ-9 item 9, the REDCap questionnaire will branch to suicide item (item 9) from Beck Depression Inventory (2nd edition). If item 9 of the Beck Depression Inventory is 2 or 3, a message will be displayed in the REDCap questionnaire making participant aware we are not an emergency service and should they need immediate help or be in danger, they need to call 9-1-1 or go directly to nearest emergency room. Additionally, if any suicide item (PHQ-9 item 9 or BDI-II item 9) is endorsed (>0), we will also display crisis resources such as (The National suicide prevention lifeline and Crisis text line) that are staffed 24/7 every day in order to direct responders who may be in crisis to appropriate crisis resources.

Study staff will review any endorsements of suicide items (>=1 on PHQ-9 item 9 and BDI-II item 9 >=2) within one business day and the CBITs Suicidality protocol will be enacted via phone. As our clinicians do not provide after-hours emergency support, the safety assessment would be performed the next business day if the alert is received after hours.

In all cases, research staff will attempt to reach participants with who have triggered risk for assessment up to 3 times within the same day. If a participant is unable to be reached, research staff will alert the PI Dr. Kaylee Kruzan and a designated on-call clinically trained masters or PhD-level clinician who will provide clinical guidance for next steps. As noted, the website will immediately refer participants scoring >=1 on PHQ-9 item 9 and BDI-II item 9 >=2 to call 9-1-1 or a staffed crisis service such as 1-800-273-TALK or The Crisis Text Line for emergency crisis services.

If the participants report suicidal ideation, plan, and intent upon follow-up interview, the PI will be notified immediately. All necessary steps will be taken to ensure the participant's safety, up to and including calling emergency services to go out to the participant's location to perform a safety check and hospitalize the participant if necessary.

Please see the DSMB meeting notes which detail that this modification and the risk management procedures were reviewed by the study DSMB and no concerns were raised.

10.0 Incomplete Disclosure or Deception:

N/A

11.0 Consent Process:

Please see attached consent document. The consent process will unfold as follows:

1. Individuals who elect to click the advertisement on MHA will be automatically redirected to a CBITs hosted website with information about the study and an option to click to a screener questionnaire, which will help determine eligibility. Prior to the screener questionnaire participants will be able to provide consent to take the eligibility screener through REDCap's e-Consent process (described in section 8.0). If consent is provided, they will automatically advance to the eligibility screener which will be hosted by the secure platform of NU REDCap. This screener will ask participants brief screening questions. Screening question answers will be automated and used to decide whether or not an individual meets inclusion criteria for the current study. Participants who do not meet eligibility will receive an automated messaging thanking them for their interest and

informing them that they are not eligible at this time (See attachment with screener for this language)

2. Screening questionnaire responses will be reviewed by research staff to ensure that all eligibility requirements are met, and that participants invited to participate in the study are representative, diagnostically, and demographically, of our target population (young adults with repeated NSSI who are not currently in treatment). Participants who meet eligibility criteria will be invited, via email, to read more about the study and will be provided with full information about the study and will then have the option of providing consent online through the REDCap e-Consent process (described in section 8.0). As part of the consent procedure participants aged 14-17 will be asked to leave the name and contact information of a trusted adult. Participants will have the option of providing the name and contact information of the trusted adult in the consent document OR on a call with a research team member prior to the interview. This will give them the opportunity to ask any questions they may have about how, when, and why a trusted adult may be contacted.
3. If participants decline informed consent, their screener data will be retained for reporting purposes, but their screener information will not be used in future research.
4. If participants consent they will receive a message that they will be contacted by an RA to schedule the interview. Participants will be contacted and the email will contain a link to a baseline survey via REDCap to gather more information on their NSSI characteristics and history (see survey attachments).
5. Participants that are ineligible will receive a message thanking them for taking the eligibility survey and indicating that they are not eligible.

12.0 Waiver of Participant Signature on Consent Form:

This study is designed to occur entirely remotely. Participant digital signatures will be collected through REDCap for participation in the study. For the eligibility screening instead, consent will be confirmed via REDCap survey by clicking an “Yes” button to the consent questions on the webform.

13.0 Waivers and Alterations of Consent Information:

In this study we are requesting a **waiver of parent consent for adolescents 14-17 years of age.**

The assent procedure will follow the guidelines outlined through expert consensus[4] including clearly stating that the intervention is not a crisis service, providing links to crisis services, and describing monitoring of data and response window.

I seek a waiver of parental consent based on the following rational. The research activities proposed as part of this project meet criteria for a waiver as outlined under section 8 of the HRP-416 (45 CFR 46.408 part c): 1) The research does not involve non-viable neonates, 2) The research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects, 3) An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and 4) The waiver is not inconsistent with Federal, State, or local law.

I expand on points 2-4 in the following paragraphs.

2) Parental permission cannot be assumed to be protective for all participants. Attempting to obtain parent consent could negatively impact the adolescent if the parent is not aware of their child's NSSI and/or if the parent is made aware that their child has lied to them about engagement in NSSI. If parents are unaware of an adolescent's NSSI or their desire for mental health support, requiring parental consent to take part in the study may cause the adolescent significant distress or ultimately be a barrier to participation. Further, some parents may not want their adolescent to access mental health support due to cultural or internalized stigma. This is particularly likely because NSSI is often misunderstood and highly stigmatized.[2,6,7] Waiving parental consent and obtaining adolescent assent may thus protect participants from adverse outcomes.[8]

Relatedly, a large majority of adolescents that engage in NSSI fail to access mental health services of any kind. A significant contributor to this lack of treatment access relates to adolescents' motivations not to share their mental health symptoms[9] and/or NSSI and suicidal thoughts/behaviors[10] with their parents. Indeed, adolescents often hesitate to share these challenges with parents, which substantially reduces their odds of accessing support[9].

Waiving parental consent increases the likelihood that participants will be honest during the study, which thus allows myself and the study team to address potential risk (e.g., suicidal ideation) if, and when, it surfaces and to provide participants with resources (e.g., National Suicide Hotlines, mental health resources, safety planning tools) that they may not otherwise have access to.

3) An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted. In addition to the risk management procedures outlined in the grant, there are several ways in which I plan to protect adolescents. 1) The assent process will include developmentally appropriate materials and simple language (appropriate for a 4th grade reading level). 2) I will ensure understanding of assent and study activities by prompting adolescents with questions to assess comprehension within the assent documents. 3) All participants will be provided with access to resources (e.g., National Suicide Hotlines, mental health resources, safety planning tools) at multiple timepoints throughout the study (Screening, Baseline, post-interview). 4) I will ask adolescent participants to provide contact information of a trusted adult prior to enrollment in any study activities. If emergency services are deemed appropriate following the CSSRS Suicide Risk Assessment, the trusted adult will be contacted and made aware of the situation. 5) Participants can ask questions about the study throughout the process (during the interview for example) and before providing assent to the study if they have concerns or questions. They may also discontinue participation at any point if they feel uncomfortable. This will be made clear in the assent documents and at the beginning of each research activity (e.g., interviews, design feedback sessions, trial).

4) A waiver of parental consent is not inconsistent with Federal, State, or local law. Mature minor laws across the country permit youth as young as 12 years old to request and receive mental health care without consent of the minor's parent, guardian, or person in loco parentis. These laws recognize that requiring parental/guardian permission for mental health concerns that are sensitive or potentially stigmatizing may inhibit adolescents' willingness to seek care for these concerns.[11] While this study does not provide validated treatment, it does provide a space for adolescents to speak about their mental health and an opportunity to receive information about resources they may not otherwise encounter on their own.

14.0 Financial Compensation:

Elicitation interviews: All adolescent participants will receive $25.00 compensation for participation which includes completion of the baseline survey and interview. Participants will be paid at the end of the study via an emailed electronic Amazon gift card.

SAB: Participants will receive $20.00 compensation for attending each SAB meeting. Participants will be paid following meetings via an emailed electronic Amazon gift card.

Longitudinal Field Usability Testing and the Clinical Trial: We will reimburse all participants for completing research assessments.

Subjects can earn up to $60 in the Longitudinal Field Usability Testing and $120 in the Clinical Trial for completing study assessments, with $20 per each assessment and $20 for the end of study interview.

Depending on Northwestern University payment guidelines and availability and study team workflows at the time of participation, payments to participants will be made available in one or a combination of the following ways:

- Amazon.com gift card: Participants will be sent a code via email that will allow them to redeem an Amazon.com gift card.
- PNC Stored Value (Visa) Card: If participants do not have an Amazon account or do not wish to be compensated through Amazon, they may request a Stored Value (Visa) Card instead. The cards may be virtual or physical as per participant preference.

Check: Participants earning more than $100 per calendar year must be paid by check. Checks require a signed W9 form. The check may be mailed to the participant's address.

15.0 Audio/Video Recording/Photography

DESIGN STUDIES

Elicitation Interviews

Interviews will be audio recorded. Subjects must consent to audio recording to be enrolled in the study. The audio recording will be transcribed before coding (see below).

Longitudinal Field Usability Testing Stakeholder Advisory Board Meetings

All interviews will be audio recorded. Subjects must consent to audio recording to be enrolled in the study. The audio recording will be transcribed before coding. Following IRB policy, data will be kept a minimum of 7 years after the completion of the study. Digital data gathered in the field will be uploaded to the Northwestern University servers.

CLINICAL TRIAL

All interviews will be audio recorded. Subjects must consent to audio recording to be enrolled in the study. The audio recording will be transcribed before coding. Following IRB policy, data will be kept a minimum of 7 years after the completion of the study. Digital data gathered in the field will be uploaded to the Northwestern University servers.

Please see Section 18 for further details on all the data collected in this study, and the storage procedures. Specific audio/photography data collected includes: interview audio files (digital file). These audio files are necessary to accurately represent participant quotes for data analysis the research. Audio recording is mandatory.

Transcribed audio will be used for data analysis. Audio files will be transcribed by a Northwestern University-approved vendor, with file transport using a secure FTP site between Northwestern researchers and the approved vendor. Transcription files will be reviewed by researchers and anonymized, if necessary, prior to loading into secure coding software (e.g., nVivo, storing data locally) for data analysis.

Individuals with access to the digital files include: the Principal Investigator (Kaylee Kruzan), and the study Co-I (David Mohr).

Following IRB policy, data will be kept a minimum of 7 years after the completion of the study. Digital data gathered in the field will be uploaded to the Northwestern University servers following each advisory board meeting.

16.0 Potential Benefits of this Research:

While there are no direct benefits to participants.

17.0 Potential Risks to Participants:

Please note: We have updated this section to reflect risks for the Longitudinal Field Usability Testing and Clinical Trial.

Longitudinal Field Usability Testing and Clinical Trial

RISKS TO PARTICIPANTS

Potential Risks: All potential risks associated with participation in this study will be disclosed in participant assent documents. Potential risks that might exist fall into three categories: (a) risks associated with the intervention; (b) risks associated with research assessments, consisting of questions about self-injury, depression, anxiety, and personal functioning, and other mental and emotional problems; (c) risks of worsening mental or emotional state. We address each in turn below.

Risks of the intervention: Meta-analyses have not found any increased risk associated with the use of DMHIs.[1] There is no reason to believe that the proposed interventions would pose greater risk than DMHIs generally.

Risks associated with research assessments: Research assessments include questions about NSSI, depression, anxiety, and other mental and emotional problems. There is no evidence that assessment alone increases risk.

Risks inherent in the study population: While participants who are at high risk for suicide (e.g., those demonstrating suicidal ideation, a plan, and intent) are excluded from the study, and the self-injury behavior within the population is by definition non-suicidal, it is nevertheless possible, given the natural course of NSSI, that some participants may show deterioration and develop suicidal thoughts and behaviors (STBs) during their participation in the study.

Risk Assessment: While the intervention and study procedures pose minimal risks, the risks inherent in the population pose greater than minimal risks.

PLANS TO MINIMIZE POTENTIAL RISKS ASSOCIATED WITH STUDY PARTICIPATION:

Plans to minimize potential risks involve assessment to detect risk and a safety protocol to ensure the safety of participants. This process will be overseen by a clinical monitor who has expertise in suicide risk assessment.

Assessment: Participants in the trial will receive automated self-report self-reports for NSSI every week. At least every 4 weeks, participants will be assessed with the PHQ-A, where the 9th and 11th items assess suicidal ideation. Participants endorsing any non-zero score on the PHQ-A item 9 OR indicating "yes" on the 11th item, will receive the BDI-II item 9 as a follow up. Participants who score at or above 2 on the BDI-II item 9 will be contacted by telephone by myself or the trained research assistant for further assessment using the CBITs Suicide Risk Assessment and Follow-up Protocol, which involves administering the Columbia Suicide Severity Rating Scale by telephone, working with the individual to develop a care plan, referring the participant to resources such as the national suicide prevention lifeline, or treatment, or considering emergency services in cases of imminent danger. If outreach is determined to be necessary the study team will respond within 24 hours, including those flagged after business hours. Participants who indicate suicidal ideation through within app text logging (e.g., in response to the conversational agent), or through phone calls or interviews will similarly be called and administered the Columbia Suicide Risk Assessment.

Ensuring participant safety: Once the PI is notified of potential suicidality, all actions necessary to ensure participant safety will be taken. This includes, evaluation of all necessary data including study records, calling the participant for further evaluation, and administering the Columbia Suicide Risk Assessment. All efforts will be made to ensure the safety of participants showing potential imminent dangerousness, up to and including recommending hospitalization, calling emergency services in the participant's jurisdiction to perform a "health and safety" check, or any other actions deemed necessary to ensure the safety of the patient. The clinical monitor, in consultation with the PI, also has the option of recommending that the patient be discontinued from the study and referred for more appropriate care. Because the RA will be the main point of contact for participants, they will be given thorough training in the assessment of STBs. While the PI will be responsible for the management of suicidal participants, it is possible that an emergent situation will arise that requires immediate attention, therefore the RA will be trained in the identification of imminent danger and procedures to ensure participant safety, including referral to crisis resources, identification of the participant's location, and contacting local emergency services. The PI will be notified of all cases of STBs and will consult with the clinical monitor. An adverse and serious adverse event (defined below) will be reported to the IRB, the DSMB chair, and the PO within the timeframes outlined under the NIH General Reporting Policy.

Recruitment and Informed assent: Methods previously used for recruiting subjects through MHA will be employed in the current study. Adolescents (14-18 years old) will be recruited nationally, from across the United States, using Mental Health America's website. All assent forms will conform to the requirements of, and approved by, the human subjects review board at Northwestern University will be developed and approved prior to any data collection. Assent procedures will be written at a 4th grade reading level to ensure that they are understandable by English Speaking participants 14-18 years old. In addition to ensuring that assent documents are developmentally appropriate, they will include individual assessments of capacity to assent to ensure (1) understanding of things they will be expected to do during the study; (2) what they would do if they no longer wished to participate in the study; (3) the potential risks for participating in the study. Informed assent will be collected from participants prior any enrollment or study procedures. As part of this process adolescents will provide the name and contact information of a trusted adult. This adult will be contacted in if emergency services are deemed necessary at any point in the study. Participants who appear eligible based on the initial screening assessment will be provided the informed assent online, which they will be asked to sign electronically. Adolescents will be provided with RA contact in case any questions arise in

the assent document. Adolescents can ask questions about the study throughout the process and before providing assent to the study if they have concerns or questions. They may also discontinue participation at any point if they feel uncomfortable. This will be made clear in the assent documents and at the beginning of each research activity. If participants do not assent, their screener data will be retained for reporting purposes, but their data will not be used in future research. All research personnel will be comprehensively trained in human subject protections, including successful completion of the applicable sections of the Collaborative Institutional Training Initiative. REDCap reports will be generated daily to alert the RA to follow-up with subjects who have not signed the digital assent form. Participants may download a copy of the assent document or contact study staff at any time to request a copy.

WITHDRAWAL OF PARTICIPANTS

Participants can discontinue the study at any time at their own request, or they may be withdrawn at the discretion of the investigator for safety, behavioral or administrative reasons. The reason(s) for discontinuation will be documented and may include:

Participant voluntarily withdraws from treatment (follow-up permitted);

Participant withdraws consent (termination of treatment and follow-up);

Participant is unable to comply with protocol requirements; (termination of treatment and follow-up);

Participant demonstrates disease progression (termination of treatment and follow-up unless continued treatment with study intervention is deemed appropriate at the discretion of the investigator)

18.0 Provisions to Protect Participant Privacy and Data Confidentiality:

Participant contact information (including name, email, and phone number) will be stored in a secure, password-protected file. Only the PI (Kaylee Kruzan), Co-I (David Mohr) and members of the research team conducting field work will be able to access the file containing contact information and reporting aliases.

Screener data: We will collect screener data for all potential participants in the study via an online questionnaire hosted by Northwestern University's secure instance of REDCap. While recruitment decisions are being made, this data will be stored on Northwestern University servers that are encrypted. For those individuals who are not included in the study, their data will be retained for reporting purposes, but their data will not be used in future research. Screener information will not be used in future research, but may be used to re-contact individuals who completed screeners to see if they would like to opt in to learning about additional research opportunities associated with this project. For those selected, their screening data will become part of the main research data, which will be stored and protected as discussed elsewhere in this protocol. Email addresses and phone numbers of participants will remain stored in an encrypted and protected database on Northwestern University's servers.

In addition, transcriptions of audio files will have any identifying information redacted prior to storing and/or analyzing the data therein.

Data collected includes:

Contact information for participants (digital file)
Signed consent forms (digital file)

Interview protocol notes from researcher (digital file)
Interview audio files (digital file)
Transcription files (digital file)

Audio files will be transcribed by a Northwestern University-approved vendor, with file transport using a secure FTP site between Northwestern researchers and the approved vendor. Transcription files will be reviewed by researchers and anonymized, if necessary, prior to loading into secure coding software (e.g., nVivo, storing data locally) for data analysis.

All digital files will be stored in secure file folders with password protection.

Individuals with access to the digital files include: the Principal Investigator (Kaylee Kruzan), the Co-Investigator (David Mohr), and members of the research team conducting field work.

19.0 Data Monitoring Plan to Ensure the Safety of Participants:

Please note: We outline the data monitoring plan for the elicitation phase only below. We will update the protocol before beginning other phases of the study.

DESIGN STUDY

Should suicidality arise during an interview , researchers will be trained to respond using CBITs suicidality protocol.

Oversight of the trial is provided by the PI Dr. Kruzan, a licensed clinical social workerThe RA will ensure that informed consent is obtained prior to engaging in research activities, and that the study is conducted according to the IRB-approved research plan.

Study data are accessible at all times for the PI and all relevant Co-Is to review. The RA will conduct analyses of accrual, drop-outs, protocol deviations on a monthly basis initially, which may drop to quarterly once we are confident that procedures are functioning adequately.

CLINICAL TRIAL

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS

Plans to minimize potential risks involve assessment to detect risk and a safety protocol to ensure the safety of participants. This process will be overseen by a clinical monitor who has expertise in suicide risk assessment.

- **Assessment:** Participants in the trial will receive automated self-report self-reports for NSSI every week. At least every 4 weeks, participants will be assessed with the PHQ-A, where the 9th and 11th items assess suicidal ideation. Participants endorsing any non-zero score on the PHQ-A item 9 OR indicating “yes” on the 11th item, will receive the BDI-II item 9 as a follow up. Participants who score at or above 2 on the BDI-II item 9 will be contacted by telephone by myself or the trained research assistant for further assessment using the CBITs Suicide Risk Assessment and Follow-up Protocol, which involves

administering the Columbia Suicide Severity Rating Scale by telephone, working with the individual to develop a care plan, referring the participant to resources such as the national suicide prevention lifeline, or treatment, or considering emergency services in cases of imminent danger. If outreach is determined to be necessary the study team will respond within 24 hours, including those flagged after business hours. Participants who indicate suicidal ideation through within app text logging (e.g., in response to the conversational agent), or through phone calls or interviews will similarly be called and administered the Columbia Suicide Risk Assessment.

- **Ensuring participant safety:** Once the PI is notified of potential suicidality, all actions necessary to ensure participant safety will be taken. This includes, evaluation of all necessary data including study records, calling the participant for further evaluation, and administering the Columbia-Suicide Severity Rating Scale. All efforts will be made to ensure the safety of participants showing potential imminent dangerousness, up to and including recommending hospitalization, calling emergency services in the participant's jurisdiction to perform a "health and safety" check, or any other actions deemed necessary to ensure the safety of the patient. The PI, in consultation with the on call clinical monitor, also has the option of recommending that the patient be discontinued from the study and referred for more appropriate care. Because the RA will be the main point of contact for participants, they will be given thorough training in the assessment of STBs. While the PI will be responsible for the management of suicidal participants, it is possible that an emergent situation will arise that requires immediate attention, therefore the RA will be trained in the identification of imminent danger and procedures to ensure participant safety, including referral to crisis resources, identification of the participant's location, and contacting local emergency services. The PI will be notified of all cases of STBs and will consult with the clinical monitor. An adverse and serious adverse event (defined below) will be reported to the IRB, the DSMB chair, and the PO within the timeframes outlined under the NIH General Reporting Policy.
- **Recruitment and Informed assent/consent:** Methods previously used for recruiting subjects through MHA will be employed in the current study. Adolescents (14-18 years old) will be recruited nationally, from across the United States, using Mental Health America's website. Assent procedures will be written at a 4th grade reading level to ensure that they are understandable by English Speaking participants 14-18 years old. Informed consent will be collected from participants prior any enrollment or study procedures. Participants who appear eligible based on the initial screening assessment will be provided the informed consent online, which they will be asked to sign electronically. Adolescents will be provided with RA contact in case any questions arise in the assent document. If participants do not consent, their screener data will be retained for reporting purposes, but their data will not be used in future research. If they do consent, the RA will reach out to them to initiate enrollment. All research personnel will be comprehensively trained in human subject protections, including successful completion of the applicable sections of the Collaborative Institutional Training Initiative. REDCap reports will be generated daily to alert the RA to follow-up with subjects who have not signed the digital consent form. Participants may download a copy of the consent document or contact study staff at any time to request a copy.

Oversight responsibility

- Oversight of the trial is provided by the Principal Investigator Dr. Kruzan. The RA will ensure that informed assent is obtained prior to engaging in research activities, and that the study is conducted according to the IRB-approved research plan. All incoming data (assessments) are automatically monitored for STB risk. A notification is automatically

sent to the RA and PI when a participant indicates risk, both are trained to identify and report risk, and clinical monitor is notified by PI.

Quality Assurance

- **Data confidentiality and security:** Data for all participants will be kept strictly confidential, except as mandated by law. All research files are kept on secure, password protected servers managed by Northwestern University Feinberg School of Medicine Information Technology. All electronic data will be stored on secure servers behind firewalls meeting all security requirements of the medical school. Any paper documentation (which I do not anticipate) is kept in locked file cabinets or a locked file room. Participants will be assigned a numerical code for identification in the files. Names and other identifiers will be kept in separate password protected files. Audio data will be stored on secure servers and will only be available for coding by study staff. To reduce the risk of loss of confidentiality through the participant's device, we will instruct participants on how to add a PIN to their phone to prevent unwanted access to the DMHI app. All data transmission of data from a participant's device to study servers will be secured using industry-standard encryption tools.
- Study data (masked as to treatment assignment) are accessible at all times for the PI and biostatistician to review. The PI, with mentorship from the biostatistician (Kwasny), will conduct analyses of accrual, drop-outs, protocol deviations on a monthly basis initially, which may drop to quarterly once we are confident that procedures are functioning adequately.

Collection and reporting of AEs and SEAs

For this study, the following standard AE definitions are used:

- ***Adverse event:*** Any unfavorable and unintended sign or symptom temporally associated with the use of digital mental health interventions, regardless of whether it is considered related to interventions
- ***Serious Adverse Event:*** Any AE that results in any of the following outcomes:
  - Death
  - Life-threatening situation
  - Event requiring inpatient hospitalization or prolongation of existing hospitalization
  - Persistent or significant disability/incapacity

- **AEs are graded according to the following scale:**
  - Mild: An experience that is transient and requires no special treatment or intervention. The experience does not generally interfere with usual daily activities.
  - Moderate: An experience that is alleviated with simple therapeutic treatments. The experience impacts usual daily activities.
  - Severe: An experience that requires therapeutic intervention. The experience interrupts usual daily activities. If hospitalization (or prolongation of hospitalization) is required for treatment it becomes an SAE.
- **The study uses the following AE attribution scale:**
  - Not related: The AE is clearly not related to the study procedures (i.e., another cause of the event is most plausible and/or a clinically plausible temporal sequence is inconsistent with the onset of the event).

- Possibly related: An event that follows a reasonable temporal sequence from the initiation of study procedures, but that could readily have been produced by a number of other factors.
- Related: The AE is clearly related to the study procedures.

Monitoring schedule and reporting procedures:

- Dr. Kruzan, as PI, and the study team will review adverse events (AEs) and serious adverse events (SAEs) individually in real-time. The PI ensures all protocol deviations, IRB/ISM/DSMB/OHRP suspension, AEs, and SAEs are reported to the IRB and the NIMH program officer according to the NIH General Reporting Policy. Protocol violations and adverse events will be reported in the annual progress report; unanticipated problems involving risks to subjects or others or unexpected SAEs related to study participation will be reported to the NIMH PO within 10 business days of the PI or RA learning of events; and deaths related to study participation will be reported immediately following PI knowledge (no later than within 5 business days); IRB/ISM/DSMB/OHRP suspension will be reported to the NIMH PO within 3 business days of receipt. All efforts will be made to report SAEs and specific treatment-associated AEs to the IRB and NIMH program officer within 24 hours.

Data Safety Monitoring Board

- A Data Safety Monitoring Board (DSMB) has been developed for this study to review and monitor participant safety, data quality and integrity, and study progress, including recruitment, retention, and adherence to the protocol. The DSMB will be chaired by Peggy Andover, PhD, an Associate Professor of Psychology at Fordham University and an expert in nonsuicidal self-injury (NSSI) with experience both in running trials of interventions for NSSI and running DSMBs. Dr. Andover will staff the DSMB will expert members who are external to the study team and independent from professional and financial conflict per NIH guidelines. The DSMB will meet prior to the launch of the clinical trial to review the protocol and establish a charter that defines what data points will be monitored, how the data will be monitored, and the monitoring schedule. Thereafter, the DSMB will meet three times a year for the duration of the trial. Members of the investigative team, including Dr. Kruzan (PI), Dr. Mohr (Primary Mentor), Dr. Washburn (Clinical expert) and Dr. Kwasny (Biostatistician) will attend the DSMB meetings as ex-officio, non-voting members to facilitate communication between the DSMB and study personnel, but may be asked to step out of meetings during deliberations, votes, and decisions. The DSMB will review study progress, data integrity, and any adverse events to determine changes in participant risk, as well as any event or concern raised by the PI or clinical monitor.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS

Potential participants will be identified by the eligibility survey. Prior to being consented, candidates will receive information about the study. Candidates who decline the consent procedure or who are screened out will have any identifying information removed from study records. Consent for the study will then be managed by research study personnel. The study team will not release the identity of any participant to any non-authorized individual, except as is necessary for participant safety or regulatory review.

COMPENSATION FOR RESEARCH-RELATED INJURY

N/A

ECONOMIC BURDEN TO PARTICIPANTS
There will be no cost to participants to receive the DMHI. It is possible that some participants might have very limited data plans, and the use of DMHI will cause them to exceed their data limit resulting in fees. The DMHI should not use unusually large amounts of data, so this is an unlikely occurrence, and the study team asks about participant data plans and will inform participants of the expected data usage prior to downloading the app. There are no procedures that will be billed to insurance.

NON-ENGLISH SPEAKING PARTICIPANTS
N/A

20.0 Long-term Data and Specimen Storage and Sharing:

Electronic and physical storage of data collected will be managed by the Principal Investigator conducting field research. When active analysis of data is complete, the electronic and physical data will be retained according to Northwestern University's data retention policies, up to and including destruction of data in the future.

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)
N/A

WAIVER OR ALTERATION OF HIPAA AUTHORIZATION
N/A

21.0 Qualifications of Research Team to Conduct the Research:

The **Center for Behavioral Intervention Technologies** (CBITs) at Northwestern conducts research on the design and evaluation of digital mental health interventions for a variety of common mental health conditions.

Kaylee Kruzan, PhD, is a Research Assistant Professor, and licensed clinical social worker, in the Center for Behavioral Intervention Technologies and the Department of Communication at Northwestern. Her areas of expertise include Communication Technologies and Nonsuicidal Self-injury. She has experience conducting interviews with young adults with NSSI and has run a clinical trial on a digital intervention for young adults with NSSI.

David Mohr, PhD, is a licensed clinical psychologist, the Director the Center for Behavioral Information Technologies (CBITs) within Northwestern's Feinberg School of Medicine, and the Co-Director of NIMH Multidisciplinary Training Program in Digital Mental Health. Dr. Mohr has overseen many projects on the design and implementation of a variety of digital mental health interventions.**Student and postdoctoral researchers** conducting field research on this project will be thoroughly trained in the semi-structured protocol, personal safety, and on skills in working with participants from vulnerable populations.

RESOURCES AVAILABLE

Recruitment will occur through Mental Health America. We have existing collaborations with MHA and have based our enrollment strategy based on an ongoing trial that uses the same enrollment procedure with a slightly older population (young adults 18-24 w/ NSSI). Additionally, the investigators have considerable experience with user-centered design,

development of digital mental health treatments, and the conduct of randomized controlled trials. CBITs has a virtual clinical trials platform that enables automated recruitment, consenting, enrollment, randomization, assessment, and provides trial management tools that can monitor data acquisition. This platform has been used for multiple clinical trials and has been described in several papers.[72,73] We feel confident in our recruitment strategy, which is based on our prior work using similar methods. We expect to enroll approximately 10 participants per month during the trial, which is very achievable given our experience with online recruitment and our virtual clinical trials platform. The lost-to-follow-up rate will be minimized by 1) paying participants $20 for each assessment and 2) encouraging participants to continue completing paid outcomes assessments even if they drop out of treatment.

REFRENCES

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