**$RESEARCH PROTOCOL INVOLVING HUMAN SUBJECTS**

This document is a **guide** for investigators; it should be edited, as applicable to the proposed study. The following outlines the **minimum information required** for IRB evaluation of a research study. Additional guidance and resources on protocol development are available.

**Study Title:** Stress and Coping Among High School Students (ALACRITY eSToRY R34 #1)

**Principal Investigator:** Margaret Weiss, MD, PhD

**Research team:**

This section was removed in November 2023 per IRB guidance. Study staff are now tracked through Cayuse.

**Protocol version date/number: 4/03/2024 v31**

**Appendix documents:**

- Component 1 Assent: 072523 (v10)
- Component 1 ICF (parent/guardian): 072523 (v11)
- Component 1 ICF (>18 youth): 072523 (v5)
- Component 2 Assent: 091423 (v9)
- Component 2 ICF (parent/guardian): 091523 (v9)
- Component 2 ICF (>18 parent/guardian): 072523 (v5)
- Component 2 ICF (>18 youth): 091423 (v10)
- Recruitment Flyer (Full Size): 012323 (v8)
- Recruitment Flyer (Small): 010522 (v4)
- Newsletter Advertisement Blurb: 120321 (v1)
- Teacher Flyer Instructions: 122121 (v1)
- Component 1 Script (youth assent): 091322 (v4)
- Component 1 Script (parent/guardian): 091322 (v4)
- Post-Screening Conversation Script: 103023 (v2)
- Component 2 Script (youth assent): 082123 (v3)
- Component 2 Script (parent/guardian): 120321 (v2)
- Component 2 Script (>18 youth): 082123 (v3)
- Component 2 Check-In Script: 091322 (v1)
- Interview Assent: 120623 (v3)
- Interview ICF (parent/guardian): 120623 (v3)
- Interview ICF (>18 youth): 120623 (v4)
- Interview ICF (clinic staff): 040324 (v2)
- Qualitative Interview Guide (youth/LAR): 12122023 (v2)
- Qualitative Interview Guide (clinic staff): 020924 (v2)
- Connect-S SDOH Screening
- Coping Self-Efficacy Scale
- CRAFFT Screening Tool
- NLS Target Form
- PCL-5 LEC
- WFIRS - S
- WFIRS - P
- JAACAP K-CAT Paper & K-CAT Supplement
- C2T Intervention Modules

## I. Background, Rationale & Literature Review

**A. Provide a summary of necessary and relevant background information that led to the development of the proposed study.**
**Summarize relevant studies supporting this proposed study. Specifically include any relevant human studies; include animal studies as relevant, especially if prior human data do not exist. Include references/citations.**

**B. Provide the rationale for, and importance of, conducting the research study, including the value the study will add to the field and/or improve understanding of the disease or condition being studied. Explain how existing literature supports the current proposed hypothesis(es).**

**Early detection of mental illness is linked to improved outcomes**
Adolescence is often when mental illness begins to emerge. For this reason, the Institute of Medicine's 2009 report recommended that the federal government prioritize prevention of mental and behavioral disorders in youth. Failure to detect early subthreshold symptoms of incipient disorders is a major impediment to prevention and diagnosis. This lost opportunity then leads to expensive crisis management, and increased use of medication and hospitalization. From a population health standpoint, identification and early intervention are critical to decreasing the burden of serious mental illness.

Early intervention can reduce the significant impact of mental health symptoms in youth and may prevent development of mental disorders. In systematic reviews of the evidence on the effectiveness of mental health promotion interventions for young people, school-based life skills and resilience programs were found to have moderate to strong evidence for improved mental health outcomes. A recent comprehensive synthesis of evidence from systematic reviews and meta-analyses on prevention of depression, anxiety, and first-episode psychosis found solid evidence that depression and anxiety disorders can be prevented, and psychotic disorders can be delayed. Similarly, for ADHD, disruptive behavior disorders, and complex comorbidity, there is increasing awareness that recognition and intervention in youth may mitigate poor adult outcomes. Indeed, community leaders in the cities involved in the proposed eSToRY Center have identified mental health as their top priority.

**Early detection of mental illness is limited, particularly in vulnerable racial, ethnic and linguistic (REL-) minority populations**
Race, ethnicity and linguistically diverse (REL) minority youth and their parents are less likely to contact a health care professional about their mental health concerns, waiting years rather than months compared with White non-immigrant families. Youth may not seek treatment because of reluctance to talk with parents or teachers, lack of insurance to cover their care, or perceiving symptoms of mental illness in pejorative terms. Online, self-paced mental health interventions administered in community settings bypass these problems. Web-based telehealth tools are particularly user-friendly to adolescents. Recent studies support the effectiveness of telehealth therapies, particularly e-cognitive behavioral therapy in adolescents. Youth have grown up in a virtual world and are comfortable with digital forms of social connection. The proposed study addresses the following important research gap: there are few empirically validated non-pharmacologic treatments to improve stress management among youth, and most especially among REL-minority youth at risk.

**Computerized Adaptive Testing (CAT) in school-based settings holds promise for early detection**
The K-CAT™ extends the adult technology contained in the CAT-MH™ to ages 7-17 based on both parent/caregiver and youth reporting. The K-CAT includes modules for depression, anxiety, mania/hypomania, ADHD, oppositional defiant disorder, conduct disorder and suicidality. The total item bank contains 2120 items distributed across parent and child ratings and can be adaptively administered in five minutes for the parent and seven minutes for the child. It has been validated against the K-SADS structured clinical diagnostic interview for each of the above disorders with AUCs of 0.83 for Generalized Anxiety Disorder (GAD), 0.92 for Major Depressive Disorder (MDD), and 0.996 for suicidal ideation or attempts. Strong correlations with extant clinical measures also demonstrated convergent validity ($r>0.60$) and test-retest reliability averaged $r=0.80$. An adolescent K-CAT-SUD measure (for substance abuse) has recently been added to the K-CAT™. Computerized adaptive testing has demonstrated efficacy in identifying mental health needs of pediatric patients and enables identification of pre-morbid risk. The K-CAT will be administered through Adaptive Testing Technologies (ATT). ATT is a secure, third party web-based platform that specializes in computerized adaptive testing and houses a control panel interface through which the K-CAT and CAT-MH can be administered.

Screening for social determinants of health (SDOH) in pediatric settings is an expanding area of practice that is essential to effective intervention. We will implement a SDOH module used by our team in primary care. Currently, the K-CAT lacks measures for prodromal symptoms for psychotic disorders, PTSD, autism, and a quantitative measure of functioning relevant to youth. Validated scales for these will be incorporated to complement K-CAT modules. We will not be screening for autism which is typically identified in the preschool years.

The proposed research project provides a novel approach to screening, early assessment, and preventive interventions for high-risk youth in REL-diverse communities.

- We assess a health promotion intervention that is specifically designed to reduce treatment disparities in REL-minority youth. This population is underrepresented in child psychiatry research. It is often excluded from clinical trials of medication or therapy because of challenges with transportation, literacy, resources or other issues.

- The study will take place during or following a syndemic including a health care crisis, economic recession, unemployment, and online learning making findings relevant to understanding the mechanisms by which hardship translates into youth mental illness.

- The innovative integration of online screening into school-based clinics in REL-minority communities is made possible by the combination of access to a new technology (CAT) in the context of a learning health community serving an REL-minority population.

- Empirical research on the impact of a resilience-based prevention intervention in youth and youth at risk is both innovative and much needed during this period of health, social and economic crisis.

II. **Aim and Hypotheses**

**A. Define the aim(s) and hypothesis(es) and clearly describe each.**

**Aim 1: Screening - Test the feasibility and acceptability of a *Screener for Adolescent Impairment and Symptoms* (SAIS). Symptom assessment on the SAIS will involve youth report on the K-CAT and function will be assessed with youth self-report on the Weiss Functional Impairment Rating Scale, which has been validated in large adolescent school populations, in different countries and settings.** After administration of the SAIS, we will refer youth to an online resilience- enhancing intervention, and youth who are syndromal to treatment. *H1: The administration of SAIS, in English or Spanish or with Portuguese or Haitian Creole interpreters, will be acceptable and feasible to youth, parents, school mental health personnel, and clinicians for a) screening for mental health symptoms, b) referring youth with moderate risk to an online resilience intervention, and c) referring youth with high risk of mental illness to treatment.*

**Aim 2: Intervention - Determine the acceptability, feasibility, and preliminary effectiveness of a novel computer-based resilience-building cognitive based therapy intervention, COPE2Thrive (C2T), on youth determined by the SAIS to be at risk for mental illness.** We will test the effectiveness of C2T on symptoms and function and assess coping self-efficacy (CSE) as a target mechanism. Repeated K-CAT measurement will allow us to identify changes in our major outcomes from baseline through three months follow-up. H2: The C2T online resilience- building intervention will demonstrate acceptability, feasibility, and preliminary effectiveness in reducing symptoms, and improving functioning, and hold promise for mitigating progression to diagnosed mental illness. As part of Aim 2 we will conduct a qualitative analysis of feasibility and acceptability of implementing C2T in the context of rapid screening and referral in a school-based clinic context.

**Aim 3: Reducing Disparity - Compare the effectiveness of screening and early intervention between more and less vulnerable (racial/ethnic and language minority and non-minority groups) on symptoms and function at follow-up**. We will implement Institute of Medicine (IOM)-concordant disparities method in order to provide an exploratory assessment of the potential of the screening, referral, and early mental health intervention on reducing disparities in access to and engagement in mental health treatment. H3: Outreach to the community with the K-CAT+ screener, followed by referral or an online resilience-building intervention, will reduce REL disparities in access to treatment. We anticipate that the early screening and prevention intervention will have a greater impact on REL-minority youth because enhanced screening will identify these populations earlier than usual and overcome known biases in recognition and referral. In exploratory analyses, we assess whether the C2T intervention had differential impacts by REL group on coping self-efficacy, symptoms, function, and conversion to diagnosed mental illness.

**B. Clearly state the objective(s) and the purpose(s) of this study.**

The objective of this study is to demonstrate the effectiveness of screening for psychiatric diagnoses with functional impairment both within the community and in patients who are awaiting treatment. This will test a triage procedure that is critical to guide access to care in referred and non-referred populations. Patients who are found to be at risk or meeting diagnostic threshold will then be allocated to a cost-effective, resiliency building intervention along with a personal contact that will provide more information on the needs and response of youth. We assess how race, ethnicity and language are impacting risk for symptoms with functional impairment, and the effectiveness of the intervention itself. The study hopes to increase cost-effective, accessible ways to reduce access and quality disparities among REL-minority youth.

III. **Research Plan**

A. Study design

**Explain the study design and the choice of research methodology.**

The SAIS will be used to stratify youth into one of three tiers:

Tier 1: These students will receive information about general services available to them (school-based & community behavioral health services) and be offered participation in C2T resilience intervention

Tier 2: These students will receive information about general services available to them (school-based & community behavioral health services) and be offered participation in C2T resilience intervention.

Tier 3: Students who fall within Tier 3 will be informed by a member of the research staff that they are expressing concerns about their well being and might benefit from treatment. No specific diagnostic information will be given since the computerized adaptive testing is not a clinical assessment, but students will receive feedback in lay man's terms as to where they expressed symptomatic or functional challenges and asked if that seems consistent with how they perceived their responses. If the child is not deemed at imminent risk of harm to themselves or someone else, acutely psychotic, currently receiving psychiatric treatment, or in need of urgent psychiatric attention imminent risk (see Suicide Risk Assessment Protocol), they will be invited to participate in the C2T intervention. If we learn that the student is a danger to themselves or others (see Suicide Risk Assessment Protocol), we will attempt to connect them with the local emergency department or 911 services. Coverage by a child psychologist and child psychiatrist will be available by phone to the research assistant if an acute issue emerges. Clinical coverage is available to the research assistants whenever the study is in progress.

The K-CAT includes modules for depression, anxiety, mania/hypomania, ADHD, oppositional defiant disorder, conduct disorder and suicidality. The symptom criteria for Tier 3 will be a score of 'severe' OR a score of 'moderate' on one or more K-CAT modules, in addition to meeting function criteria. The function criteria for Tier 3 will be a mean score of 1.0 or more on WFIRS (which is 2 SD outside the population norm), in addition to meeting the symptom criteria. Referral for Tier 3 requires both significant psychopathologies as defined above, and impairment from those symptoms. We anticipate that the majority of students who are actively suicidal will automatically be referred to Tier 3, based on their having met the symptom threshold. The K-CAT suicide risk module identifies any suicidal ideation and does not provide a risk score for actual suicidal behavior. Up to a quarter of adolescents have some degree of suicidal ideation, without at-risk suicidal behavior. Our pilot of the K-CAT confirmed that the suicide risk module was very sensitive to low-risk suicidal ideation. For this reason, if we identify a student who receives an elevated score on the suicide module, the student will be prompted to complete the C-SSRS to determine imminent risk. If the student scores high-risk on the C-SSRS, the RA will implement the Suicide Risk Assessment Protocol (see below) and page one of the clinicians. If the student does not score high-risk on the C-SSRS, they will receive a handout with information on referral services and be invited to participate in the COPE2Thrive intervention. The student will also be asked for assent to inform the parent/guardian and provide them with the same resources.

The clinical trial of the C2T intervention will collect the following battery of measures consisting of parent and youth report, completed independently and confidentially. The consent will stipulate that only where clinically or legally required does the parent have access to the youth report or *vice versa*. Since parental consent is required for treatment, if a student is identified as being symptomatic but not at high risk of suicide, we will inform them that treatment is indicated and request assent to inform their parents of the need for treatment. The C2T online intervention program is available in English. Participants who wish to take the modules in Spanish, Haitian-Creole or Portuguese will have access to an interpreter. CHA interpreters will be available to cover any dialect-specific translation needs. C2T participants will also be offered an optional weekly phone or text check-in while they are completing the intervention to address any concerns or questions that may arise. This check-in will be conducted by a member of the research team using the Component 2 Check-In Script. Interpreter services will be available for participants who prefer to check-in in Spanish, Portuguese, or Haitian Creole. If any acute concerns arise during these check-ins the Suicide Risk Assessment Protocol will be followed (see below).

Parent report:
- K-CAT
- WFIRS-P

The parent report measures will be sent electronically to the parent/guardian's email via a secure link from REDCap. Once the parent has completed the WFIRS in REDCap, they will be prompted with a link to take the K-CAT in ATT.

Adolescent self-report:
- K-CAT

- WFIRS-S
- PTSD Checklist for DSM-5 (PCL-5) with Life Events Checklist for DSM-5 (LEC-5) and Criterion A (which includes an inventory of adverse childhood experiences)
- CRAFFT for substance abuse
- Coping Self Efficacy Scale
- Target Impairment Scale
- Connect-S (Social Determinants of Health): a six-item scale which evaluates feeling unsafe, food insecurity, housing, utilities and access to transportation, childcare, medical care
- C-SSRS (Columbia Suicide Severity Rating Scale) a series of simple, easy to understand language that help identify if someone is at risk suicide, and assess the severity and the immediacy of that risk

This battery of measures will be referred to as the **Comprehensive Evaluation for Youth (CEY)**. The CEY will be administered at baseline, post-intervention, and at 3 months follow-up to determine if treatment effects endure over the moderate term. The total time of administration of CEY in English is estimated to be 60 minutes, or 70 minutes if administered through an interpreter. An interpreter is only required for the K-CAT as all other measures will be available in the subject's own language.

The K-CAT will be repeated at baseline, completion, and three months follow-up to the C2T group to track change over time. Scores on the youth K-CAT will be the primary outcome. All other outcomes are secondary outcomes and exploratory. All analyses will be done both intents to treat and per protocol.

We will use a stepped wedge research design, which randomizes students to clusters that allow for a rolling recruitment in which each student serves as their own control until they "crossover" from the control group to the treatment group. We will complete the screening of 400 students with recruitment of the 108 youth into one of three clusters, each cluster starting C2T at either one, two, or three-week intervals starting at week 1 and ending at week 23 of the study. Each student serves as their own control.

The K-CAT modules are the same in both the SAIS and the CEY. Youth who participate in Component 2 will have completed the initial SAIS, and will complete the CEY at baseline, completion and 3-month follow-up. The baseline done during the SAIS has to be repeated as a baseline for the clinical trial in Component 2 because there will be a time lag between the two. A timeline depicting when each instrument will be administered has been included below.

| **COMPONENT 1** | |
|---|---|
| SAIS: Initial Screening | |
| *Youth* | *LAR* |
| • WFIRS-S<br>• K-CAT<br>  ○ C-SSRS<br><br>*The C-SSRS will only be administered if the K-CAT suicide module is flagged. | N/A |

| **COMPONENT 2** | |
|---|---|
| BASELINE: Comprehensive Evaluation for Youth (CEY) | |
| *Youth* | *LAR* |
| • WFIRS-S<br>• K-CAT<br>  ○ C-SSRS*<br>• PCL-5<br>• CRAFFT<br>• Coping Self-Efficacy Scale<br>• Target Impairment Scale | • WFIRS-P<br>• K-CAT |

| | |
|---|---|
| • Connect-S<br><br>*The C-SSRS will only be administered if the K-CAT suicide module is flagged. | |
| COMPLETION of C2T: Comprehensive Evaluation for Youth (CEY) | |
| *Youth* | *LAR* |
| • WFIRS-S<br>• K-CAT<br>  ○ C-SSRS*<br>• PCL-5<br>• CRAFFT<br>• Coping Self-Efficacy Scale<br>• Target Impairment Scale<br>• Connect-S<br><br>*The C-SSRS will only be administered if the K-CAT suicide module is flagged. | • WFIRS-P<br>• K-CAT |
| 3-MONTH FOLLOW-UP: Comprehensive Evaluation for Youth (CEY) | |
| *Youth* | *LAR* |
| • WFIRS-S<br>• K-CAT<br>  ○ C-SSRS*<br>• PCL-5<br>• CRAFFT<br>• Coping Self-Efficacy Scale<br>• Target Impairment Scale<br>• Connect-S<br><br>*The C-SSRS will only be administered if the K-CAT suicide module is flagged. | • WFIRS-P<br>• K-CAT |

The suicide risk assessment will occur as follows:

1. If the student scores 'severe' on the K-CAT suicide module, they will fall into the Tier 3 category. At this time the C-SSRS will be triggered and the student will complete the additional screening. If the student scores high-risk on the C-SSRS (red), the Suicide Risk Assessment Protocol (outlined below) will be implemented. The C-SSRS is the gold standard for assessment of high-risk suicide behavior. If the student is not deemed at imminent risk of harm to themselves or someone else, acutely psychotic, or in need of urgent psychiatric attention (see Suicide Risk Assessment Protocol) they will be invited to participate in COPE2Thrive.
2. If the student opts in to the check-ins during their participation in C2T and expresses any acute risk of self-harm, suicide, violence, or other safety concern, the research team member conducting the check-in will contact the on-call clinician as per the suicide/high risk protocol. If the safety concern is related to suicide or self-harm, the on-call clinician will verbally administer the CSSRS and conduct a risk assessment in accordance with suicide risk assessment protocol beginning at #6. If the safety concern is related to violence or otherwise, in addition to the CSSRS, the clinician will thoroughly assess the concerns through a clinical interview in accordance with the risk assessment protocol beginning at #6

**SUICIDE RISK ASSESSMENT PROTOCOL (HIGH-RISK)**:

1. Student completes WFIRS and K-CAT
2. RA/RC reviews K-CAT results. If student scores in the severe category, RA/RC will administer the C-SSRS. If results are red, child is high-risk and a risk assessment by a clinician is required.
3. RA/RC pages on-call clinician (Margaret Weiss, Ellie Castine or Nick Carson)
4. On-call clinician will confirm receipt of message & immediately follow through as per usual clinical standards for follow up of a high risk situation

5. RA/RC shares C-SSRS results with on-call clinician
6. Clinician assesses risk using C-SSRS responses and/or clinical interview
7. Clinician takes appropriate action according to their assessment of the risk involved. These actions may include: referral to the emergency room, a section 12, notification of the parent in accordance with the law, notification of mobile crisis, provision of referral materials and/or suicide prevention resources, or other measures appropriate to the situation and best practice clinical care.
8. Clinicians will write up detailed notes and justification for their decisions which will be kept in a confidential research record for the student which will be saved behind the CHA firewall.

**B. Study Location**

**Indicate where all elements of the study will take place, including the consent process, data analysis, and record and data storage. Include detailed information about the facility to confirm that the location is adequate to ensure subject safety and privacy, as well as data/record security.**

Student assents will take place either in person in a private space at the location they were recruited (CHA Teen Health Centers, Cambridge, Somerville, and Everett High Schools, or community program space), or virtually via GoogleVoice, Google Meet, or phone (available in English, Spanish, Portuguese and Haitian-Creole) . Interpreters will be available when needed. Parental informed consent will be obtained verbally via GoogleVoice, Google Meet, or phone (available in English, Spanish, Portuguese and Haitian-Creole)

SAIS and CEY will be administered by the project RA/RC(s) either in the Teen Health Centers, in a private space at schools/community spaces, or remotely using Google Meet so that a RA/RC may supervise virtually. In the case of a virtual screening, RA/RC will send participants a unique REDCap link to the SAIS/CEY assessment via email at the time of their screening. RA/RC will remain on Google Meet with the participant while they complete their assessment. Participants will be encouraged to mute their microphones and turn their video off to ensure privacy while taking the assessment. We will use REDCap, a secure web application for building and managing all online surveys, except the K-CAT, and databases that meet HIPAA compliance standards for data collection. While REDCap can be used to collect virtually any type of data, it is geared to support online or offline data capture for research studies and operations. CHA REDCap will be used to collect identifiable information. The identifiable information included in REDCap will be: email address, date of birth, gender, race and ethnicity the student identifies as, the student's primary language spoken, the student's language spoken at home,whether they have received care at CHA before, their COVID status, and the address where they are currently located (if the screening is taking place virtually). ATT will not be collecting any PHI, as a link to access ATT will be sent directly through REDCap. All research team members have submitted CHA REDCap User Agreements as well as a REDCap IT Review Form. CHA IT has also reviewed ATT to verify that it is a secure platform for the use of this study. Survey instruments will be translated into Portuguese, Spanish and Haitian-Creole by CHA Translation Services. ATT also offers the K-CAT questions to be read aloud for the participants in English and Spanish.

The intervention C2T will be available to the students online and students will have a unique log-in to access their program modules. The modules may be completed either at home or in school in the students' own time. Students who do not speak English or Spanish will complete the intervention with the help of an interpreter. C2T is a secure online digital intervention program. After inputting their unique access code participants will be prompted to create an account on the website. This account information includes an email address, name, and password. Participants input this information on their own, and we will not have access to it. The website will not have access to any other participant information other than what they provide for their account setup. The only information we receive is the completion certificate provided by the student, not the program. CHA IT has reviewed the website for data security. Students will have the option of weekly check-in phone calls or text messages from a member of the research team to discuss how C2T is going, which will take place through GoogleVoice. CHA IT has reviewed GoogleVoice for data security. Per CHA IT's request, once AvayaRed becomes available it will be used instead of GoogleVoice.

All data analyses will be conducted on CHA network computers. All study records will also be stored on CHA network computers (Component explanations are in Section D). Only the RAs/RCs and select data analysts will have access to patient identifiable information. Other study team members will see only coded data or aggregated results of data analyses.

**C. Collaboration**

**If this is a collaborative effort with another institution, explain the collaboration and attach a copy of the other institution's current IRB-approved protocol, consent form and IRB approval letter.**
**If an IRB authorization agreement (IAA) has been proposed, contact the chairboffice@challiance.org to discuss the information that must be included in the protocol and submitted to the IRB office.**
**If, as part of a collaboration with another institution, electronic and/or hard copy study records and/or data will be**

**created/collected at the other site, ensure that data transfer procedures are detailed in the Procedures section. If records/data will be retained at the collaborating site, confirm in this section of the protocol that a data sharing/data transfer agreement has been executed by CHA Office of Sponsored Research and the collaborating institution.**

CHA is the only site for this project.

**D. Subject Population(s)**

**Describe the study population in detail, including age range, gender, language, disease/condition, etc. State the maximum number of subjects to be enrolled in *each* group, as applicable, <u>and</u> in total.**

This project will include high school students in CHA's service area (Cambridge, Everett, Lynn, Malden, Revere, Somerville & Winthrop). The eSToRY Center focuses its efforts on adolescents because early detection of mental illness and assessing the appropriate interventions is linked to improved outcomes. This project will also include parents/LARs as participants in Component 2, as they will be completing survey instruments about their child. Component 3 includes the adolescents in Aim 1 as well as 400 matched youth in the EHR.

The project components are as follows:

**Component #1** - Screening (Aim 1)
We will screen 400 youth, including racial/ethnic minorities and females at rates similar to the general community population. Specifically, we expect the sample to be 44% non-Latino White, 22% Latino, 21% Black and 6% Asian. We expect 58% of the sample to be female. Given these demographics, we anticipate that we will be well powered for any comparative analyses between REL and non-REL youth.

**Component #2** - C2T Intervention (Aim 2)
We expect to include 108 youth in C2T. We estimate that the randomly clustered students in C2T may be more likely to identify as REL-minority compared to the general population given that the REL-minority population is at greater risk for emotional consequences of social distress. As part of understanding the feasibility and acceptability of C2T we will also be conducting semi-structured interviews with 10 pairs of youth and their parent/guardians.

**Component #3** - Reducing Disparity (Aim 3)
We will assess the impact of K-CAT screening and referral on REL disparities in access to MH treatment, comparing the youth screened in Aim 1 with CHA EHR records to matched youth in the EHR. We will also conduct an exploratory moderation analysis assessing how the effectiveness of C2T differs for REL-minority youth compared to White English-speaking youth.

**State if any specific population(s) will be excluded and detail the rationale. Scientific justification must be provided to exclude subjects based on race, gender, including women of child-bearing potential, or age (children, elderly).**

**NOTE: If vulnerable populations (e.g., pregnant women, neonates, fetuses, children, prisoners, persons with impaired decision making) will be enrolled, address in the recruitment and consent sections the additional precautions that will be taken to avoid undue influence and/or coercion. As it relates to vulnerable populations, ensure applicable Federal regulations are addressed and satisfied in the protocol.**

**Detail all inclusion criteria. Detail all exclusion criteria.**

Screening will include high school students in CHA's service area (Cambridge, Chelsea, Lynn, Malden, Everett, Revere, Somerville, and Winthrop). Adolescents will be excluded from participation in the C2T intervention if they have any current psychiatric history/treatment or use of psychoactive medication. This will be verified by checking with the student. Adolescents with a current psychiatric history or use of psychoactive medication will not be excluded from the initial screening. Twelfth graders may participate in the initial screening and the C2T intervention Subjects who are not fluent in English, Portuguese, Spanish or Haitian Creole will be excluded. Only subjects demonstrating a functional reading level so as to understand the consent and showing evidence that they can meet the expectations of what is demanded as judged by the RA/RC during the consent will be included. Students who are already engaged in behavioral health treatment will be excluded. All participants who have screened , will be eligible for inclusion in the qualitative interviews, and participants who complete all COPE2Thrive modules, as well as participants who start COPE2Thrive but do not complete it will be eligible for the post-C2T CEY evaluation. Students who do not complete all the C2T modules will still complete the CEY at the point they notify us they will be ending the program and are still eligible for participation in the qualitative

interviews. This CEY at last observation carried forward will be used in the analysis.

For the Aim 3 EHR analysis, matched control youth will be included based on the following criteria: adolescents with primary care visits at CHA but no Teen Health Center visits in Cambridge, Everett, or Somerville. Control youth will be matched to the youth participants screened in Aim 1 that have CHA EHR records using propensity score matching techniques based on K-CAT, EHR socio-demographics, substance use, physical health conditions, social determinants of health data, and merged neighborhood-level covariates.

**Address whether a subject may participate in another research study while participating in this study.**

Study participants are eligible to participate in another research study while participating in this study. Study participants in Component #2 cannot participate in another research study that involves mental health treatment as it might contaminate the findings of this study.

**If non-English speaking persons will be enrolled, refer to CHA policies on consent form and study document translation, consent processes for enrolling non-English speaking persons, etc.**

The student assent and parent consent forms will be translated into Spanish, Portuguese and Haitian-Creole. The parental consent will be conducted with a CHA interpreter if the parent is more comfortable in a language other than English. The K-CAT is available in English and Spanish. Participants wishing to take the K-CAT in a language other than English or Spanish will be connected with a CHA interpreter to complete the surveys in their preferred language. Additionally, interpreters for Spanish, Portuguese, and Haitian-Creole will be available if participants wish to complete weekly check-in phone calls or text messages in a language other than English.

**REMINDER: CHA considers every subject who signs an informed consent form (ICF) as enrolled, whether or not that subject completes the study. In determining the number of subjects to be enrolled the PI should take into consideration the likely subject attrition rate.**

**E. Recruitment**

**Detail recruitment methodologies. Include in an appendix to the protocol all advertisements and/or flyers and state where they will be posted. State the plan for ensuring that any posted advertisements, including online postings, will be updated, as needed and will be removed at the conclusion of recruitment.**

**Describe in detail how and where recruitment is performed and by whom.**

For Component #1 of this project, subjects will be recruited primarily through Cambridge Rindge Latin High School, Somerville High School and Everett High School. Recruitment will be expanded to teen-focused programs in the community and CHA clinics that see adolescents. The research team will document receipts of clear consent from each site to recruit through email documentation, written agreement from a representative of the organization, or through a signed letter of support when feasible. In all cases, the study team will maintain a clear documentation of approval to recruit at each site. Recruitment activities at teen/parent-focused community and summer programs will include sharing flyers for the study and having RA/RCs table or present information about the study to teens at the programs. Recruitment activities at CHA clinics that see adolescents will involve posting flyers in common spaces and sharing information about the study with providers so that they may share flyers with patients. Staff at these sites will refrain from answering questions about the study and defer to the RA/RC contact information on the flyer. Recruitment flyers may also be posed around the community (on public bulletin boards, store windows, telephone polls etc.) in accordance with local guidelines around posting. The school-based teen health center clinic staff training will be led by Chief of Pediatrics Dr. Hagan (who oversees the Teen Health Center staff), and Drs. Weiss and Castine. Training will include protocols for identifying students eligible to participate. The staff at the teen health clinics and other CHA clinics that see adolescents will help identify students eligible for Component #1 and direct them to the QR code on the flyer. The project Research Assistant/Coordinator will obtain youth assent and parental consent for participation in the study. For recruitment in the Teen Health Clinics and CHA clinics that see adolescents, clinic staff will not access patient PHI to determine eligibility. Flyers advertising the study will be posted on the front door and inside the Teen Health Clinic. Teen Health Clinic staff routinely visit classrooms to advertise the clinic, so during this time they will mention the study and hand out flyers. The extent to which teen health center staff will be involved in recruitment involves providing flyers to students and referring them to the RA/RC(s) for more information. Staff at all recruitment sites will refrain from answering questions about the study and defer to the RA/RC contact information on the flyer. After obtaining written approval from the school principals, RAs/RCs will expand recruitment activities into the schools. This may include: setting up a table outside to have greater visibility to students, mentioning the study in a clinic newsletter, visiting classrooms and extra-curricular activities to talk about the study, posting flyers in other parts of the schools, or putting flyers in teacher mailboxes. In the case that in-person recruiting is no longer a viable option, the

research team will work with the clinics and principals to identify other suitable options for reaching students (any additional activities will be approved in writing from the principals). A QR code will also be added to the flyer so that students can more easily contact the RA/RCs. More information about these activities is outlined below:

- A blurb describing the study that may be included in clinic newsletters has been submitted to the IRB for stamped approval.
- Upon written approval from the principals, flyers may be placed into teacher mailboxes along with instructions specifying that they should defer all study-related questions to the study team. These instructions have been submitted to the IRB for stamped approval. RA/RCs may also visit classrooms and extra-curricular activities to share information about the study.
- The QR code on the flyer leads to a secure CHA GoogleForm which requests their name, age, grade, preferred contact method and phone number or email address. All responses will be stored in a locked GoogleSheet that only the RAs/RCs will have access to. Once the RA/RC contacts the student, it will be recorded in the secure recruitment log.

Participants will also be recruited from the CHA Child Psychiatry waitlist. We have received approval from Dr. Nicholas Carson, Medical Director for child and adolescent outpatient psychiatry services, to access the waitlist and are requesting a waiver of consent to contact eligible youth and their parents/guardians. Prospective participants will initially be contacted either by GoogleVoice, AvayaRed, phone, or email to introduce the study. It will be made clear that participating in the project will not have any impact on their status on the waitlist. Should a participant get off the waitlist and into therapy during their participation in C2T, they will no longer be eligible and will discontinue their participation in C2T.

The participants who assent and whose parents/guardians consent to the screening will complete SAIS and subsequently will be tiered into three categories based on their scores as described above. Students who fall within Tier 1 will receive CHA behavioral health and resource guides for teens. All students will be eligible to participate in C2T, independent of how they are classified by Tier, unless they meet one of the exclusion criteria described below. This addresses our awareness that a majority of youth are distressed and might benefit from resiliency training. This will also allow us to assess whether the intervention could be considered as a universal intervention as part of a school curriculum, and how different levels of wellness or distress impact interest in participating in the program and response to the program. Students who fall within Tier 3 will be informed by a member of the research staff that they scored high on a specific module or modules and will be given recommendations for additional services and supports, while clarifying that this evaluation is for research purposes and not diagnostic. Tier 3 students will also be eligible for the COPE2Thrive (C2T) resiliency-based intervention and offered participation in the C2T study with the exception of students that are at imminent risk of harm to themselves or someone else, acutely psychotic, or in need of urgent psychiatric attention (deemed upon clinician assessment - see Suicide Risk Assessment Protocol), or students who are currently in treatment. Parental consent will be obtained prior to making referrals for additional services. If we learn that the student is a danger to themselves or others, we will attempt to connect them with the local emergency department or 911 services. Coverage by a child psychologist and child psychiatrist will be available by phone to the research assistant in any acute situation. Clinical coverage is available to the research assistants whenever the study is in progress (see Suicide Risk Assessment Protocol).

All students will receive generic feedback from RAs/RCs on what their relative domains of strength are according to their WFIRS results during a conversation between RA/RC and participants after the screening. The strengths shared and questions asked during this conversation help to avoid the risk of increasing a sample bias towards youth who are more symptomatic and allow for participant motivation and instances of sample bias to be recorded in study records (REDCap). Most importantly this also means participation in the study screening will provide youth with useful information on their strengths. A Post-Screening Conversation Script has been provided in the appendix documents. The RA/RC will note participant answers to post-screening conversation questions in the participant's REDCap record.

Rolling recruitment for the qualitative interview portion of the study will take place either after participants have completed the screening portion of the study or the COPE2Thrive intervention and CEY-completion survey, or after a participant drops out of COPE2Thrive and completes a CEY-completion survey. 30 participants (a mixture of youth and their LARs) will be selected to participate in qualitative interviews in order to assure representation of completers, non-completers, youth who refuse the intervention, responders and non responders, and the full spectrum of psychopathology.. Project RA/RCs will approach student participants for recruitment into the qualitative interview portion of the study any time after they have screened or at the time of their CEY-completion screening. If interested, RA/RCs will seek verbal assent using CHA DocuSign. If the student is not interested in participating in COPE2Thrive, the RA/RC will still offer a qualitative interview. If the student declines both C2T and the qualitative interview, RA/RC will ask the student why they were not interested in C2T and make a note in the recruitment log. This will aid in our understanding of what makes C2T appealing or not appealing to students. LAR participants will also be recruited to participate in the qualitative interview portion of the study at the time of their CEY-completion survey. If interested, RA/RCs will seek consent for participation in the qualitative interviews using CHA DocuSign. Participants who complete the screening portion or all COPE2Thrive modules, as well as participants who start COPE2Thrive but did not complete it, will be recruited for the qualitative interviews and CEY-completion surveys. Those who drop out of the COPE2Thrive intervention may be recruited for participation in the qualitative interview and the post C2T CEY surveys at the time they alert the RA/RC of their decision to drop out. Clinic staff from each of the three teen health

centers will be recruited for participation in qualitative interviews via verbal request. Clinic staff will be recruited based on their degree of familiarity with the research project and consistency of research procedure observation at the clinic.

For Component #3, there will be no recruitment, as it is a secondary data analysis of retrospective EHR/K-CAT data, which could not practically be carried out without a waiver of consent (see section G).

**F. Study Procedures**

**Describe the timing, administration/performance, and location of ALL study procedures, including screening procedures, cognitive assessments, *etc*.**

For Component #1, the RA/RC(s) will greet/contact students, inform them of the study, and if there is interest, begin the youth and parent consent process. The RA/RC will also reach out to students who signed up to learn more about the study through the QR code on the recruitment flyer via text, email, or phone call to begin the youth and parent assent/consent process. The RA/RC(s) will elicit verbal parent/guardian consent by reviewing all information and required elements of consent with the parent/guardian using the Component 1 ICF and share a copy of the consent form via email, text or mail. This conversation will take place either through GoogleVoice, by phone, or in person. GoogleVoice is a secure application that allows the RA/RCs to call from a randomly generated number. It does not collect any information from the participant. A more secure version (paid license) of GoogleVoice will be used once the license is obtained. Per CHA IT's request, Once AvayaRed becomes available it will be used instead of GoogleVoice. Once student assent and parental consent are obtained, the SAIS will be administered by the RA/RC(s). RAs/RCs will also be available by email or text if participants or parents/guardians have additional questions about the study or consent process.

For Component #2, once eligible students have been identified after an initial screening during Component 1 using the SAIS, the RA/RC(s) will obtain assent from the youth and consent from the parent/guardian for participation in the C2T intervention. The youth will then be randomly assigned to one of 3 total clusters for rolling admission into the study (Cluster 1 crosses over at study week1, Cluster 2 at study week 2, and Cluster 3 at week 3). At each weekly crossover, students in a cluster are eligible to receive C2T and can randomly crossover from the control group to the C2T intervention group. During the assent conversation, the Research Assistant(s) (RAs/RCs) will discuss the benefits of participation in potentially building resilience and coping with stress. The student will then be asked if they consent to participating in the C2T intervention and the RA/RC(s) will follow up with the youth's parent/guardian to elicit their informed consent and will receive a signed consent (similar to the process described above for the screener). Before starting the web-based COPE2Thrive (C2T) intervention, the RA/RC will provide information on C2T to the student, either virtually or in a designated area with a computer in the teen health center, including how to access the online platform and how to view and respond to the content. Participants will be asked if they would like to receive weekly check-ins via phone call or text message from a member of the research team. These conversations will take place on GoogleVoice and will be for the purpose of checking on the progress of the C2T intervention. The CEY will be administered by the project RA/RC(s). The CEY module will take approximately 60 minutes to complete. The parent/guardian will then be sent the parent report measures included in the CEY. For children who endorse significant symptomatology with functional impairment, with their child's assent, parents will be informed that their child's responses to our initial questions indicated that their child is showing signs of emotional and/or behavioral difficulties and may benefit from a referral for treatment. As required by law, if the child's responses indicate that they are at serious risk of harm to themselves or others, the clinicians will inform their guardians and take appropriate action as indicated to ensure the child's safety. Once enrolled, each student will have a unique login to access the C2T online intervention for each of the seven modules.

Project staff will conduct the qualitative interviews for both student and LAR participants. Project staff will be trained by Dr. Cortés and Dr. Progovac in the IRB-approved study protocol for reporting and safety concerns. Staff will also be familiar with the COPE2Thrive program and will have access to the modules through a trial program prior to conducting the interviews.. Qualitative interviews with clinic staff will be conducted by project RA/RCs and/or other appropriate members of the research team. Interviews will occur virtually using Google Meet, GoogleVoice, AvayaRed or phone and will last about 60 minutes each. Interpreters will be available if the participant is more comfortable in a language other than English. Interviews may last longer than 60 minutes if an interpreter is required. Participants will be informed that they may choose to stop the interview at any time for any reason. Audio of each interview will be recorded using Google Meet and transcribed using Google Meet. CHA IT has approved Google Meet. Recordings of interviews will be saved to a secure folder in the CHA Google Drive. RA/RCs will review Google Meet transcripts for accuracy and to remove all identifiable information. Once reviewed, interview transcripts will be saved to a secure folder in the CHA Google Drive. Transcripts will then be uploaded to Dedoose for coding.

For Component #3, we will use a propensity score matching technique to match the youth recruited in Component 1 to matched controls. We will use propensity score matching techniques used in previous CHA studies, to balance treatment students in CHA's teen health clinics with control of high school-aged patients in primary care. Matching will be based on the EHR socio-demographics, substance use, physical health conditions, and merged neighborhood-level covariates. We will be looking for two sets of outcomes from

the EHR data. The first is access to treatment (operationalized as any psychotropic medication or primary care- or specialty mental health treatment in the follow-up period). The second is the use of acute treatment (operationalized as ED use and psychiatric hospitalization). Information collected from the EHR will include demographics (race/ethnicity, sex, age), mental health, substance use, physical health diagnoses (from ICD codes), services use (outpatient, inpatient, ED service use), medications, and insurance status. Merged neighborhood-level covariates will be merged to participant addresses from publicly available area-level datasets as in previous studies. These will include Socio-economic status covariates, block-group level economic factors, block-group level built environment factors, county-level economic factors. Additionally, county-level health related factors will be downloaded from the Area Health Resource File (AHRF). Exploratory moderation analysis will also be conducted to assess how the effectiveness of C2T differs between REL- minority youth, and white English-speaking youth. Individuals with CHA EHR records will be matched to a control group for analysis. Although not all 400 youth screened in component 1 will have CHA EHR records, this group should be large enough to maintain statistical power for primary analyses. For secondary analyses, missing data imputation methods will be used to impute characteristics for the group that does not have EHR data.

**If subjects will be randomized to a group, explain randomization procedures.**

Each student participating in the C2T intervention will be randomized to one of 3 clusters using block randomization. As opposed to simple randomization to the 3 clusters (which may by chance allocate more youth to some blocks and fewer youth to other blocks), block randomization ensures that each of the 108 consented, eligible youth will be placed into 1 of the 3 clusters of the stepped wedge trial (a total of 36 youth for each of the 3 blocks). The block randomization program incorporates random number generators to allow for random permutations of the cluster assignment order and balanced assignment (exactly 36 per block) to each of the study clusters.

**State which study team member(s) (by role, e.g., PI, study physician, research coordinator) will perform each of the study procedures. Include a copy of each study team member's CV/resume so that the IRB may assess his/her qualifications to perform assigned study tasks.**

This section was removed in November 2023 per IRB guidance. Study staff are now tracked through Cayuse.

**REMINDER: Submit all interview guides, scripts, questionnaires, instruments scales to be used in this study.**

All instruments, scripts, and questionnaires are attached.

**Clearly identify which procedures, tests, visits, *etc*., are part of standard care and which are performed solely for research purposes.**

**State which tests are routinely performed for clinical care but are providing data for the research (and are billable to insurance companies), and which tests are only performed for research purposes (not billable to insurance companies).**

The screeners and follow-up surveys (SAIS and CEY) are part of this project, are not part of the standard of care, and are administered solely for research purposes.

**Describe the fate of any identifiable information collected in the study, emphasizing confidentiality of labeling of the sample and the sample's destruction or storage.**

Component #1 - The RA/RC(s) will keep a log of subjects approached for participation, those who assent, consent, drop out, and those who complete the screening. Contact information for eligible participants on the waitlist will be obtained using the phone number and email listed in EPIC. Only the IRB-approved Research Assistants/ Coordinators and Project Manager will have access to this file. This file will be kept in a GoogleSheet within the CHA Google workspace with restricted permissions only to be accessed by project RAs/RCs and Project Manager. We will only keep the minimum necessary data to verify the identity of potential participants. The only purpose of keeping this data is to ensure we won't recontact them in the future regarding participation in the study. Screening results collected via REDCap and ATT will be saved on the Health Equity Research Lab's drive within CHA firewalls. Designated member(s) of the data analyst team responsible for coding will have access to the file containing identifying information for participants. All other data analysts and team members will only have access to coded data or analyses that aggregate these data.

Component #2 - The CEY will be collected at baseline, post-intervention and 3 months follow-up. The students will show their certificate of completion for C2T modules (either on paper or by logging in to the C2T application) to the project RA/RC. The

RAs/RCs will record the modules as completed. The RA/RC will keep a log of subjects approached for participation, those who assent, consent, drop out, and those who complete the study. RA/RCs will keep a log of subjects approached for participation in the qualitative interviews, those who assent, consent, drop out, and those who complete the interviews. Only the IRB-approved RA/RCs and Project Manager will have access to this file. The file will be kept in a Google Sheet within the CHA Google Workspace with restricted permissions only to be accessed by the project RA/RCs and Project Manager. Google Meet recordings and transcripts of each interview will be uploaded to a restricted access folder in Google Drive within the CHA Google Workspace with restricted permissions only to be accessed by the interviewer, project RA/RCs and Project Manager. RA/RCs will review interview transcripts to remove all identifiable information prior to transcript coding.

Component #3 - The RA/RC(s) will compile a locked Google Sheet within the CHA Google workspace containing participant IDs and their corresponding MRN. Only the IRB-approved Research Assistants/Coordinators and data analyst team will have access to this file. Subject's name and birthdate will be used to verify the MRN; once that is completed only the MRN will be used to link subject data collected in the study to the EHR. The subject's address will be used to geocode the data, for linking to census and other area-level variables. The final analytical file will not contain any identifying information other MRN and an ID internal to EPIC, that no one other than IT personnel have access to.

Data will be prepared, analyzed, and stored using a CHA network computer behind the CHA firewall and if greater computer power is required, data will be analyzed on the Google Cloud Platform (GCP) in an area protected by the CHA firewall. We will have data use agreements for all of the databases that will be merged with the CHA EHR records. DUA agreement procedures will be strictly followed. The greatest risk is a data breach and we view this risk as minimal. With the precautions taken that are outlined in Sections F, H, I and J, the identification of individuals in these datasets is considered unlikely. This risk is mitigated by the measures we will take to secure the data (described in greater detail in “Confidentiality”). In the unlikely event of a data breach, we will immediately report the breach to Compliance, and work with them to identify compromised data and corrective action. We will also report the breach to the IRB within 5 business days in accordance with IRB policy.

Participants will be informed that the research team will make every effort to ensure the information they share will be kept confidential. No one outside of the research team will have access to identifying information for participants, including providers or school staff, except if the participant expresses any thoughts of suicidality, thoughts of plans to hurt someone else, or reports of abuse requiring legal mandated reporting. Participants will be informed in the assent/consent that this information would have to be shared in this extenuating circumstance. Only the Research Assistants/Coordinators and data analyst will have access to the participants’ name, email address, and phone number for assent/consent purposes. This information will be kept in a Google Sheet, within the CHA Google workspace, with restricted permissions only to be accessed by the IRB-approved project RAs/RCs and data analyst. Only the data analyst will see uncoded and identifiable data before creating aggregate data.

**State the length of time study procedures/visits will take and the expected duration of each subject’s participation, as well as how long the study will take to complete**

**Component #1 Screening** - The SAIS (KCAT and WFIRS) are estimated to take 20-30 minutes combined in English, and 40 minutes in a language other than English and Spanish. The K-CAT is estimated to take 7 minutes if administered in English or Spanish, and 15 minutes if administered through an interpreter.

**Component #2 Intervention** - The C2T program consists of 7 modules which take 20-30 minutes each to complete. The intervention cohort will take the CEY at baseline, completion, and 3-months follow-up. The CEY is estimated to take 60 minutes combined in English/Spanish, and 70 minutes in a language other than English and Spanish. The parent report is estimated to take 20-30 minutes to complete in English/Spanish and 40 minutes to complete in a language other than English and Spanish. Weekly check-in phone calls or text message conversations will take approximately fifteen minutes and will be conducted via phone call or text message using GoogleVoice. The 20 open-ended semi-structured qualitative interviews will be conducted after completion of the initial screening or the COPE2Thrive intervention. Each interview will last approximately 1-hour and will be conducted remotely via CHA Google Meet. Interviews may last longer than 1 hour if an interpreter is required.

**Transportation: Describe subject transportation arrangements, as applicable, with emphasis on post-visit transportation.**

Post-visit transportation is not applicable to this study. The SAIS and CEY will be administered to the students online.

**Withdrawal/Termination criteria: State the specific circumstances under which a subject’s participation will be terminated by the Investigator. Address any necessary safety precautions for withdrawal (tapering drug doses, evaluative x-ray, exit interview, etc.)**

In Component #2, a student’s CEY scores will be reviewed on the day they are obtained to screen for any acute concern or escalation

to a diagnosed mental condition that requires referral for treatment. The data will be reviewed by the RA/RC(s), and a clinician will be available as needed to triage and refer to clinical service as indicated. Any student who escalates from Tier 2 to Tier 3 on the CEY will be given information about accessing clinical services but will remain eligible for the C2T intervention. If they do not wish to complete the intervention, their data will be analyzed as intent to treat, and the last observation carried forward. Students who get off of the waitlist and into treatment while participating in C2T will no longer be eligible for the C2T intervention and their data will be analyzed as the last observation carried forward. Students who appear to be unable to understand the questions, or otherwise judged to be unable to reliably participate in the C2T intervention will be removed from the study but will be included in the ITT analysis if they have already started the intervention. Students who do not demonstrate that they have actually completed the C2T intervention as described above will only be included in an ITT analysis.

**Procedure Timeline: Consider creating and attaching a study flow chart or table illustrating subject visits and tests or procedures to be performed at each visit.**

Please see the attached procedure flowchart.

**If blinding (masking) is involved, describe the procedures. State who will hold the code and the circumstances and procedures for breaking the code, including under emergency settings, nights, weekends, holidays, etc.**

There will be no blinding/masking involved.

**G. Informed consent**

**Refer to CHA policy A-COM-0004 (Informed Consent for Research and Authorization for the Use and Disclosure of Protected Health Information) for details on CHA's research consent policy, including applicability, definitions, procedures, etc., and criteria for waiver or alterations of informed consent.**

**The PI must provide a prospective subject or the LAR with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information. A subject or his/her LAR is to have adequate opportunity to read the ICF, ask questions and obtain answers, and discuss and consider whether or not to participate in the study or not. A written copy of the ICF is to be given to the person signing the ICF, and a copy mailed to the parent.**

**a. Consent Process**

**Describe the informed consent process, including who will give subjects detailed and comprehensive information about the study. State who among the study team will perform this process, including who will obtain and document subjects' written consent.**

Co-I Hagan will train clinic staff about the study implementation timeline and processes for referral in order to facilitate study recruitment and workflow. Parental consent and child assent will be obtained using translated materials (Spanish, Portuguese and Haitian-Creole) and phone interpretation. A Research Assistant/Coordinator will provide youth support as needed to complete the SAIS screener and CEY baseline and follow-up surveys. Interpreter/translation services will be provided for all procedures and documents as needed.

The Research Assistants/Coordinators will be the individuals carrying out the consent conversation with the student and the parent/guardian for Component #1 and Component #2. Project RA/RCs will also carry out the consent process for students and LARs for the qualitative interview portion of the study.

**If a waiver or alteration of consent is being sought, state the rationale and ensure that the regulatory requirements for a consent waiver are addressed.**

For Component #1 (initial screening) we are requesting a general waiver of documentation of consent under 45 CFR 46.117(c)(1)(ii): "the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context" for the following reasons:

- This research presents no more than minimal risk of harm to the subjects; in fact, the study actually may reduce risk to participants who have underlying concerns that would otherwise not have been caught or addressed. Additionally, the use of the PHI in this study involves no more than minimal risk to the privacy of individuals.

- The activities of screening are currently occurring in practice in other ways without written consent. For example, the use of the Youth Risk Behavior Survey which involves students answering questions similar to those in our screener, including suicidality, without written parental consent or follow up procedures. This is currently being done in all Massachusetts High Schools.

We are also requesting a waiver of consent to contact prospective participants from the CHA Child Psychiatry waitlist due to the following reasons:

- The research is not regulated by the US Food and Drug Administration;
- We would not be able to reach these prospective participants without the requested waiver;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
    - The use of the PHI involves no more than minimal risk to the privacy of individuals based on the presence of the following elements:

        a) An adequate plan to protect identifiers from improper use and disclosure, as described in Study Procedures. Additional language clarifying procedures has been added to the protocol.
        b) An adequate plan to destroy identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or retention is required by law. We note in Privacy and Confidentiality that we will destroy the code at the termination of the research study. Additional language clarifying these procedures has been added to section M "Privacy and Confidentiality".
        c) The PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule. The ALACRITY eSToRY Center grant supports smaller research projects within it that are expected to use data from the larger project. These smaller projects will be submitted to the IRB for approval prior to commencement.
- and - Whenever appropriate, the subjects will be provided with additional pertinent information after participation (e.g., through summaries of the research shared on the lab's website).

For Component #3, we are requesting a HIPAA waiver. We are also seeking a waiver of consent/assent for the matched control group due to the following reasons:

- The research is not regulated by the US Food and Drug Administration;
- The research involves secondary data analysis and therefore involves no more than minimal risk to the subjects;
- Due to the large sample size, the research could not practicably be carried out without the requested waiver or alteration;
    - This applies to both the Comparison group and Intervention group, since Component #3 was added to the research protocol well after Component #1 began and would require an arduous process of re-consenting participants when the loss to follow-up due in part to very involved consenting processes already exists as a burden and risk to the study.
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
    - The use of the PHI involves no more than minimal risk to the privacy of individuals based on the presence of the following elements:

        a) An adequate plan to protect identifiers from improper use and disclosure, as described in Study Procedures. Additional language clarifying procedures has been added to the protocol.
        b) An adequate plan to destroy identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or retention is required by law. We note in Privacy and Confidentiality that we will destroy the code at the termination of the research study. Additional language clarifying these procedures has been added to section M "Privacy and Confidentiality".
        c) The PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule. The ALACRITY eSToRY Center grant supports smaller research projects within it that are expected to use data from the larger project. These smaller projects will be submitted to the IRB for approval prior to commencement.
- and - Whenever appropriate, the subjects will be provided with additional pertinent information after participation (e.g., through summaries of the research shared on the lab's website).
    - This only applies to subjects in Component #1, as it would not be appropriate to contact the Comparison group for this purpose.

**REMINDER: Informed consent as a whole must present information in sufficient detail relating to the**

**research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate.**

**Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent form must be organized and presented in a way that facilitates comprehension.**

**b. Consent location and timing**

**State when and where the consent discussion will take place.**

Completion of study assent and consent will take place in a private space with an internet connection at the Teen Health Centers, high schools, teen community programming space, or virtually using GoogleVoice (CHA IT has approved the use of GoogleVoice) or AvayaRed. Verbal consent and assent will be obtained and noted in REDCap, and a copy of the assent/consent form will be shared with both parents and students either in hard copy form or texted/emailed. Both child assent and parental consent will take place prior to the initial screening for study eligibility and repeated prior to child participation in C2T intervention. If a child turns 18 while participating in the study, they will be re-consented. Students who are 18 at the time of their consent for participation in C2T will be asked for consent prior to study team members contacting their parent to participate in the parent/guardian surveys. Students who are 18 will not be excluded if they do not consent to the research team contacting their parent, or their parent does not consent to participating in the study.

**c. State the methods that will be used to ensure that participants understand the study and procedures. Specify who will carry out the assessment and where and how it will be documented.**

All aspects of the consent form will be discussed in detail. For Component 1, RAs/RCs will review all information and required elements of consent using the consent form. Both students and their parents/guardians will be offered an opportunity to have all questions answered. Capacity to consent/assent will be determined based upon a discussion of the study during the consent process, followed by a series of questions to assess the participant's understanding of: the purpose of the research, foreseeable risks and anticipated benefits of study participation, and the participant's understanding of the voluntary nature of research and the elements of consent. Because the informed consent of a parent/guardian is required prior to participation, no additional risk is presented to participants or their parent/guardians by obtaining youth assent prior to parent/guardian informed consent. All study data will be maintained securely in password-protected electronic files and in locked file cabinets.

**d. Subject Decision-Making Assessment: State how and by whom it will be determined whether a subject has the capacity to give informed consent, or whether their legal guardian or legally authorized representative will give informed consent. For subjects whose ability to give informed consent may be compromised by cognitive and/or decisional impairment (examples may include individuals with a psychiatric disorder, an organic impairment, a developmental disorder, or those suffering from a terminal illness, degenerative disease, severe physical handicap or dependence on drugs or alcohol), complete Appendix I.**

**e. If minors and/or persons with impaired decision-making will be enrolled, detail the assent and permission processes, including how assent will be documented.**

**REMINDER: It is strongly advised that researchers document in each study participant's files details of the consent process and discussion, including who was present for the discussion, any questions asked by a subject and the answers provided, as well as any other pertinent details.**

**REMINDER: If minors will be enrolled and will attain age 18 years while in the study, their consent must be obtained at age 18 years. The protocol must state details related to this procedure, if applicable.**

The Research Assistants/Coordinators will carry out the consent conversation with the student and parent/guardian. The steps in this process are as follows: Research Assistant(s)/Coordinators (RAs/RCs) will share an informational flyer with an overview of the study with student and discuss study procedures. The RA/RC(s) will read through all information and required elements of assent in the Component 1 Assent form with the student to gain verbal assent from the student. The RA/RC(s) will ask for a parent/guardian phone number or email address and contact them to obtain consent for the student. In contacting the parent/guardian, the RA/RC(s) will obtain verbal consent by reading through all information and required elements of consent in the Component 1 ICF with each

individual and sending the consent form to them via email, text, or mail. If the parent/guardian prefers the conversation in a language other than English, the RA/RC(s) will contact CHA's Interpreter Services and have the conversation translated for the parent by the Interpreter. If the RA/RC(s) are unable to reach the parent/guardian, we will not be able to obtain consent and the youth will not be able to participate. If a parent would like to discuss at a later date or requests time to consider their decision, the RA/RC(s) will follow up with them on a routine basis. Youth and parents will be informed that all information they provide is confidential and will not be shared, unless mandated by state law for safety purposes. If a child is eligible for C2T, the RA/RC(s) will reach out to the student to let them know that they are eligible for the COPE2Thrive intervention. If the student is interested in learning more, the RA/RC will provide the student with more information about the intervention and obtain assent. RA/RC will refer to the Component 2 assent script to obtain assent from the minor for participation in the COPE2Thrive intervention. If a youth assents, the RA/RC(s) will contact the parent/guardian to obtain consent for the minor's participation in the COPE2Thrive intervention. If the parent/guardian prefers the conversation in a language other than English, the RA/RC(s) will contact CHA's Interpreter Services and have the conversation translated for the parent by the interpreter. The parent/guardian consent will take place using CHA DocuSign (in extenuating circumstances a paper form may be used). While the Research Assistant/Coordinator is still in contact with the parent/guardian, they will review the signed CHA DocuSign or paper version of the consent to ensure it is complete. The consent will then be saved electronically to the patient's study file. Should a participant turn 18 before the study ends, the RA/RC(s) will follow the script for young adults (>18) to initiate the consent process. The assent/consent processes will be done in such a way that students and parents have ample time to process the information, ask questions, and to consider whether they wish to participate. If a child falls into tier 3 but refuses assent to inform parents of the need for treatment, we will not break confidentiality unless there is evidence of imminent risk (see Suicide Risk Assessment Protocol). If the child is not deemed an imminent risk they will be invited to participate in C2T, at which point a separate assent/consent process will take place. RA/RCs will seek youth assent for the qualitative interview portion of the study directly following the initial screening (if C2T is declined) or following the student's CEY- completion assessment. Assent will be obtained using CHA DocuSign (or a paper form if necessary). RA/RC will seek consent for the qualitative interview portion of the study by reaching out to the student's LAR directly following the LAR's CEY- completion assessment. Consent will be obtained using CHA DocuSign (or a paper form if necessary).

Project team will seek clinic staff consent for qualitative interview participation by reaching out to the staff directly (either virtually or in-person). Informed consent will be obtained using CHA DocuSign (or a paper form if necessary).

**H. Risk/benefit assessment**

**State all risks associated with participation in this study, including physical, psychological, social, economic, and any other risks. Give consideration to study assignment, as applicable (Arm A, Arm B, placebo, active substance, *etc*.):**

The study does not involve invasive physical procedures and we anticipate risks to participants to be minimal. Risks involved in screening include identification of symptoms of mental illness that the subject was unaware of and that raises concern about their own well-being. It is also possible that students who have experienced a previous trauma may be 'triggered' by completion of the UCLA trauma scale. However, this can equally be understood as a potential benefit in raising awareness and improving access to treatment. There is also risk in identifying mental illness in a youth for whom the youth does not want their parent to be aware of, thus potentially creating a situation of parent-child conflict. The consent will explicitly state that the study is not a diagnostic evaluation, but that information will be provided if a serious potential concern is identified. The consent/assent will indicate that feedback will be limited to reporting back to the youth whether or not referral for treatment was indicated. Guidelines for informing parents of youth results will follow Massachusetts legislation. In order to mitigate risk to youth who are identified as Tier 3, we will ask for the youth's assent to notify parent/guardian and will provide both the youth and parent/guardian with a list of resources that may help them access treatment if they so choose. The risk to such youth is likely to be lower than it would have been if the difficulties with mental illness had gone undetected.

It is possible that by recruitment from the waitlist, we may encounter more seriously ill patients than from the community. Reasons which argue against this happening is that the waitlist has already been triaged and acute patients placed in treatment. In addition, we have found that only 1/3 of the seriously ill patients identified in the community have had access to or been referred to treatment. If they are not in our system we will follow the same procedure previously described for management of Tier 2 or 3 in the clinical protocol. If we contact someone on the waitlist who is no longer interested or appropriate to remain on the waitlist, we will encourage them to contact the outpatient intake department to let them know. This decreases risk to the patient and provides a valuable service to our outpatient department. More importantly, if this procedure is found to be feasible to use, C2T with check-ins would become a model for a possible intervention to address the crisis or lack of access to care during the mental health crisis.

Completion of the C2T intervention and measures will take time that might have been spent on other activities but will likely offer significant advantages in building resiliency. The addition of the C2T check-ins decreases the risk of the study by increasing the frequency, vigilance and patient centered nature of our contact. Another possible risk is that some participants may feel

uncomfortable answering certain questions or may feel a burden of answering questions. Several steps will be taken to minimize potential risks. The informed consent form will explicitly state that participation is voluntary and that the participant may skip or refuse to answer any question at any time.

**State the potential benefit to individual subjects participating in the study.**

The student participants in the C2T might receive benefits from participating in the program. If the program is effective, the students could build resiliency skills, lower mental health symptoms and improve functioning. Completion of the screening is also likely to raise awareness in students of any subsyndromal mental health challenges they may face, and to provide education on symptoms associated with mental illness. Identification of students with suicidal ideation and plans or mental illness, with appropriate and timely referral for treatment, is a benefit of the project. The study may also contribute to a culture of resiliency and awareness in schools that have recently experienced significant trauma secondary to the current syndemic. A benefit of the project will be identification of and referral for treatment for acute mental illness that would otherwise have gone undetected. Another benefit of the project will be providing schools with group data of levels of distress in their communities, that may inform and facilitate innovation in their social and emotional learning programs. Adolescents in the project may additionally experience some satisfaction with having participated in a research study where the objective is improved youth wellbeing. Once the screening process is established in the school, and staff are trained in C2T, we anticipate that these tools might become an ongoing part of usual care or part of the school's social and emotional learning curriculum. The WHO, CDC, UN, UNICEF, and the Surgeon General have all found that there is at a minimum a 40% increase in mental illness among youth. The addition of weekly phone/text 'check ins' increases the benefit of the study to youth because they will have access to support that adds a personalized context to the C2T program. The waitlist includes many patients who are referred to integrated care or for counseling who have been waiting for more than one year with no intervention. By providing the screening we will be assisting in triaging these patients so that if we come across a patient that is urgent but not emergent we will provide that information with their consent to intake so that they are prioritized for treatment. For those patients who are mildly ill, immediate but personalized access to C2T may either mitigate the length of treatment that is needed later or potentially eliminate the need altogether.

**REMINDER: Payment is never to be considered a "benefit" of participation.**

## I. Data and Safety Monitoring Plan

**Define adverse (AE) and serious adverse events (SAE) for this study.**

Given that the nature of this study involves assessing youth at an elevated level of risk, we would define an adverse event as a student becoming distressed by the questions themselves, although this would suggest that such a student would benefit from appropriate feedback. A serious adverse event would be if any student identified as actively suicidal, and this will be managed by the usual clinical procedures for mental health crises. In order to ensure appropriate response to suicidal ideation, serious drug use, high risk activities or significant SDoH concerns, SAIS or CEY data will be reviewed by the site RA/RC on the day it is completed, and any concerns raised will be elevated to the clinical investigators. Any concerns that arise during weekly C2T check-ins will be elbated to the clinical investigators who will follow the high risk protocol as appropriate. Clinicians in the project will provide rotating 'on call' availability to address any acute clinical situation. If a student scores red (high-risk) on the Columbia Suicide Rating Scale (C-SSRS), the RA/RC will page the on-call clinician in accordance with the Suicide Risk Assessment Protocol. The clinician will then contact the patient to provide clinical follow-up as indicated by their clinical risk evaluation. Clinicians conducting a suicide risk evaluation will follow through on whatever clinical emergency procedures are indicated. Patients found to be at acute and imminent risk will be directed to the ED and sectioned if appropriate. Patients who are found to be at risk, but do not meet inpatient level of care, will be managed appropriately according to the clinical level of risk as judged by the clinician (see Suicide Risk Assessment Protocol). Adverse events in which a child is in serious risk will be shared with the parent/guardian in accordance with state law. The consent forms will stipulate that information obtained will be kept confidential, with the exception of information putting the child at serious risk, as required by law. The Research Assistant/Coordinator will be the first point of contact in identifying an AE or SAE, with report to clinical investigators who will be available by page.

**Describe how AEs will be ascertained and processed, including the timeframe and who on the research team (*e.g.*, individual role) is responsible for processing reports.**

In the case of an adverse event, we will follow CHA's IRB's policies to ensure patient safety and appropriate response. We will report any SAE or AE to the IRB within 5 business days of discovery. Any significant protocol violations will also be reported to the IRB.

**Refer to CHA policy A-COM-0007 (Reporting to the IRB of Adverse Events and Unanticipated Problems Involving Risks to Study Participants or Others) when developing the data and safety monitoring plan.**

**Explain the data monitoring plan for this study, including the frequency of monitoring, who on the study team will perform the monitoring, and what will be monitored.**

The frequency of monitoring for adverse events will be on the day that the information is collected. Students will be given contact information for a study staff member in the event that concerns arise following the completion of any study component. All such contacts will be logged. Only the data analyst on the project will have access to subject identifiers for participants in order to conduct the analyses. The information that will be monitored are as follows: medical record number, address, information for medical visits (date, provider type and location of visit, diagnoses, expenditures).

**If a Data and Safety Monitoring Board (DSMB) exists for the study, include a copy of the charter.**

N/A; no DSMB exists for this study.

**Describe accountability procedures as they relate to drugs, devices, and data, including who will be accountable, in addition to the PI, on the research team (*e.g.*, individual role) to interface with the pharmacy (drugs) or sponsor (devices) or other entities.**

The project's screening and clinical trial will be closely monitored by PIs, Dr. Weiss and Dr. Castine. The PIs will monitor the psychiatric review of the SAIS screening tool, appropriately referring high risk youth to indicated treatment. The Research Assistant/Coordinator will review the results of the SAIS on the day it is completed and contact the study clinicians with any concerns. Those who score red on the suicidal risk score of the C-SSRS will be screened for suicide risk by a clinician involved in the study according to the best practice clinical procedures for follow up of any high risk situation. The RAs/RCs will monitor the progress of the students participating in the COPE2Thrive intervention by checking in regularly with the youth participating in the intervention to monitor progress. This project does not require the formation of a Data Safety and Monitoring Board.

**J. Study Records, Data, and Biospecimens Storage**

We will use Research Electronic Data Capture (REDCap), which is a free, secure (HIPAA compliant), web-based, and user-friendly electronic data capture (EDC) tool for research studies, and Pathology Specimen Locator. The system was developed by a multi-institutional consortium initiated at Vanderbilt University. The REDCap file will be saved on the Health Equity Research Lab's drive within CHA firewalls. K-CAT data collected using ATT will subsequently be consolidated into the REDCap database, which will be saved on the Health Equity Research Lab's drive or on the CHA Google Cloud Platform, both within CHA firewalls. Only the Data Analyst and RAs/RCs will have access to this file. Verbal assent and consent will be noted in the student's REDCap record and in the call log, which is stored behind the CHA firewall.

**Address the location where study records, including signed consent forms, will be stored.**

**Detail where hard copy and electronic data will be stored and for how long.**

Electronic data and consents will be stored at the Health Equity Research Lab for seven years as required by IRB policy. Electronic assent/consent forms and logs will be stored in REDCap behind the CHA firewall, as well as in a restricted access GoogleDrive folder that only RAs/RCs and the Project Manager will have access to. Original paper assent/consent forms will be locked in a file cabinet at 1035 Cambridge St, Cambridge MA, 02141.

**State who will have access to study records, and data.**

Members of the CHA research team will have access to aggregated tables (demographics, analyses) without identifying information. Only those members of the CHA analyst team designated for coding will have access to identifiable data.

**K. Costs**

**State all costs to subjects associated with participation in this study.**

There are no costs for the patient associated with this study. The C2T program will take a total of 7 hours, some of which may occur during the school day.

**L. Subject Payment**

**State if subjects will be paid for participation, including the amount.**

**State the method/form (e.g., cash, gift card, check) of payments and how they are administered (e.g., given directly to participants at study visits, mailed to subjects, emailed to subjects).**

**Specify the payment schedule, including the prorated plan should a subject withdraw or be withdrawn from the study prior to his/her completion.**

The incentive for completion of the SAIS is a gift of a $10 Tango gift card.

In Component #2, students will be offered gift certificates of $65 for incentive to begin the intervention, $15 upon completion of the online modules, and another $20 upon completion of the program and follow-up evaluation. Parents/guardians will also be given a $5 gift card to complete each portion of their screener (upon beginning the intervention, upon completion, and at 3-months follow-up). Students who participate in the qualitative interview portion will be offered a $25 incentive in the form of a Tango gift card. Parents/guardians who participate in the qualitative interview portion will be offered a $50 incentive in the form of a Tango gift card. There is no incentive for clinic staff interviews

Tango gift card rewards will be emailed to study participants by the project RAs/RCs. Some participants may experience limited access to internet or computer literacy, so in order to accommodate this range of needs we are offering physical gift card incentives to those with extenuating circumstances. These will be mailed to the participant's preferred address. This mailed correspondence will just include the gift card and no other documentation (e.g., a note or letter) that could directly link the subject to this specific study.

**Specify if travel costs will be reimbursed.**

Travel expenses will not be incurred in this project.

**REMINDER: Full payment cannot be held until the end of the study as that is potentially coercive.**

**M. Privacy and Confidentiality:**

**Describe study procedures to protect subject privacy and confidentiality. Identify all parties who will have access to research records, such as research staff, internal and external auditors, sponsor, monitor(s), DSMB(s), IRB(s), etc.**

Once participants are enrolled in C2T, only the RA/RC(s) and the data analyst(s) responsible for coding will have access to individual identifiers. Only the members of the data analyst team will have access to identifiers in order to perform the coding procedures. All other data analysts will use the coded data. Other research team members will only see analyses that aggregate the individual data into cross-tabulations or statistical modeling results.

Subjects requiring referral information will be identified for safety purposes by the clinicians acting as emergency back-up to the RA/RC(s). All preliminary tables and final results will be aggregated so that participants are not identifiable. All investigators analyzing these data will be required to adhere to CHA's strict human subjects training protocols and will operate within the CHA firewall. Only coded datasets will be available to other Co-Investigators and research team members for analysis.

The datasets used in the eSToRY Center analyses are tied to protected health information (PHI) in electronic health records and system wide computer adaptive testing (CAT-MH) from CHA. Because these datasets are tied to PHI in electronic health records and other merged datasets, the results of these studies will not be made publicly available. However, we will work to make publicly available a limited dataset that includes de-identified, non-PHI information, sharing these data with the NIMH's data archive site, National Database for Clinical Trials Related to Mental Illness, and ClinicalTrials.gov.

The preparation of the clinical-socio contextual data warehouse (CHA-IRB-21-22-120) will involve merging data using identifiable information. Description of identifiers for the data include: medical record number, address, DOB, information for medical visits (date, provider type and location of visit, diagnoses, expenditures), social determinants of health (employment, financial barriers to treatment, housing) at the individual (as derived from SDOH screeners in the EHR and Connect-S) and neighborhood levels (as derived from Census data).

The data warehouse will use electronic health record (EHR) data from CHA patients that includes phrases from clinical notes, structured clinical data (questionnaire responses, medications, diagnoses, vital signs, lab values, visit dates) and individual-level social determinants of health (SDOH) data. These data are merged as follows:

- by medical record number to insurance claims data
- by address to census-block and county social determinants of health data and healthcare supply characteristics

The data analyst team on the project will be the only staff to have access to subject identifiers in order to merge data sets. Identifiable information include name; medical record number; addresses; and all dates, including date of birth and service dates.

Once the data are merged, the data analysts will create a coded data set with all identifiable information being masked. “Masking” involves replacing the Protected Health Information elements with a randomly generated code. Without the code, the data will be unable to be linked to the living individuals. In the course of publication, reviewers often request revisions to the analyses, which may require a renewed examination of the raw data. Therefore, the code will be destroyed at the termination of the research project.

When data analysis approaches or results need to be discussed with study consultants, the analyses and results will only be shared in aggregate and any identifiable information will only be available to the data analyst team. Aggregated results will contain no identifiers. We will take every possible precaution to maintain patient privacy protections.

With authorization from Dr. Nicholas Carson, Medical Director for child and adolescent outpatient psychiatry services, a request will be submitted to CHA Marketing to extract contact information (name, phone, email address) for patient caregivers from the relevant Epic waitlist, or "workqueue" (Referral/Authorization Workqueue BH Child Intake - Scheduling [34248]). This contact information will be entered directly into our participant log, which is a HIPPA compliant Google doc securely stored behind the CHA Firewall.

**If data will be coded or de-identified, state who will perform the procedures, when, how, and where data will be stored.**

**If data will be coded, state who will create the code, where and by whom the key to the code will be kept, who will have access to the key to the code, and how long the key to the code will be maintained.**

The RA/RCs will create the codes to identify participants for Components 1 and 2. For Component 3, the code will be created by the data analyst; this analyst will keep the code in a file that is not shared with other research staff. The key to the code will be maintained for the duration of the center grant (4 years) at which point it will be destroyed. ata will only be accessible by the analyst and stored for the duration required by the IRB (currently 7 years).

**Address how the Health Insurance Portability and Accountability Act (HIPAA) will be satisfied in relation to this research study.**

We are seeking an alteration of HIPAA authorization, under the Privacy Rule, for Component 1 to remove the signature requirement, as we are requesting a waiver of documentation of asset/consent for verbal assent/consent and the following apply:

- The use or disclosure of protected health information involves no more than minimal risk to the privacy of the subjects based on:
  - An adequate plan to protect the identifiers from improper use or disclosure (outlined in this protocol);
  - An adequate plan to destroy the identifiers at the earliest opportunity, unless there is a health, legal, or research justification for retaining the identifiers (outlined in this protocol);
  - Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information (provided in the assent/consent form);
- The research could not practically be conducted without the alteration;
  - The written assent and consent documentation procedures are a barrier to recruitment in a project which by definition is community-based and set up to be virtual.
- The research could not practically be conducted without access to and use of the protected health information.

Component 2 of this research study will satisfy HIPAA requirements by following the signed HIPAA authorization rule on the CHA IRB website, which states that “A HIPAA Authorization is an individual study participant’s signed permission to allow a CHA researcher to use or disclose the subject’s PHI.” The authorization is included in the Informed Consent Forms.

A HIPAA waiver has been granted for Component 3 of this study.

**Address if a Certificate of Confidentiality will be or has been obtained.**

As noted in the IRB application template, any project receiving NIH funding that collects or uses identifiable, sensitive information is automatically deemed issuance of a CoC. NIH awardees do not need to request a CoC. Researchers with a CoC may ONLY disclose

identifiable, sensitive information in the following circumstances:

- if required by other Federal, State, or local laws, such as for reporting of communicable diseases
- if the subject consents; or
- for the purposes of scientific research that is compliant with human subjects' regulations

AND must ensure that anyone who is conducting research as a sub-awardee or receives a copy of identifiable sensitive information protected by the policy understands they are also subject to the disclosure restrictions, even if they are not funded directly by NIH.

**N. Alternatives**

**State the alternatives to participation in this research study.**

The alternative to participating in this study is to not participate. Participants will be informed that participation in the project will not have any impact on their education, treatment in the Teen Health Center, or any care they receive at CHA.

**O. New Information**

**State the process for how new information obtained during the course of this study will be conveyed to study subjects and how it will be documented.**

The study publications will be sent to Cambridge Rindge Latin School, Everett High School, and Somerville High School. Schools will also have the option of including a summary of the study findings for staff and parents in school news bulletins.

**P. Research-Related Injury**

**Include information regarding payment for a research-related injury, including who is financially responsible for such payment, where treatment may be obtained, and the study team member to be contacted in the event of an injury.**

The study team envisions any potential harm to participants to be low if at all because the study does not involve invasive physical procedures, and any potential loss of confidentiality has several safeguards in place to minimize risk. The project will potentially raise awareness of emotional distress but not over and above that which the subject is already aware of. Wherever students are identified as Tier 3 (not high-risk), a Research Assistant/Coordinator will provide students with a list of referral information. Upon assent from the student, a RA/RC will also notify their parent/guardian and provide them with the same referral information. Clinicians will be on call to the RA/RC(s) during the hours in which the study is conducted to facilitate the management of any acute clinical concerns that emerge (See Suicide Risk Assessment Protocol).

**Q. Statistical Analysis**

**Describe the analytic and statistical methods to analyze data, including any interim analysis. If randomization will be used, include the method of randomization and randomization ratio (1:1; 3:1; *etc.*).**

**Include power calculations and specify the statistical tests that will be used to test each hypothesis.**

**Design.** We plan a stepped wedge design to evaluate the preliminary effectiveness of COPE2THRIVE in Component 2. We begin with unadjusted comparisons (over time and between treatment and control groups) using ANOVA for symptom (K-CAT) and function (WFIRS) outcome scores. Second, to more rigorously assess the preliminary effectiveness of the intervention on outcomes, we conduct an intent to treat analysis using Generalized Estimating Equations (GEE), controlling for age (continuous), gender, primary language (English, Spanish, Portuguese, other non-English language) and race/ethnicity (non-Latino white, non-Latino black, Latino, other race/ethnicity), focusing on the significance of the treatment by time interaction coefficients as representative of preliminary effectiveness.

GEE accounts for the clustering of individual observations over time and is robust against misspecifications of the working correlation matrix when specifying the correct dependent-variable distribution and canonical link function. When appropriate, we will transform data to normalize distributions, using the appropriate link and variance functions (e.g., gamma distribution with logit link for K-CAT symptom and Weiss function scores), comparing Akaike's Information Criteria (AIC) to determine the best fit for each of the models.

**Power analysis**. The C2T intervention, with 108 subjects, 3 clusters of 36, assuming a clinically meaningful effect size of 0.4,

within-period correlation of 0.1, inter-period correlation 0.01, and within-individual correlation of 0.2, will provide 80% power to detect significant changes in child-reported K-CAT symptom scores and WFIRS functional outcomes. Since the CRLS teen clinics have annual visits from 935 youth in the age range that matches the inclusion criteria of this study, there are more than enough students available to obtain our required sample size, even accounting for ineligibility and refusal to consent.

**R. Study results**

No study results will be given directly to subjects. Study results will be presented with dissemination purposes in academic conferences as well as with completion of manuscripts.

**S. Outcome:**

**Describe what results are expected, the criteria for success or failure, and the end point of the study.**

**Primary - Youth-reported symptom score on the K-CAT**
The K-CAT is an online screening tool that assesses a range of psychiatric symptoms. The K-CAT provides a combined numeric score for each module that will be used to determine thresholds (e.g., mild, moderate, severe) that are based on validated quantitative comparisons. Change in the numeric level of these symptoms will be the primary outcome of the testing of the preliminary effectiveness of the C2T intervention.

All secondary analyses are exploratory in nature.

**Secondary outcome 1 - Youth-reported function**
*Weiss Functional Impairment Rating Scale (WFIRS)* The youth reported WFIRS asks youth to rate their own functional impairment over the past month, across subdomains of family, school, life skills, child's self-concept, social activities, and risky activities.

**Secondary outcome 2 - Parent-reported symptom score**
*The parent K-CAT* will be used to measure changes in parent reported symptoms scores.

**Secondary outcome 3 - Parent-reported function**
*Weiss Functional Impairment Scale (WFIRS) Parent* asks the parent to rate the youth's functional impairment over the past month, across subdomains of family, school, life skills, child's self-concept, social activities, and risky activities.

**Secondary outcome 4 - COPE2Thrive Interest**
Data on the characteristics of the population of students interested in C2T will be analyzed. These include symptom severity and impairment severity, gender, grade level, race/ethnicity, school, language, and time of invitation to C2T. We will run an analysis to see if we can identify predictors of interest, participation, and completion of COPE2Thrive.

**Exploratory:**
Exploratory analyses will be done on the other CEY outcomes. Exploratory analysis will also be conducted on transcripts from the qualitative interviews in order to learn more about participants' experiences during the study and with the COPE2Thrive intervention. Additional exploratory analyses will include: evaluation of differences in outcome in patients who maintain check-ins but discontinue C2T, vs. patients who only complete C2T, vs. patients who use both, real time qualitative information about how the program is used, stratification of screening results to distinguish between patients recruited from the community and from the clinic so that we can compare similarity and differences of referred vs. unreferred populations. At the present time of 41 patients approached, no eligible Tier 2 or 3 patients have enrolled. We will therefore look at the extent to which using the waitlist and using check ins increases interest in participation.

**T. Data/Biospecimen Banking**

**Include details, procedures, etc., related to data or biospecimen banking, as applicable.**

## APPENDIX I: VULNERABLE POPULATIONS

I. If the recruitment plan includes any of the groups below, explain how they will be protected and how consent/permission/assent will be obtained, as applicable. In general, Federal regulations allow subjects identified as part of vulnerable populations (*i.e.*, minors; pregnant women, neonates, & fetuses; and prisoners) to be included if the research involves only minimal risk to them, or if they will directly benefit.

The vulnerabilities of this population include that they are minors, and this is covered above.

II. Minors

A. Recruitment procedures are to be stated.

B. Assent/Permission

a. Procedures to be followed to obtain and document minor assent and parent/guardian permission are to be detailed, including who will have the discussions, when, where, etc. Submit, as applicable, minor assent forms, parent/guardian permission forms, scripts, handouts, etc. Details should include how a minor's understanding will be assessed and by whom, including the individual's qualifications to make such an assessment. Details related to documenting a minor's assent are to be stated (e.g., minor will write his/her name on an assent form, oral discussion will take place and be documented by designated study staff, etc.). NOTE: Mere failure to object to participation is not to be construed as assent.

C. Consideration and procedures are to be stated if the minor will attain age 18 years while in the study. Details should include what will happen to the data if a subject does not provide consent at age 18 years, or if the subject is lost to follow-up and does not provide consent at age 18 years.

III. Cognitively or decisionally impaired

This may include individuals with a psychiatric disorder, an organic impairment, a developmental disorder, and those suffering from a terminal illness, degenerative disease, severe physical handicap or dependence on drugs or alcohol. NOTE: In order to enroll subjects with impaired decision-making capacity the IRB must specifically grant approval for their enrollment. Such IRB approval will be documented in the IRB approval letter to the PI.

A. Assent/Permission

a. Procedures for obtaining the assent of a subject and the permission of his/her guardian/legally authorized representative (LAR) are to be stated, including who will have the discussion, when, where, etc. State how the LAR will be identified and detail how he/she will be approached about study enrollment.

Submit, as applicable, assent forms, LAR/guardian permission forms, scripts, handouts, etc. Details should include how a prospective subject's understanding will be assessed and by whom, including the individual's qualifications to make such an assessment. Details related to documenting a subject's assent are to be stated (e.g., subject will write his/her name on an assent form, oral discussion will take place and be documented by designated study staff, etc.). NOTE: Mere failure to object to participation is not to be construed as assent.

Detail who will give the LAR detailed and comprehensive information about the study and obtain and document their written permission. State the qualifications of the person(s) who will perform this study activity.

b. Details about whether a subject may regain cognitive or decision-making capacity, if applicable, and therefore be able to provide his/her own consent to study participation is to be addressed. Details should include how this will be

assessed, by whom, at what time points during the study, and what will happen to the data if the subject declines to provide his/her consent upon regaining cognitive or decision-making capacity.

IV. Students and/or Employees: To reduce potential coercion or interference with normal job duties, if students or employees are to be recruited as research subjects:

A. Include a letter from the Department Chair from which the students or employees are to be recruited indicating the Chair's review of the protocol and acknowledgement and understanding of the study, as well as his/her permission to recruit the students or employees.

B. If students from a public or private school system are to be recruited, the method of identification of and contact with the students must be explained. It will be necessary to obtain permission from the school's officials (*e.g.,* Superintendent) to conduct the research at a specific site (school). Minor assent and parent/guardian permission requirements, as above, are also necessary.