CLINICAL STUDY PROTOCOL

A digital game targeting suicide prevention in adolescents who report substance misuse

(Formative Work and Pilot Study)

Principal Investigator

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Sponsor

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Synopsis

Purpose

Suicide is the second leading cause of death in adolescents aged 14-18 years. In this age group substance use is a risk factor for suicidal thoughts and behaviors. Specifically, adolescents who misused prescription opioids were more likely to experience suicidal thoughts and behaviors than adolescents who did not. The role of school-based health centers (SBHCs) holds promise as they offer accessible medical and behavioral health services. However, there is a lack of research on effectiveness of behavioral health services delivered in SBHCs, including those that target suicidal thoughts and behaviors. Compelling evidence shows “serious games” (i.e., games for a purpose other than solely entertainment), as digital experiences, can promote health, reduce risk factors, enhance protective factors through skill-building, and target prevention. To date, no serious game focused on suicide and opioid misuse has been developed or evaluated in schools. Therefore, we will create supportED focused on suicide prevention.

Objectives

Formative Work: Our primary aim is to design and develop a digital game that models the process of a safety planning intervention. To do so, we will explore and better understand peer or student perceptions around potential warning signs, coping strategies, and seeking help among youth who may be at greater risk of suicide due to misuse of substances. We will conduct focus groups with adolescents, college-aged youth, and school-based mental health providers. In addition, we will aim to conduct approximately 10 individual interviews with adults who may have misused substances during their youth and will be able to reflect on what they wish they knew during then (aged 18-80). Interviews will last approximately 60-90 minutes for one session and will be conducted via Zoom. Findings will inform the development of a digital game to reduce the risk of suicide among adolescents who misuse opioids. Once a prototype of the game is developed, we will conduct play-test focus groups with adolescents and school-based mental health providers to finalize the game.

Pilot Study: In year 2, we will assess user experience, acceptability, and feasibility of the game experience as well as explore the following proximal outcomes such as but not limited to adolescent well-being, intentions to use a safety planning intervention, coping strategies, substance misuse in last 30 days, and associated risk factors related to suicidal risk (e.g., hopelessness, impulsivity, etc.).

Study Population

Formative Work: High-school-aged students between the ages of 16-19, college-aged youth between the ages of 18-22, adults aged 18-80 and school-based mental health providers aged 18-80.

Pilot Study: Sixty (60) high-school-aged students between the ages of 13-19.

Number of Participants

Formative Work: We will conduct six focus groups with a total of 30 participants (10 high-school aged adolescents [aged 16-19], 10 college-aged youth [aged 18-22], and 10 adult school-based behavioral health providers [aged 18-80]) during development. We will also conduct approximately 10 interviews with adults who may have misused substances during their youth and will be able to reflect on what they wish they knew during then (aged 18-80). We will conduct play-testing focus groups with input from adolescents and/or college-aged youth each (n=10-20), high school youth aged 16-22, and focus groups of school-based mental health providers and/or providers who specialize in addiction who are aged 18-80 (n=10-20) to assess user experience (e.g., acceptability and usability) and feasibility of protocol to prepare for a larger pilot STUDY that will require a new protocol (N=60).

Pilot Study: We will conduct a pilot study with a total of 60 high-school aged adolescents [aged 13-19], who attend a high school with a school-based provider.

Study Design

Formative Work: The protocol will be conducted over the course of two years. The outline below highlights the study design. We will conduct focus groups to inform the development of a digital game and discuss approaches to enhance user experiences, acceptability, and feasibility of the game experience. First, we will conduct six focus groups with a total of 30 participants, including 10 high-school-aged adolescents,10 college-aged youth [aged 18-22], 10 providers. In addition, we will conduct approximately 10 interviews with adults [aged 18-80] who may have misused substances and will be able to reflect on what they wish they knew during their adolescence to inform the content of the videogame with a focus on content related to potential warning signs, coping strategies, and seeking help to prevent suicidal thoughts and behaviors among youth who misuse opioids. Focus groups/interviews will occur in-person or via Zoom over the course of six months. Each group/interview will meet for approximately 1-1.5 hours after school hours. The study will be introduced to parents/guardians and students and then, if interested, information sheets will be provided in paper form or electronically. When the study is introduced to parents/guardians and students, we have always stressed that a stipulation of our studies requires reliable transportation to/from our studies if conducted in person. If COVID-19 restrictions apply, we may modify this process and share flyers with educators who will share with their students and/or parents/guardians or email information sheets to parents/guardians when email is provided. No forms will be signed in our procedures. In certain cases where transportation is not available by family or school, we will provide a bus pass.

Focus groups/interviews will be approximately 60-90min. A semi-structured focus group/interview guide will be developed, pilot tested, and used in focus groups/interviews. The focus group/interview guide will align with constructs from a safety planning intervention,[a,b] a well-recognized, evidence-based suicide prevention intervention, and

include questions related to potential warning signs of emotional distress, coping strategies, and seeking help to prevent suicidal thoughts and behaviors among youth who misuse opioids. Focus groups/interviews will be led by a facilitator, who is also a certified school counselor and licensed professional counselor, and a co-facilitator who will take field notes. Focus groups/interviews will be audio-recorded. Transcripts will be transcribed verbatim by a third-party transcription service who our Lab has worked with prior. All participants will receive instructions on not using identifiable information (e.g., names, school, peer/colleague names, etc.) while being audiotaped and will be provided a study number prior to the start of audiotaping. Participants will be instructed to state their study number prior to speaking. Audiotapings will be transcribed and will be destroyed 24 months after the completion of the study and after review of their content has been completed. Transcriptions will not be sent to other institutions and will not be used for purposes other than this study and future publications related to this study. Should any identifiable information be shared in the focus groups, it will be redacted from transcripts. Participants will receive a $25 gift card to participate.

We will follow the same protocol for play-testing focus groups in order to finalize the game.

Pilot Study: Once the prototype of a game is ready, we will conduct a pilot study to evaluate the usability and acceptability of the game, and feasibility of delivering the game in schools. We will enroll 60 who attend one of our partner school sites. We will also explore proximal outcomes such as but not limited to adolescent well-being assessment, intentions to use a safety planning intervention, coping strategies, substance misuse in last 30 days, and associated risk factors related to suicidal risk (e.g., hopelessness, impulsivity, etc.). See below for additional details on measures. Our research team will be trained by Dr. Blumberg's team and a Pitt Methods workshop on suicide prevention research prior to commencing the study in all procedures, risk and protection methods, and safety related to conducting suicide **prevention** research as well as attend a summer workshop on best practices in conducting suicide prevention research. Eligible individuals will be assigned to either the 1) supportED group (n=30) or 2) control group (n=30). Both groups will also receive NIDA and NIMH pamphlets on substance misuse and mental health at the end of the session. Prior to receiving pamphlets, those in the supportED group will engage with the game for one session (~45min) while the control group will engage with a non-health-related game for the same duration. Given schools do not have a standardized approach to address suicide prevention, we opted to use an attention/time control condition. Participants will use a dedicated device (e.g., tablet, laptop, or desktop) to access their digital experience on the web. The research staff will be present to monitor gameplay, to provide support, if needed, and to field questions in person. There will also be a school-based provider on site for direct referrals, as needed, given the sensitive topic. The total duration of the game and number of sessions is consistent with those found in safety planning and with the amount adolescents engaged with our empowerED game.

The Yale University Human Subjects Committee (the committee that reviews, approves, and monitors research on human subjects) may inspect study records**.** All published results will be group data. Information that will be collected during the focus group interviews will be erased 24 months after the completion of the study and after review of their content has been completed.

Formative and development work: (1 year)

- We will work iteratively with our target audience of 16-19-year old adolescents within schools, college-aged youth for their reflections of their 16-19 year selves, and school-based mental health providers to develop videogame content, collecting qualitative data for the videogame and refining our logic model with input from 2 focus groups of 5 high school adolescents each (n=10), aged 16-19, 2 focus groups of 5 college-aged youth each (n=10), aged 18-22 and 2 focus groups of 5 school-based mental health providers aged 18-80 (n=10), and approximately 10 interviews with adults who may have misused substances during their youth and will be able to reflect on what they wish they knew during then (n=10).
- We will create the "Game Playbook" specific to this new digital Game Playbooks are our game manuals. We create behavior change gameplay manuals to accommodate the specific needs of a multi-disciplinary game development team. The playbooks outline the theoretical foundations and gameplay elements. This ensures targeted theoretical principles and behavior change mechanisms and constructs are included in the videogame.
- We will build the new digital game by creating new content, developed from focus groups and from the suicide and opioid/substance misuse prevention literature, for our game development team, DigitalMill, Inc.
- We will conduct play-testing focus groups with input from adolescents and/or college-aged youth each (n=10-20), high school youth aged 16-22, and focus groups of school-based mental health providers and/or providers who specialize in addiction who are aged 18-80 (n=10-20) to assess user experience (e.g., acceptability and usability) and feasibility of protocol to prepare for a larger pilot study that will require a new protocol (N=60).

Pilot Study (Year 2):

- We will conduct a pilot study with (N=60) adolescents between the ages of 13-19. We will examine the usability and acceptability of the game experience among adolescents, and the feasibility of protocols and procedures in delivering the game experience by piloting assessment measures in schools.

- We will also explore proximal outcomes as potential means for behavior change in supportED vs. control group at 3 months. Examples include but are not limited to the following measures on: 1) intentions to use safety plan; 2) coping strategies;

and, 3) suicidal thoughts and associated risk factors (e.g., pessimism, helplessness, limited social support, and despair).

Study Duration

The anticipated duration of this study will be two years.

Year 1: Participants will engage in twelve focus groups and approximately 10 interviews over one-year period for approximately 60-90 minutes each.

Year 2: Participants will engage with the gameplay or a non-health-related game over one-year period for approximately 45 minutes each.

Outcome Variables

The outcomes are exploratory and preventative by nature.

Formative Work: We will explore participants' perceptions on their peers' or students' potential triggers, coping strategies, and resources related to opioid misuse and suicide prevention as outlined in safety planning.[5]

Pilot Study: We will ask questions about user experience, including usability and acceptability. We will ask questions about feasibility. Feedback on what they view as acceptable/feasible will be critical to developing successful technological gameplay experience targeting mental health supports and suicide prevention among youth who have misused substances.

Locations/Facilities

Formative Work: The study will be conducted virtually with participants from across the United States via Zoom and/or at previously long-standing and established partner school sites. We will also recruit from existing partnerships in Connecticut and Miami-Dade County Public schools, such as but not limited to Maloney (Meriden, CT; N=1191), Hamden (Hamden, CT; N=1598), and Platt (Meriden, CT: N=970), Ronald W. Reagan Doral (Miami, FL; N= 1440), Miami Lakes Educational Center (Miami, FL; N= 1015), Alonzo and Tracy Mourning (Miami, FL; N=1528), School for Advanced Studies West (Miami, FL; N=119), and Barbara Goleman (Miami, FL; N=2882).

Pilot Study: The study will be conducted among high schools with school-based behavioral providers, including previously long-standing and established partner school sites. We will also recruit from existing partnerships in Connecticut and Miami-Dade County Public schools, such as but not limited to Maloney (Meriden, CT; N=1191), Bassick High School (Bridgeport, CT; N=970), Ronald W. Reagan Doral (Miami, FL; N= 1440), Miami Lakes Educational Center (Miami, FL; N= 1015), Alonzo and Tracy Mourning (Miami, FL; N=1528), School for Advanced Studies West (Miami, FL; N=119), and Barbara Goleman (Miami, FL; N=2882). See letters of support.

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1 - Background/Literature Review

1.1 Background

Suicide is the second leading cause of death in adolescents aged 14-18 years[a]. In this age group, substance use is a risk factor for suicidal thoughts and behaviors. Specifically, adolescents who misused prescription opioids were more likely to experience suicidal thoughts and behaviors than adolescents who did not[b].The role of school-based health centers (SBHCs) holds promise as they offer accessible medical and behavioral health services. However, there is a lack of research on effectiveness of behavioral health services delivered in SBHCs, including those that target suicidal thoughts and behaviors[c]. Safety Planning, a brief psychosocial intervention that identifies coping strategies and sources of support, is considered a best practice to alleviate suicidal crisis in the emergency department setting[d-m]; however, to date, there are no studies that evaluate safety planning in schools. In addition, compelling evidence shows "serious games" (i.e., games for a purpose other than solely entertainment), as digital game, can promote health, reduce risk factors, enhance protective factors through skill-building, and target prevention[n-p]. To date, no serious game in the form of a safety planning intervention focused on suicide and opioid misuse has been developed or evaluated in schools. Therefore, we will conduct formative research (e.g., focus groups) to build a digital game focused on suicide prevention among youth who misuse opioids. Research demonstrates that asking youth about suicide does not increase risk for suicidal behaviors and ideation.[ff]

2 - Rationale/Significance/Problem Statement

2.1 Rationale

Suicide is the second leading cause of death in adolescents aged 14-18 years.[a] In this age group, substance use is a risk factor for suicidal thoughts and behaviors.[f] Specifically, adolescents who misused prescription opioids were more likely to experience suicidal thoughts and behaviors than adolescents who did not.[b] The role of school-based health centers (SBHCs) holds promise as they offer accessible medical and behavioral health services. However, there is a lack of research on effectiveness of behavioral health services delivered in SBHCs, including those that target suicidal thoughts and behaviors.[c] Compelling evidence shows "serious games" (i.e., games for a purpose other than solely entertainment), as digital games, can promote health, reduce risk factors, enhance protective factors through skill-building, and target prevention[n-p] .To date, no serious game focused on the intersection of suicide and opioid misuse has been developed or evaluated in schools.

Our **specific aims** include the following:

Aim 1: Adaptation Activities (Year 1): Aim 1a: Using methods developed by our multidisciplinary team, who has extensive experience developing videogames for adolescents, we will conduct six focus groups with 30 participants including 10 high school-aged adolescents, 10 college-aged youth, and 10 school-based behavioral health providers as well as approximately 10 interviews with adults who may have misused substances during their youth and will be able to reflect on what they wish they knew during then. We will learn about their experiences related to their peers' or students' potential warning signs, coping strategies, and resources in seeking support related to youth who misuse opioids and suicide prevention. We will extract themes using rapid analytic techniques to inform content and storylines. **Aim 1b:** In collaboration with our long-standing partnership with DigitalMill and the national School-Based Health Alliance (SBHA), we will adapt a theory- and evidence-based videogame that will be called ***supportED*** by integrating constructs from self-determination theory and social cognitive theory, as well as techniques from Motivational Interviewing to enhance engagement**.** It will model the evidence-informed practice of safety planning.[m]

Aim 2: Evaluation Activities (Year 2): In collaboration with CT and MDCP schools, where we have partnerships, we will conduct a pilot study with 60 adolescents (aged 13-19). We will examine usability and acceptability of the gameplay experience, and feasibility of delivering the game and piloting protocols in schools. We will also explore proximal outcomes as potential means for behavior change in supportED vs. control group at 3 months on: 1) intentions to use safety plan; 2) coping strategies; and, 3) suicidal thoughts and associated risk factors (e.g., pessimism, helplessness, limited social support, and despair).

Completion of these aims will generate an evidence-informed, novel approach to addressing the intersection of suicide and prescription opioid/substance misuse among adolescents and, ideally, reduce the risk of suicide among a population who may experience greater risk

2.2 Significance

Suicide is the second leading cause of death among adolescents ages 14 through 18, accounting for 2,039 deaths annually in the U.S in 2018.[a] In the last 10 years, the incidence of suicide among high school-aged students increased by 62%.[e] By grade, a significant increase in having attempted suicide was observed for 12th-grade students (4% to 9%). Substance use in this age group is a significant risk factor for suicidal thoughts and behaviors. Specifically, adolescents who misuse prescription opioids are one and a half times more likely to have suicidal ideation, to make a suicide plan, or to attempt suicide.[b] School-based health centers (SBHCs) increase access to and reduce barriers to behavioral health services, and are positioned well to address this work. For this stage of our study, the goal is to design a videogame to reduce the risk of suicide in adolescents who are at greater risk due to lifetime prescription opioid misuse. To achieve this goal, we will create a digital game, modeling the process of safety planning. Using the methods developed by our multidisciplinary team that has extensive experience developing videogame for adolescents, we will conduct six focus groups, including four focus groups with 10 high school-aged adolescents and 10 college-aged youth, as well as two focus groups with 10 SBHC providers. We will also conduct approximately 10 interviews with adults who may have misused substances during their youth and will be able to reflect on what they wish they knew during then. Data from focus groups will inform relatable stories that are engaging and offer opportunities for skill development. To assess user experience (e.g., acceptability and usability) and feasibility of protocol, we will conduct a total of six focus groups for play testing: focus groups with adolescents and/or college-aged youth each (n=10-20), high school youth aged 16-22, and focus groups with school-based mental health providers and/or providers who specialize in addiction who are aged 18-80 (n=10-20) to assess user experience (e.g., acceptability and usability) and feasibility of protocol to prepare for a larger pilot study that will require a new protocol (N=60).

3.1 Purpose

Through the use of focus groups, we will better understand and explore participant's perceptions of their peers' or students' related to potential warning signs, coping strategies, and resources to seek help in an effort to reduce the risk of suicide among their peers or students who misuse opioids. We will extract themes using rapid analytic techniques to inform content and storylines. Additionally, in collaboration with our long-standing partnership with DigitalMill and schools, we will adapt a theory- and evidence-based videogame that will be called supportED by integrating constructs from self-determination theory and social cognitive theory, as well as techniques from Motivational Interviewing to enhance engagement. It will model the evidence-informed practice of safety planning.[d]

3.2 Hypothesis

We will test the hypothesis that individuals who engage with supportED will find the prototype engaging and acceptable (e.g., easy to use, relatable, and helpful) among youth. We will also test if the prototype is feasible to deliver in schools. We also hope to report decreases in outcomes in comparison to the control group through our exploratory findings although the sample is not large enough to correlate.

3.3 Objectives

Our primary aim is to develop and pilot-test a videogame to reduce suicide risk in adolescents who report substance misuse. The approach follows well-established guidelines using rigorous methods to develop theory-informed videogames with demonstrated benefits in proximal outcomes (e.g., knowledge, beliefs, attitudes, and behaviors),56-59 utilizes long-standing successful partnerships in schools doing this work, and integrates robust expertise in suicide prevention research. Using the successful methods from prior studies, we will design and adapt a previously developed game (empowerED) informed by focus group data for content (Aim 1). We will then pilot test this game (Aim 2).

4 - Study Participants

4.1 Study Population

Formative Work: The study will enroll high-school-aged adolescents (aged 16-19), college-aged youth (aged 18-22), and adult school-based behavioral health providers (aged 18-80). Study enrollment and focus groups/interviews will be conducted virtually with participants across the United States and in collaboration with previous partnership in Connecticut and Miami-Dade County Public schools, such as but not limited to Maloney (Meriden, CT; N=1191), Bassick (Bridgeport, CT; N=970), Ronald W. Reagan Doral (Miami, FL; N= 1440), Miami Lakes Educational Center (Miami, FL; N= 1015), Alonzo and Tracy Mourning (Miami, FL; N=1528), School for Advanced Studies West (Miami, FL; N=119), and Barbara Goleman (Miami, FL; N=2882).

Pilot Study: The study will enroll high-school-aged adolescents (aged 13-19) who report substance misuse (n=60). Study enrollment be conducted with participants in collaboration with previous partnership in Connecticut and Miami-Dade County Public schools, such as but not limited to Maloney (Meriden, CT; N=1191), Bassick (Bridgeport, CT; N=970), Ronald W. Reagan Doral (Miami, FL; N= 1440), Miami Lakes Educational Center (Miami, FL; N= 1015), Alonzo and Tracy Mourning (Miami, FL; N=1528), School for Advanced Studies West (Miami, FL; N=119), and Barbara Goleman (Miami, FL; N=2882)

4.2 Number of Participants

Formative Work: We will conduct six focus groups with a total of 30 participants (10 high-school aged adolescents [aged 16-19], 10 college-aged youth {aged 18-22], and 10 adult school-based behavioral health providers [aged 18-80]) during development. We will conduct approximately 10 interviews with adults who report misuse of substances in their youth. We will conduct approximately 6 play-testing focus groups with input from adolescents and/or college-aged youth each (n=10-20), high school youth aged 16-22, and focus groups of school-based mental health providers and/or providers who specialize in addiction who are aged 18-80 (n=10-20) to iteratively improve and finalize the game.

Pilot Study: The study will enroll 60 high-school-aged adolescents (aged 13-19) (n=60).

4.3 Selection Criteria

Formative Work:

High-school aged adolescent participants must: 1) attend a high school; 2) be aged 16-19; 3) English-speaking; 4) be willing to engage in discussions around mental health (e.g., potential warning signs, coping strategies, and help-seeking behaviors) related to suicide prevention and opioid misuse; and 5) if attending via Zoom, have access to Internet and a device for Zoom.

College-aged participants must: 1) attend a college/university; 2) be aged 18-22; 3) English-speaking; 4) be willing to engage in discussions around mental health (e.g., potential warning signs, coping strategies, and help-seeking behaviors) related to suicide prevention

and opioid misuse; and 5) if attending via Zoom, have access to Internet and a device for Zoom.

Adult school-based behavioral health provider and/or providers with expertise in addiction medicine participants must: 1) provide behavioral health services in a high school (if school-based) or provide addiction medicine services (if expertise in addiction medicine), 2) be aged 18-80, 3) English-speaking, 4) be willing to engage in discussions around mental health (e.g., potential warning signs, coping strategies, and help-seeking behaviors) related to suicide prevention and opioid misuse; and 5) if attending via Zoom, have access to Internet and a device for Zoom.

Pilot Study:

Inclusion criteria: For the pilot study, participants must: 1) attend a high school that has a school-based provider; 2) be between the ages of 13-19; 3) fluent in reading English during the consent process; 4) be willing to sit for a single session to complete pre-/post-assessments, engage with the game (~45min), and participate in a post-gameplay focus group (if in the experimental group) for 60min; and 5) provide assent and parental/guardian consent (if<age 18).

Exclusion criteria: Any student who is actively suicidal and/or moderately severe to severely depressed will not be eligible and will be immediately referred to the school-based provider on site to who will follow school protocol (e.g., contact 211, notify parent/guardian, and/or contact their local emergency department, etc.), as needed. Student may return to rescreen for participation according to the criteria on page 16.

Rescreening: Participants will not have to repeat the questions related to static variables (such as demographics and past experiences), but the baseline assessment of dynamic variables will need to be repeated and meet eligibility requirements .

4.4 Recruitment Procedures

Formative Work: Participants will receive a $25 gift card to participate in focus groups and playtesting sessions. Flyers will be circulated throughout schools.

Pilot Study: For the pilot study, participants will receive a $25 gift cards as compensation for completion of assessments at each time point. We will share with educators, school-based providers, and our youth advisory board who will share with students. Students may then share with other students (e.g., snowball sampling). The flyers contain a QR code for students to input their first/last name, phone number, and email address. If they are younger than 18, they must input parent/guardian first and last name, phone number, and email address. Research staff will then contact them to obtain consent/e-consent. When needed, study staff will be available to parents/guardians for information sessions should they have any questions.

4.5 Risks

The potential risks associated with this study have to do with maintenance of the confidentiality of the identities of the participants enrolled in the study and information relating to them. As with all of our studies, we will train study researchers in maintaining

confidentiality. Prior to the start of the focus groups, researchers will discuss potential risks including breach of confidentiality.

Given engagement in discussions with the research team about its content may pose a potential psychological risk in that we address sensitive issues around mental health, substance use, and its consequences, Dr. Fernandes (who is a Certified School Counselor and Licensed Professional Counselor, and has extensive expertise working with adolescents, college-aged youth, and schools) will be on site for all study sessions in Miami and Connecticut with research staff, when available, to connect participants to school-based personnel as a resource should any distress or concern arise. Dr. Fernandes has a long-standing relationship with school partners and will refer students to their school-based personnel for additional support.

If there are additional concerns raised with regards to active substance use or mental health, or if participants need additional or more intensive attention, the research staff will seek medical advisement from Dr. L. Fiellin, a medical doctor with expertise in addiction medicine, or Dr. H. Blumberg, a psychiatrist. All students will receive resources for support and hotline information from NIDA and NIMH. Students who report moderate to high suicide risk and/or depression will be directly connected immediately to the on-site school-based provider who will follow their school's protocol to help navigate care or file a referral (examples include conducting a safety planning intervention, connecting to outpatient clinic, notifying parent/guardian, and/or contact with local crisis intervention team and transport via ambulance to local emergency department as deemed necessary). Students will be flagged by our RedCap system as moderate-/high-risk as a result of their answers on the PHQ-8, GAD-7, CHRT, or ASQ measures, which will result in an immediate email notification to research staff on site who will immediately refer or connect the student to the on-site school-based provider.

If a student indicates moderately severe to severe symptoms of depression, student will be flagged and immediately connected to the school-based provider for a risk assessment and follow school protocol. If student is cleared by the school social worker, student may continue in the study and the school social worker will follow up with student in two weeks.

If a student screens positive for suicide (but is not acutely suicidal), student will be flagged and immediately connected to school-based provider for a risk assessment and follow school protocol. If student is cleared by school social worker, student may continue in study and the school social worker will follow up with student in two weeks. If student is acutely suicidal, student will be flagged and immediately connected to school-based provider who will follow school protocol (e.g., contact 211, contact parent/guardian, etc.). They will be ineligible to participate in the study on this day. Student may not return to rescreen for participation for at least 2 weeks and only when they are no longer actively suicidal. Eligibility for rescreening will be based on the resolution of the moderate or severe suicidality and may include being on active treatment, clearance by the school social worker according to school policy, or completion of brief treatment. Documentation of the resolution of the acute suicidality state will be documented upon assessment for eligibiligty for rescreening.

If any student were to become triggered as a result of the sensitive nature of the topics, the school-based provider will be able to offer and/or refer to school-based emotional support and/or referral services. The school-based provider will not be a part of handling any of the research protocols; however, the provider will be present and available for support services, as needed. They will receive a $75.00 gift card for their time.

This study presents minimal risks to the participants and adverse events or other problems are not anticipated.

Adverse Events (AEs):

Violation of confidentiality: Any breach of confidentiality.

Discomfort due to assessment procedures: Discomfort created by answering survey questions. Embarrassment in disclosing sensitive personal information.

Disclosure of information about current and/or intended physical harm to persons; current and/or intended abuse of children that would be reported to a child welfare agency; and/or an investigation of such allegations(s) that could ensue.

Dissatisfaction with the game activities: In this case it would be the gameplay experience. While gaming addiction is a recognized entity, it is very rare and, in the setting of playing a serious game, very unlikely. If there are any concerns of developing serious addictive behaviors in our pilot study participants, we have team members who are experts in the field of addiction medicine and will address these issues immediately.

Serious Adverse Events (SAEs):

SAEs include death, life threatening injury or condition, hospitalization, persistent or significant disability/incapacity, and other conditions which in the judgment of the investigators represent significant hazards. In the rare evident of an SAE, we do not expect them to be related to our study.

Procedures for research team management of AEs, SAEs and other study risks such as mandatory reporting requirements:

This study presents minimal risks to the participants and adverse events or other problems are not anticipated. In the unlikely event that such events occur, Reportable Adverse Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or unanticipated problems involving risks to subjects or others will be reported in writing within five calendar days to the IRB (using the appropriate forms from the website and electronic submission system) and the NCATS PO. The PI will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project through regular study meetings and via email as they are reviewed by the PI. We will use procedures to detect and respond to adverse events that ensure prompt discovery of any adverse events and to minimize their effects. There is adequate surveillance and protections to discover adverse events promptly and keep their effects minimal.

Procedures for training and supervision of all research personnel have been developed as part of our previous and current studies. All members of the research team are familiar with procedures for identifying and reporting possible adverse reactions. All members of the research team are trained in mandatory reporting and will notify the PI immediately of any concerns raised about participant mental health (suicidality), substance use, abuse of any kind, and so forth.

If an adverse event occurs study personnel will notify the PI as well as the appropriate Information Security Officer (ISO) and follow all necessary procedures. All adverse events are reported using the Yale Institutional Review Board (IRB) standard template for reporting adverse events. The PI reviews all adverse events, classifies the attribution of adverse events (e.g., definitely, probably, possibly related; unlikely or unrelated) and grades the severity of the event, utilizing the FDA's definition of serious adverse events, on a 6-point scale (0=no adverse event or within normal limit; 1=mild; 2=moderate; 3=severe; 4=life-threatening; 5=fatal). Serious unanticipated or anticipated adverse events will be reported promptly to the IRB within five calendar days and to the NCATS PO within 24 hours by phone and/or email and will submit a written report to the PO no more than two days later.

The PI will evaluate all adverse events and determine whether the event affects the Risk/Benefit ratio of the study and whether modifications to the protocol (e.g., Risks to Subjects) or consent form (e.g., Risks and Inconveniences) are required.

The PI will be responsible for monitoring the data and conducting performance and safety reviews, at the specified frequency. Either the PI or the IRB have the authority to stop or modify the study. The monitoring by the IRB will occur annually at the time of re-approval. The PI will conduct data and safety review at least quarterly and at any time a serious adverse event occurs. During the review process, the PI will evaluate whether the study should continue unchanged, requires modification or amendment to continue, or should be closed to enrollment.

4.6 Anticipated Benefits

The study may have no direct benefits to the participants, but may help researchers find out something that will help educators, clinicians, and/or adolescents.

4.7 Vulnerable Populations

Given participants will include minors (aged 13 through 17) who will participate in focus groups, information sheets will be shared prior to enrollment with minors and their parents/guardians.

For the pilot study, adolescent assent and parent/guardian consent/e-consent will be required for minors.

4.8 Consent/Assent Procedures

Formative Work: Given our study focuses on prevention and aims to better understand perceptions of peers and students, this protocol is eligible for a waiver of documentation of consent. The study will be introduced to parents/guardians and students and then, if interested in participating, information sheets will be provided via paper form or electronically. For participants under the age of 18, parents/guardians who do not wish for their children to participate will communicate disapproval to the research staff or remain silent/walk out for the purpose of demonstrating no interest to participate without

communicating to staff. Both options will result in non-participation by the adolescent. If COVID-19 restrictions apply, we may modify this process and share flyers with educators who will share with their students and/or parents/guardians. No forms will be signed in our procedures. This protocol is one we have used in our previous qualitative work and has been approved by the Yale IRB.

Pilot Study: For the pilot study, we will obtain informed written or digital consent from adolescents above the age of 18 and informed written or digital consent from parents or guardians with adolescents under the age of 18. We will obtain informed written or digital assent from all participants. We will share flyers with educators, school-based providers, and our youth advisory board who will share the flyer with students. Students may then share with other students (e.g., snowball sampling). The flyer contains a QR code where students will input their first/last name, age, grade, and email address and parent/guardian first and last name, phone number, and email address. Research staff will then contact them to obtain consent/e-consent. When needed, study staff will be available to parents/guardians should they have any questions.

5 - Methods

Pilot Study: Treatment – Device

5.1 Intended Use for Device (provide the following information for each device being investigated in the study)

supportED is a digital prevention game focused identifying warning signs, coping strategies, and resources for seeking help. The overall goal is to prevent suicide in youth who may be at risk due to substance misuse. The formative work of this game included focus groups and playtesting to develop a prototype of the game. In the subsequent pilot study, we will be investigating the usability/ feasibility of delivering the game in schools. This is not a pivotal study, as it is not powered to demonstrate efficacy of the game (n=60). For this reason, preliminary outcomes will only be exploratory in nature. Given the preliminary nature of the research, and primary outcomes of usability, feasibility, and acceptability we anticipate supportED to be classified as a non-significant risk device.

supportED is not designed to be a replacement for or of substantial importance in diagnosing, mitigating, or treating mental health, substance misuse, and suicidal thoughts and behaviors in youth. It is an external web-based game that does not present potential for serious risk. supportED models the process of a safety planning approach, an evidence-based approached to prevent suicide in emergency departments, through interactive storylines presented in the game. The game focuses on identifying warning signs, coping strategies, and resources for support with the goal to promote youth mental health and prevent the initiation or escalation of substance misuse.

5.2 Device Administration and Schedule

Eligible individuals will be assigned to either the 1) supportED group (n=30) or 2) control group (n=30). Both groups will also receive NIDA pamphlets on substance misuse for youth at the end of the session. Prior to receiving pamphlets, those in the supportED group will engage with the game for one session (~45min) while the control group will engage with a non-health-related game for the same duration. Given schools do not have a standardized approach to address suicide prevention, we opted to use an attention/time control condition. Participants will use a dedicated device (e.g., tablet, laptop, or desktop) to access their digital experience on the web. The research staff will be present to monitor gameplay, to provide support, if needed, and to field questions in person. Dedicated devices will be

prepped prior to sessions with participants (programmed as control or game). The school-based provider will be present for immediate referrals, if needed.

Currently our game does not record ANY personal information or even individual game information. We do not ask for a personal registration or login.

Twine by default does save information locally to the device running the Twine game off the Web server. No information is saved server-side and local information can be removed by deleting local-storage using the Web browser command to do so.

We envision most, if not all, players playing through an entire sitting in one session so saving locally shouldn't be a need, and devices will have local saves wiped if under-the-control of the research team.

We are considering disabling saves as well. However, Twine does maintain some saved state during play and it likely is cached (locally of course)

5.3 Method of Assignment/Randomization (if applicable)

Using a 1:1 randomization procedure, eligible individuals will be assigned to either the 1) supportED group (n=30) or 2) control group (n=30). Randomization will be stratified by assigned sex at birth (male or female).

5.4 Device Calibration

There is no necessary calibration process as supportED is a webbased game. If there are any concerns or issues with the functionality of the game, Ben Sawyer of Digital Mill will be available to assist. Participants will answer study related questions through a secured data management system, RedCap. The game itself will not be utilized to record any data.

5.5 Storage Conditions

supportED is a web-based game that will be delivered to participants via tablets, phones, or desktops. Participants will engage with the game under the supervision of the study team to ensure proper use of the game and care for the devices. Although our game does not collect any identifiable data, tablets will be locked and stored in a secure location.

5.6 Concomitant therapy

N/A there are no restrictions

5.7 Restrictions

Participants will engage with the device for a restricted period of 45 minutes (one-time session).

6 - Study Design

6.1 Study Design

The protocol will be conducted over the course of two years. The outline below highlights the study design.

Formative Work: We will conduct focus groups to inform the development of a digital game and discuss approaches to enhance user experiences, acceptability, and feasibility of the game. First, we will conduct six focus groups with a total of 30 participants, including 10 high-school-aged adolescents, 10 college-aged youth, and 10 providers, to inform the content of the videogame with a focus on content related to potential warning signs, coping strategies, and seeking help to prevent suicidal thoughts and behaviors among youth who misuse opioids. Focus groups will occur in-person or via Zoom over the course of six months. Each group will meet for approximately 1-1.5 hours after school hours. The study will be introduced to parents/guardians and students and then, if interested in participating, information sheets will be provided via paper form or electronically. When the study is introduced to parents/guardians and students, we have always stressed that a stipulation of our studies requires reliable transportation to/from our studies if conducted in person. In certain cases where transportation is not available by family or school, we will provide a bus pass.

Focus groups will be approximately 60-90 minutes. A semi-structured focus group guide will be developed, pilot tested and used in focus groups. The focus group guide will align with constructs from a safety planning intervention,[5,6] a well-recognized, evidence-based suicide prevention intervention, and include questions related to potential warning signs of emotional distress, coping strategies, and seeking help to prevent suicidal thoughts and behaviors among youth who misuse opioids. Focus groups will be led by a facilitator, who is also a certified school counselor and licensed professional counselor, and a co-facilitator who will take field notes. Focus groups will be audio-recorded. Transcripts will be transcribed verbatim by a third-party transcription service who our Lab has worked with prior. All participants will receive instructions on not using identifiable information (e.g., names, school, peer/colleague names, etc.) while being audiotaped and will be provided a study number prior to the start of audiotaping. Participants will be instructed to state their study number prior to speaking. Audiotapings will be transcribed and will be destroyed 24 months after the completion of the study and after review of their content has been completed. Transcriptions will not be sent to other institutions and will not be used for purposes other than this study and future publications related to this study. Should any identifiable information be shared in the focus groups, it will be redacted from transcripts. Participants will receive a $25 gift card to participate.

We will follow the same protocol for play-testing focus groups to finalize the game.

Pilot Study: To examine usability, acceptability, and feasibility, we will conduct a pilot study. We will enroll 60 high-risk adolescents who attend one of our partner school sites. We will also explore proximal outcomes.

Our research team will be trained by Dr. Blumberg's team and the Pitt Methods workshop prior to commencing the study in all procedures, risk and protection methods, and safety related to conducting suicide **prevention** research. Eligible individuals will be assigned to either the 1) supportED group (n=30) or 2) control group (n=30). Both groups will also receive NIDA/NIMH pamphlets on substance misuse and mental health for youth at the end of the session. Prior to receiving pamphlets, those in the supportED group will engage with the game for one session (~45min) while the control group will engage with a non-health-related game for the same duration. Given schools do not have a standardized approach to address suicide prevention, we opted to use an attention/time control condition.

Participants will use a dedicated device (e.g., tablet) to access their digital experience on the web. The research staff with Dr. Fernandes always there will be present to monitor gameplay, to provide support, if needed, and to field questions in person. A school-based provider will be present for direct referrals, as needed. The total duration and number of sessions is consistent with those found in safety planning and with the amount adolescents engaged with our empowerED game.[q] To pilot the feasibility of protocols, we will collect proximal outcomes, as possible mechanisms for behavior change. Proximal outcomes include but are not limited to the following measures: 1) intention to use safety planning; 2) coping strategies; and 3) severity of suicidal thoughts and associated risk factors (e.g., pessimism, helplessness, limited social support, and despair). We will also measure severity of suicidal ideation and attempts

We will collect participant demographic data including self-reported sex at birth, gender identity, sexual orientation, race, and ethnicity to determine subgroup similarities and/or differences. We will collect assessment data before and immediately after the participants engage with the game as well as at 3 months following gameplay. The primary outcomes of the proposed study are to examine: 1) the usability (e.g., ease of use) and acceptability (e.g., gameplay satisfaction) of the game among adolescents; and 2) the feasibility of delivering the game and piloting protocols in schools. To assess usability, acceptability, and feasibility, directly following supportED game completion, we will collect focus group data on participants' experiences. The following proximal outcomes, as mechanisms for behavior change, will be measured: 1) intentions to use safety plan;[r] 2) coping strategies through adaptive and maladaptive subscales;[s] and 3) severity of suicidal thoughts and associated risk factors using the Concise Health Risk Tracking Self-Report (CHRT-SR) comprised of the following subscales: Propensity (including domains of Pessimism, Helplessness, Limited Social Support, and Despair), Impulsivity, and Suicidal Thoughts.[t] We will measure substance misuse in past 30[u] days as a possible mediator. These scales will be self-reported by adolescents.

All of our data will be self-reported data; therefore, we will use data collection methods such as confidential self-administration that have been effective in our trials to minimize social desirability bias in self-reported data. Participants will receive $25 gift cards as compensation for completion of assessments at each timepoint (e.g., baseline/post-game and 3-month follow up)

The Yale University Human Subjects Committee (the committee that reviews, approves, and monitors research on human subjects) may inspect study records**.** All published results will be group data. Information that will be collected during the focus group interviews will be erased 24 months after the completion of the study and after review of their content has been completed.

1. **Formative and development work**: (1 year)
2. We will work iteratively with our target audience of 16-19-year old adolescents within schools, college-aged youth for a reflection of that age range, and school-based mental health providers to develop videogame content, collecting qualitative data for the videogame and refining our logic model with input from 4 focus groups of 5 high school-/college-aged youth each (n=20), aged 16-19 and 2 focus groups of 5 school-based mental health providers aged 18-80 (n=10).
3. We will create the “Game Playbook” specific to this new digital game. Game Playbooks are our game manuals. We create behavior change gameplay manuals to accommodate the specific needs of a multi-disciplinary game development team. The playbooks outline the theoretical foundations and gameplay elements. This ensures targeted theoretical principles and behavior change mechanisms and constructs are included in the videogame.
4. We will build the new digital game by creating new content, developed from focus groups and from the suicide and opioid misuse prevention literature, for our game development team, DigitalMill, Inc.
5. We will conduct play-testing focus groups with input from focus groups of 5 high school-/college-aged youth each (n=20), aged 13-19 and focus groups with adults who specialize in addiction medicine 18-80 (n=10) to assess user experience (e.g., acceptability and usability) and feasibility of protocol to prepare for a larger pilot study that will require a new protocol (N=60).
6. **Pilot Study:**
7. We will conduct a pilot study with (N=60) adolescents between the ages of 13-19. We will examine the usability and acceptability of the game among adolescents, and the feasibility in conducting the study in schools.
   Inclusion criteria: For the pilot study, participants must: 1) attend a high school that has a school-based behavioral provider; 2) be between the ages of 13-19; 3) be

fluent in reading English as determined in consent process; 4) be willing to sit for a single session to complete pre-/post-assessments, engage with the game (~45min), and participate in a post-gameplay focus group (if in the experimental group) for 60min; and 5) provide assent and parental/guardian consent (if<age 18).

8. We will also assess proximal outcomes as potential means for behavior change in supportED vs. control group at 3 months. Examples include but are not limited to: 1) intentions to use safety plan; 2) coping strategies; and, 3) suicidal thoughts and associated risk factors (e.g., pessimism, helplessness, limited social support, and despair).

6.2 Study Duration

The anticipated duration of this study will be two years. Participants will engage in focus groups over one-year period for approximately 60-90 minutes each. Participants will participate in a pilot study in year 2.

6.3 Outcome Variables

Formative Work: Our study is qualitative by nature. We will explore participants' perceptions on their peers' or students' warning signs, coping strategies, and resources to seek help related to substance misuse and suicide prevention as outlined in safety planning. We will also ask questions about what they would like in a technological game with regard to usability and acceptability. We will ask providers questions about feasibility. Feedback on what participants view as acceptable/feasible will be critical to developing successful technological games targeting suicide.[v]

Pilot Study:

The findings from the proposed study have strong potential for positively impacting adolescents who report opioid/substance misuse and who may be at greater risk for suicidal thoughts and behaviors. It will be the first to provide evidence that a suicide prevention videogame offers an engaging approach and is feasibly conducted in schools with adolescents. With schools seeking technology-based approaches and videogames providing an engaging platform for adolescents, the proposed study has the potential to serve as a necessary first step for long-lasting implications on the health and well-being of adolescents.

6.4 Study Procedures

Formative Work: Participants will engage in six 60-90-minute focus groups led by a licensed professional counselor, and a co-facilitator who will observe and take notes. Focus groups will be audio-recorded and held in a private room within the school if conducted in a school or held via Zoom if conducted virtually. Participants will be asked questions developed from a semi-structured focus group guide, which will first be pilot tested. Questions will be grounded in constructs of a safety planning intervention, as well as self-determination,[w] and social cognitive theories,[x] and techniques used in Motivational Interviewing.[y] Participants will

be asked to not share any identifiable information. Should any be shared, it will be redacted from transcripts. Participants will receive a $25 gift card to participate. Same procedures will be in place for play-testing focus groups.

Pilot Study: We will pilot test *supportED* to examine usability, acceptability, and feasibility. We will enroll 60 adolescents who attend one of our partner school sites. To determine feasibility in piloting protocols, we will also explore proximal outcomes. Eligible individuals will be assigned to either the 1) supportED group (n=30) or 2) control group (n=30). Both groups will also receive NIDA/NIMH pamphlets on substance misuse for youth at the end of the session. Prior to receiving pamphlets, those in the supportED group will engage with the game for one session (~45min) while the control group will engage with a non-health related game for the same duration. Given schools do not have a standardized approach to address suicide prevention, we opted to use an attention/time control condition. Participants will use a dedicated device (e.g., tablet) to access their digital experience on the web. The research staff with Dr. Fernandes always there will be present to monitor gameplay, to provide support, if needed, and to field questions in person. A school-based provider will be present for immediate referrals, as needed.

The total session lasting approximately 90 minutes. The facilitator will ask adolescents to sign assent form and provide clarification or answer any questions about the study procedure. Prior to the session, we will share flyers with educators, school-based providers, and our youth advisory board who will share with participants. Students may then share with other students (e.g., snowball sampling). The flyers contain a QR code for students to input their first/last name, phone number, and email address. If they are younger than 18, they must input parent/guardian first and last name, phone number, and email address. Research staff will then contact them to obtain consent/e-consent. When needed, study staff will be available to parents/guardians should they have any questions. Before students are able to participate in the research study, they must have a signed assent and parent/guardian consent if under 18.

When the gameplay portion of the session begins, participants will play the game on an iPad or desktop device. A member of the research team or the facilitator will be there to provide assistance at all times. After completing the game, adolescents will be asked to participate in a questionnaire session and focus group about their overall gameplay experience. This will be facilitated by one of the members of the research team. The responses of the participants will be gathered and documented as data, which will be kept confidential. If at any point a student is flagged as moderate to high risk due to concerns related to substance misuse, depression, and/or suicide, they will be immediately referred to the school-based provider who will be on site during baseline and 3-month follow up. If a student is triggered by the sensitive nature of the topics, their school-based provider will be able to provide emotional support and/or referral to services. These same procedures will be utilized in local CT schools and in Miami-Dade County public schools.

DATA COLLECTED: We will collect name of student and parent/guardian if under 18, their email addresses and phone numbers to obtain assents/consents. This information will be de-identified prior to the start of research. We will collect participant demographic data including self-reported sex at birth, gender identity, sexual orientation, race, and ethnicity to determine subgroup similarities and/or differences. We will collect assessment data before and immediately after the participants engage with the game as well as at 3 months following gameplay. The primary outcomes of the proposed study are to examine: 1) the usability (e.g., ease of use) and acceptability (e.g., gameplay satisfaction) of the game among adolescents; and 2) the feasibility of delivering the protocols and procedures of conducting the study in schools. To assess usability, acceptability, and feasibility, directly following supportED game completion, we will collect focus group data on participants' experiences. The following proximal outcomes, as mechanisms for behavior change, will be measured including but not limited to: 1) intentions to use safety plan;74 2) coping strategies through adaptive and maladaptive subscales; 75 and 3) severity of suicidal thoughts and associated risk factors using the Concise Health Risk Tracking Self-Report (CHRT-SR) comprised of the following subscales: Propensity (including domains of Pessimism, Helplessness, Limited Social Support, and Despair), Impulsivity, and Suicidal Thoughts. We will measure substance misuse in past 30 days as a possible mediator. These scales will be self-reported by adolescents. Participants will receive $25 gift cards as compensation for completion of assessments at each timepoint (e.g., baseline/post-game and 3-month follow up).

6.5 Withdrawal Procedures

Participation in the formative work and pilot study is voluntary. Participants may withdrawal at any point. This will be explicitly stated prior to the start of each focus group, interview, or research session.

6.6 Locations/Facilities

Formative: The study will be conducted virtually via Zoom and/or at previously long-standing and established partner school sites. We will recruit from existing partnerships in Connecticut and Miami- Dade County schools, such as but not limited to Maloney (N=1191), Bassick (N=970), Ronald W. Reagan Doral (N= 1440), Miami Lakes Educational Center (N= 1015), Alonzo and Tracy Mourning (N=1528), School for Advanced Studies West (N=119), and Barbara Goleman (N=2882).

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6.7 Data Collection

Formative Work: A research assistant will take notes during the focus groups, and a third-party transcription service, who our lab has worked with prior, will transcribe audio recordings verbatim. We will review field notes and focus group transcripts.

Pilot Study:

Currently our game does not record ANY personal information or even individual game information. We do not ask for a personal registration or login.

Twine by default does save information locally to the device running the Twine game off the Web server. No information is saved server-side and local information can be removed by deleting local-storage using the Web browser command to do so.

We envision most, if not all, players playing through an entire sitting in one session so saving locally shouldn't be a need, and devices will have local saves wiped if under-the-control of the research team.

We are considering disabling saves as well. However, Twine does maintain some saved state during play and it likely is cached (locally of course)

We MAY however implement the following depending on further IRB guidance:

1. A 'simple' password that blocks the site where the game is played from the public internet. This password would not be individual but would be a simple single password that any participant would need to know to enter the page.

This password would be changed periodically and would cease to work overall when the site was closed after initial trials.

2. We may add server-side recording of event-based analytics (i.e. user choices)

This data would be de-identified automatically because there would still be no initial login using an personally identifiable account or token.

We are considering using Google Analytics for this purpose or saving data to a Google Sheet.

In all cases of such analytics recording we would include a page accessible to all player (perhaps even requiring an acknowledgement) that their gameplay data is saved but is not identifiable.

There are no other plans or default actions that record player actions / data. There is no personalized login system that could enable such identifiable data.

Specific practices would be made to reduce the proliferation or retention of even unidentifiable game data in the short term (e.g. wiping local browser storage) and on a long term basis deleting long-term analytics data once its use for research and analysis is completed.

6.8 Data Collection Sources

Formative Work: The focus group guide will be organized based on the constructs of a safety planning intervention (e.g., potential warnings signs related to emotional distress, coping strategies, and resources for seeking support).

Pilot Study: We will assess the user experiences (e.g., acceptability and usability) as well as feasibility of delivering protocols of the digital game. From our playtesting focus groups (i.e.,

where we obtained feedback to finalize the prototype), will modify two approaches: the think-aloud method and cognitive interviewing. The think-aloud method and cognitive interviewing are mainly used to analyze how human participants perform and interact with a prototype or interface of a product. By conducting either of these methods when testing the usability of a product, issues with the prototype can be identified and fixed. The think-aloud method specifically requires participants to speak aloud their thought processes and ideas as they perform a specific task or solve a problem. Sometimes the method is carried out one-on-one with a participant and a research/note taker, while other times video recordings can be used.[z] By having the participants verbally articulate their thought process, the researchers will be able to gain insight on potential issues or complications with the game design and/or playtesting process. In context of the Pilot Study, aspects from the think aloud method and cognitive interviewing will be applied simultaneously in our post-gameplay focus group, which allows for feedback and discussion on the content of the game, as well as the process through which the game is being presented for playtesting. Along with the use of these methods to gather feedback on the digital game, quantitative measures are also being gathered through the use of the **User Engagement Scale- Short Form (UES-Short Form),** and **Acceptability of Intervention Measure (AIM) as examples**. These scales along with qualitative data collection and observation will assess the usability, acceptability, and feasibility of the game.

The User Engagement Scale-Short Form (UES-Short Form) is a validated, 12-item self-report measure that assesses six domains of engagement where responses are measured on a 5-point Likert scale where 1= strongly disagree and 5= strongly agree.

The Acceptability of Intervention Measure (AIM) is a validated, 4-item self-report measure of perceived acceptability where responses are measured on a 5-point Likert scale where 1 = completely disagree and 5= completely agree.

Lastly, feasibility of delivering protocols and procedures will be measures through observation of modifications to conduct study, duration of gameplay, and reasons if did not finish game to end. Participants will also answer qualitative questions (e.g. does the game work? can the game be implemented in schools?) that will be developed by the study team. By gathering both qualitative and quantitative data and feedback on the protocol design of the digital game, appropriate revisions can be made to future versions of the game.

We will also explore proximal outcomes such as but not limited to adolescent well-being, intentions to use a safety planning intervention, coping strategies, substance misuse in last 30 days, and associated risk factors related to suicidal risk (e.g., hopelessness, impulsivity, etc.). Our specific measures and proximal outcomes are outlines below:

Coping Strategies
Change in coping strategies will be assessed using the brief COPE scale at baseline and 3-months follow-up. Brief COPE adaptive and maladaptive subscales are validated, 28- item, 4-point self-report measures. Brief COPE measures assess 14 conceptually different coping reactions. Responses are measured on a 4-point likert scale where 1= I haven’t been doing this at all and 5= I’ve been doing this a lot.

Mindfulness

To assess facets of mindfulness, we will utilize The Five Facet Mindfulness Questionnaire (FFMQ). The FFMQ is a validated, 15-item self-report measure that assesses facets of mindfulness. Responses are measured on a 5 point-likert scale where 1= never or very rarely true, and 5= very often or always true.

Emotion Regulation
Emotion regulation will be assessed using the State-Difficulties in Emotion Regulation (S-DERS) scale, a 21-item self-report measure. Responses are measured on a 5-point likert scale where 1= almost never and 5= almost always.

Adolescent Well-Being
Adolescent well-being will be measured using The Adolescent Well-Being assessment, which is a validated, 16-item school-based, self-report measure with 11-items focused on well-being, and 5-items focused on student demographics.

Intentions to Use a Safety Plan
Intentions to use a safety plan is a 7-item measure adapted from Addis et al., 2013. Responses are measured on a 5-point likert scale where 1= strongly disagree and 5= strongly agree.

Knowledge about the Safety Planning
Participants will complete surveys through a secured, data management system (RedCap). 6-items will assess learning goals of the game developed by the study team (e.g. warning signs, coping strategies, resources for support).

Concise Health Risk Tracking - Self Report
Concise Health Risk Tracking Self-Report (CHRT-SR) is a validated, 14 item, 5-point self report measures comprised of the following subscales: Propensity, Impulsivity, and Suicidal Thoughts. Responses are measured on a 5-point likert scale where 1= strongly disagree and 5= strongly agree. We will also utilize the Ask Suicide-Screening Questions (ASQ), a validated set of 4 questions to assess suicide risk.

Change in Symptoms of Anxiety
The General Anxiety Disorder-7 (GAD-7) is a validated, 7-item self report measure that assesses symptoms of anxiety. Responses are measured on a 4-point likert scale where 0=not at all and 3=nearly everyday.

Change in Symptoms of Depression
The Patient Health Questionnaire (PHQ-9) is a validated, 9-item self-report measure that assesses symptoms of depression. Responses are measured on a 4-point likert scale where 0=not at all and 3=nearly everyday.

Help-Seeking Behavior
The General Help Seeking Questionnaire (GHSQ) is a validated, 20-item self-report measure that assesses professional and non professional help seeking behaviors. Responses are measured on a 7-point likert scale where 1=extremely unlikely and 7=extremely likely.

Substance Misuse in the Past 30-Days
Substance misuse of alcohol, tobacco/vaping, cannabis, legal and illegal opioids in the past 30-days will be measured as a possible mediator. These measures are self-reported.

Suicidal thoughts and behaviors in Past 30-days – Self-Report

The Ask Suicide Screening Questions (ASQ) has used a self-reported 4-item questionnaire with youth to measure the occurrence of suicidal thoughts and behaviors. The 4 questions asked targeted a different aspect of suicidal thoughts: past wishes of death (“wish you were dead?”), suicidal ideation (“have thoughts of killing self?”), suicidal thoughts with a plan (“had a suicidal plan?”), and suicidal behavior (“tried to kill self?”).

6.9 Standard Tools

N/A

7 - Statistical Analysis

7.1 Sample Size

For Content: 30 participants, including 20 high-school/college-aged youth and 10 adult providers, will make up our six focus groups. Approximately 10 interviews with adults who may have misused substances during their youth and will be able to reflect on what they wish they knew during then.

For Play Testing: 30 participants, including 10-20 high-school/college-aged youth and 10-20 adult providers, will make up our six focus groups.

For Pilot Study: 60 participants, high-school aged youth [ages 13-19], across 6-10 high schools with school-based behavioral providers.

7.2 Planned Analyses

Formative Work: Data will be analyzed using rapid analytic techniques to ensure timely analysis.[cc] We will review field notes and focus group transcripts. We will develop a templated table to summarize each transcript.[dd] We will then create a codebook outlining the components of safety planning to code each summary. Three team members will code each summary for researcher triangulation. We will consolidate summaries into two matrixes (adolescents and providers) to capture similar/different themes with supporting quotations. When there are discrepancies, we will discuss until full consensus. We will keep documentation of decisions, meetings, peer debriefings, and a reflexive journal as part of our audit trail to enhance the rigor and meet the trustworthiness criteria.[ee] Data collected in the study will reside in our computerized database and electronic storage mechanisms. All data analyses will be performed under IRB approved protocols.

Pilot Study: We will assess usability, acceptability, and feasibility gathered through the use of the **User Engagement Scale- Short Form (UES-Short Form)** and **Acceptability of Intervention Measure (AIM)**. These are validated scales that will determine the reactions to the gameplay experience. We will also assess the usability, acceptability, and feasibility of the game in our post gameplay focus groups. We will also explore proximal outcomes of supported by comparing scores in intentions, coping strategies, and suicidal thoughts and associated risk factors by changes in response rating from before to after. We will also

compare scores in the severity of suicidal ideation and attempts. We will test the hypothesis that individuals who engage with supportED will report decreases in outcomes in comparison to the control group. We will conduct a longitudinal analysis using a hierarchical linear mixed model approach to compare participants in the game group to participants in the control on reported outcomes from baseline to 3-month follow-up assessments (i.e., baseline, post-gameplay, and three months). We will also use logistic regression models to determine if any relevant baseline variables are associated with changes in outcomes. We will also examine whether changes in outcomes varied by treatment group, sex at birth, sexual orientation, race, ethnicity, gameplay duration, and/or gameplay experience to determine similarities and/or differences among subgroups. **All of these analyses will be exploratory.** P-values smaller than 0.05 will be considered statistically significant.

7.3 Data Relevance

n/a

7.4 Data Coding

Formative Work: The data will be coded using an inductive qualitative data analysis approach. We will create a codebook outlining the components of safety planning to code each summary. Three team members will code each summary for researcher triangulation. We will consolidate summaries into two matrixes (adolescents and providers) to capture similar/different themes with supporting quotations. When there are discrepancies, we will discuss until full consensus. We will keep documentation of decisions, meetings, peer debriefings, and a reflexive journal as part of our audit trail to enhance the rigor and meet the trustworthiness criteria. For playtesting we will use Qualtrics to collect their feedback through cognitive interviewing and the think aloud methods. We will also have a note-taker complete a debrief summary after each session. Participant experience will be collected and analyzed using rapid analytic techniques to quickly draft a report for the game development company with suggested revisions to finalize the prototype for the pilot study.

Pilot Study: For the pilot study, qualitative data will be analyzed using techniques from a reflexive thematic analysis approach and rapid analysis. Coding is organic and allows for the researchers' subjective skills and experience to be highlighted. Debrief summaries will be completed after each session.

7.5 Data Analysis Tools

Formative Work: We will use a qualitative analysis software (e.g., NVIVO or Dedoose) to analyze the data.

Pilot Study: A web-based computer system (RedCap) will be used for data collection, management, and monitoring. The web-based data system Clinical Trial Management System (CTMS) is under the auspices of the Yale Center for Medical Informatics who is responsible for data management.

7.6 Data Monitoring

Formative Work: Because this study has minimal risk, a Data and Safety Monitoring Board will not be established.

Pilot Study: A Data and Safety Monitoring Board will be established. We are in the process of establishing a Data and Safety Monitoring Board (DSMB). The DSMB will be comprised of two experts in clinical trials (one with expertise in substance use prevention and/or adolescents) trials and will provide oversight in a number of areas including for the selection, enrollment, or consenting of participants, or determination of eligibility.

8 - Data Handling and Record Keeping

8.1 Subject Data Confidentiality

Participants will be asked to not share any identifiable information during focus groups. Should any identifiable information be shared in the focus groups, it will be redacted from transcripts.

A number of precautions will be actively integrated into the research procedures to protect the confidentiality and anonymity of all participants. All research study staff will be required to complete training in research ethics. All data entry and analyses will be completed with ID numbers only. The research staff will follow standard confidentiality procedures for research programs.

A web-based computer system (RedCap) will be used for data collection, management, and monitoring. The web-based data system Clinical Trial Management System (CTMS) is under the auspices of the Yale Center for Medical Informatics who is responsible for data management. It is a web-accessible, multi-disciplinary database for study- or disease-specific clinical research data designed to store the focused data required for clinical trials and clinical research studies. This system has proven to be very efficient and reliable in other clinical trials. It will be used by the research assistant to administer the research instruments from any computer with Internet access. The CTMS will be used to generate a number of web accessible reports and reminders to help monitor and manage the data collection process to assure completeness of evaluation. The system can check for data inconsistencies, omissions, and errors regularly. Data questions or problems will trigger data queries and analyses of missing data will be done periodically to assure that all forms are entered and available for analysis. CTMS staff have received HIPAA training and Human Subjects Protection training. Users will certify that they are HIPAA trained and will act in full compliance of HIPAA regulations. Specifically, individual profile data and data on application use by study participants will be collected and de-identified through irreversible hashing methods prior to storage to ensure privacy protection is satisfied. De-identified data will be encrypted in transit and securely transferred for storage and analyses.

The web data-entry interface allows data entry to be performed from anywhere on the Internet and uses 128-bit secure sockets layer security to protect the confidentiality of the data. The CTMS maintains an electronic audit trail of all modifications to a study's data, including the user who made the change, date and time, each data item changed and its previous value and new value. Yale houses and maintains the security and backup of all servers and workstations. The CTMS's Oracle database is housed in a central machine room maintained by Yale. Passwords and subject identifying data will be stored encrypted in the database server. Several levels of database backup are performed regularly, including full daily and incremental backup.

8.2 Data Quality Assurance

We will keep documentation of decisions, meetings, peer debriefings, and a reflexive journal as part of our audit trail to enhance the rigor and meet the trustworthiness criteria.

The organizational structure used to ensure quality of data in this project include: 1) Extensive training and close supervision of research personnel in data collection and

management; 2) Preliminary review of all data for completeness and coding errors by data manager/analyst; and 3) Utilization of error-checking statistical procedures. The PI supervises data procedures. All error corrections are fully documented in the research records of the study. All research personnel are required to participate in and document training in protection of human subjects and the responsible conduct of scientific research. In addition, the Clinical Trials Management System (CTMS) will be used to generate a number of web accessible reports and reminders to help monitor and manage the data collection process to assure completeness of evaluation. The system can check for data inconsistencies, omissions, and errors regularly.

8.3 Data Storage/Security

Names, phone numbers, addresses, email addresses, parent/guardian names, parent/guardian phone numbers, and parent/guardian email addresses will all be collected.

Data collection forms will be designated by ID numbers only. A separate master file of names, addresses, contact persons, and telephone numbers, along with the study ID numbers will be maintained in a locked file cabinet in the PI's research offices. All data entry and analyses will be completed with ID numbers only. The research staff will follow standard confidentiality procedures for research programs.

8.4 Study Records

Protocol

Information Sheets

Focus Group/Interview Guide

Audiotaped focus group recordings

Informed Written Assent/Consent

Participant Assessments

8.5 Retention of Records

Information that will be collected during the assessments and interviews will be erased 24 months after the completion of the study and after review of their content has been completed.

9 - Study Considerations

9.1 Research Personnel Training

Procedures for training and supervision of all research personnel have been developed as part of our previous and current studies. All members of the research team are familiar with procedures for identifying and reporting possible adverse reactions. All members of the research team are trained in mandatory reporting and will notify the PI immediately of any concerns raised about participant mental health (suicidality), substance use, abuse of any kind, etc.

9.2 Unanticipated Problems and Protocol Deviations

Any protocol deviations or unanticipated problems will immediately be reported to the PI. Protocol deviations or unanticipated problems will be reported to the IRB as per their written policies and procedures.

If an adverse event occurs study personnel will notify the PI as well as the appropriate Information Security Officer (ISO) and follow all necessary procedures. All adverse events are reported using the Yale Institutional Review Board (IRB) standard template for reporting adverse events. The PI reviews all adverse events, classifies the attribution of adverse events (e.g., definitely, probably, possibly related; unlikely or unrelated) and grades the severity of the event, utilizing the FDA's definition of serious adverse events, on a 5-point scale (0=no adverse event or within normal limit; 1=mild; 2=moderate; 3=severe; 4=life-threatening; 5=fatal). Serious unanticipated or anticipated adverse events will be reported immediately to the IRB within five (5) calendar days by phone and/or email and will submit a written report to the PO no more than five (5) calendar days later.

Medical advisement will be available by the PI's primary mentor, Dr. Lynn Fiellin, and co-primary mentor, Dr. Hilary Blumberg, as needed.

9.3 Study Modification and Discontinuation

We will update the protocol any time a change has been made to the study and re-submit to IRB. Once approved by the IRB, changes will be implemented into the study.

9.4 Study Completion

This phase of the study will complete within two years from the start date.

9.5 Funding Source

This study was made possible by CTSA Grant Number KL2 TR001862 from the National Center for Advancing Translational Science (NCATS)/National Institutes of Health (NIH).

9.6 Publication Plan

At the end of the study and once data analysis has been completed, results will be submitted to a peer-reviewed journal and a community report may be shared with our partners.

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