CLINICAL STUDY PROTOCOL

KIDS FACE FEARS PRAGMATIC TRIAL FOR CHILD ANXIETY

NCT03707158
H-37862
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Funder
PCORI

Protocol Version
December 22, 2020

Statistical Analysis Plan- pages 76-79

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Synopsis

Primary Objective • To compare the acute and longer-term effectiveness of Therapist-Led CBT (telehealth, office-based, or hybrid) versus Guided Online CBT (with minimal clinician involvement) for treating youth anxiety identified in pediatric healthcare.
Secondary Objectives The secondary objectives are: • To determine whether key factors predict or moderate differential treatment engagement or response, in turn informing treatment personalization for various patient subgroups • To explore quantitative and qualitative data to understand perspectives, preferences, background factors, clinical and treatment engagement variables, and organizational factors that impede or facilitate implementation of, and patient engagement with, the comparators in pediatric health settings.
Primary Outcome Variables • Youth anxiety symptoms - measured via the PROMIS Pediatric Short Form Item Bank v2.0-Anxiety. • Life interference - measured via the Child Anxiety Life Interference Scale; CALIS • Treatment Responder Status – measured via the Pediatric Anxiety Rating Scale; PARS • Family Perceived Effectiveness – measured via caregiver- and youth self-report • Treatment Satisfaction – measured via caregiver- and youth self-report
Secondary and Exploratory Outcome Variables Treatment engagement and barriers, broader youth psychopathology (i.e., internalizing problems, externalizing problems, and attention problems), youth sleep difficulties, caregiver internalizing symptoms (i.e., depression symptoms, anxiety symptoms, and stress symptoms), and therapist perceptions of treatment response. Other secondary analyses will examine predictors and moderators of differential outcomes, including: demographic factors, clinical factors, caregiver and youth attitudes, and language of care (English versus Spanish), among other factors.
Study Duration The study project has a duration of 5 years.
Study Design

The study design entails a large-scale, streamlined, pragmatic Randomized Controlled Trial (RCT), in which eligible anxious youth presenting to pediatric health care settings will be randomly assigned to receive therapist-led (telehealth, office-based, or hybrid care) versus guided online CBT for youth anxiety and monitored for up to 1 year.
Intervention Cognitive Behavior Therapy (CBT) is a well-supported standard of care for the treatment of anxiety in children and adolescents. This study is a pragmatic comparative effectiveness design comparing two modalities for administering CBT: Therapist-led CBT (telehealth, office-based, or hybrid care) vs. Guided Online CBT (with minimal therapist involvement).
Study Population We will include youth ages 7-18 years of age presenting to pediatric health care sites, including community health centers serving primarily low-income and traditionally underserved populations, affiliated with four major academic medical centers, each distinguished by renowned programs in behavioral health integration: Boston Medical Center in Boston, MA; Nicklaus Children's Hospital in Miami, FL; John's Hopkins Hospital in Baltimore, MD, and Seattle Children's Hospital in Seattle, WA.
Number of Participants We require 150 participants per treatment group, for a total of 300 participants.

Abbreviations

Abbreviation	Explanation
ADHD	Attention-deficit/hyperactivity disorder
AHRQ	Agency for Healthcare Research and Quality
BMC	Boston Medical Center
BUMC	Boston University Medical Campus
CALIS	Child Anxiety Life Interference Scale
CBT	Cognitive Behavioral Therapy
CCF	Center for Children and Families
CRF	Case Report Form
DE	Design Effect
FIML	Full information maximum likelihood
FISMA	Federal Information Security Management Act
FIU	Florida International University
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act

IRB	Institutional Review Board
KFF	Kids Formats of Anxiety Care Effectiveness study For Extending the Acceptability and Reach of Services
Kids FACE FEARS	Kids Formats of Anxiety Care Effectiveness study For Extending the Acceptability and Reach of Services
LAR	Legally authorized representatives
LR	Likelihood ratio
ML	Maximum likelihood
PCORI	Patient Centered Outcomes Research Institute
PRO	Patient Reported Outcome
RA	Research Assistant
RCT	Randomized Controlled Trial
RE-AIM	Reach, Effectiveness, Adoption, Implementation, Maintenance
REDCap	Research Electronic Data Capture
SD	Standard Deviation
SES	Socioeconomic status
SSRI	Selective Serotonin Reuptake Inhibitor

Table of Contents

1 - Introduction

1.1 Introductory Statement

This document is a protocol for a human research study, Kids FACE FEARS (**F**ormats of **A**nxiety **C**are **E**ffectiveness study **F**or **E**xtending the **A**cceptability and **R**each of **S**ervices). The purpose of this protocol is to ensure that this study is to be conducted according to PCORI guidelines, applicable government regulations, and participating institutional research policies and procedures. Each site will adhere to their institution's human subject research policy. This study protocol and statistical analysis plan details the trial's rationale, stakeholder partnerships, treatment conditions, participant recruitment, assessment schedule/strategy, provider training/consultation, and analytic plan.

1.2 Project Synopsis

Pediatric anxiety constitutes a serious public health concern. Cognitive-behavioral therapy (CBT) is a "gold standard" treatment, preferred by families over pharmacological options, but barriers limit CBT accessibility. Modern CBT formats include varying levels of therapist involvement and differential technologies to overcome barriers, but little is known about their effectiveness in typical care settings. The Kids Formats of Anxiety Care Effectiveness study For Extending the Acceptability and Reach of Services (Kids FACE FEARS) trial addresses these gaps. The Kids FACE FEARS trial (*N*~300 youth; ages 7-18 years) is a multisite, pragmatic randomized trial comparing Therapist-Led CBT (telehealth, office-based, or hybrid) versus Guided Online CBT (self-administered/self-paced, with minimal therapist support) for treating anxiety identified in pediatric care. English- and Spanish-speaking families are enrolled from high-volume, urban pediatric healthcare sites affiliated with major medical centers in four metropolitan regions. Children with elevated anxiety (and their families) are randomized to receive one of the two treatment comparators. Families participate in major assessments conducted at baseline, midtreatment, posttreatment, and one-year follow-up. Data for the study are drawn from caregiver-reports, youth self-reports, ratings of independent evaluators who are masked to treatment condition assignment), therapist-reports, and administrative logs. Exclusion criteria are minimal relative to other large-scale youth anxiety treatment trials. Treatment is provided by natural providers at the participating clinical settings (i.e., clinicians not employed by the Kids FACE FEARS investigative team, and not working in anxiety specialty settings).

Primary study aims focus on comparative effectiveness between the two treatment conditions on symptom severity, impairment, and patient-centered outcomes. Secondary aims focus on examining factors that predict heterogeneity of treatment response outcomes across youth (i.e., predictors and moderators), and exploring factors that impede or facilitate the treatment implementation and engagement.

2 – Background and Rationale

2.1 Pediatric anxiety and its sequelae constitute a very serious public health concern.

Anxiety disorders are the most common psychiatric problems affecting children and adolescents,[1–4] with one-fifth of the population meeting criteria for an anxiety disorder by the time they reach adulthood.[3] Pediatric anxiety is associated with considerable burdens including school absenteeism, academic underachievement, social difficulties, family dysfunction, somatic symptoms, and frequent medical visits.[5–8] When left untreated, pediatric anxiety often persists into adulthood and can worsen with time, increasing risk for substance use, psychiatric comorbidity, educational under-attainment, more medical visits, poor quality of life, lost wages and job productivity, suicidal thoughts and behaviors, and substantial costs to society.[9–15]

Pediatric anxiety rates have been rising across the past decade,[16–20] against a backdrop of increased political division and social unrest, widening disparities and inequities, potentially harmful social media impacts, rising climate concern, and a global pandemic with far-reaching ripples and hardships. In the United States (U.S.), minoritized status confers particular risk for anxiety, especially for youth of color, language-minority youth, and children of foreign-born caregivers.[21–25] At the same time, minoritized youth are often underrepresented in pediatric anxiety research.

2.2 Cognitive-Behavioral Therapy is Well-Supported in Treating Pediatric Anxiety.

Efficacious treatments for youth anxiety can decrease lifelong symptoms, functional burdens, costs, and the subsequent onset of comorbid problems (e.g., depression, substance use).26–30 Cognitive-behavioral therapy (CBT) is a “gold standard” psychological treatment for mild-to-moderate anxiety,31–34 and is preferred by families over pharmacological approaches.35 CBT is goal-directed, brief and time-limited, can be manualized and broadly disseminated, and is divided into two general phases: (1) skills building; and (2) exposure practice.

Dozens of large randomized trials indicate the majority of anxious youth are markedly improved after CBT, significantly outperforming waitlist, bibliotherapy, active support, and placebo comparators.31–33,36 In the landmark, multisite Child/Adolescent Anxiety Multimodal Study (CAMS),34 for example, 60% of youth treated with CBT were classified as treatment responders by independent evaluators (IEs), compared to 55% of youth treated with sertraline and only 23% of youth treated with placebo. For those with severe anxiety, a combination approach of CBT plus sertraline (associated with an 80% responder rate) was required for response,37 although medication approaches introduce side effect concerns for families to consider. More recent work has also called into question whether added benefits observed from multimodal treatment reflect true medication augmentation effects or simply a placebo effect added to existing CBT gains.

2.3 Treatment Gaps: Problems in the Availability, Accessibility, and Acceptability of CBT for Pediatric Anxiety.

Despite the demonstrated efficacy of CBT for youth anxiety, up to 80% of anxious children do not seek or receive help.[3] Among individuals with anxiety disorders who do receive treatment, the median delay from disorder onset to time of initial treatment contact ranges from 9-23 years.[38] Such failures and delays in treatment utilization underscore major problems in the availability, accessibility, and acceptability of care. Several barriers interfere with the receipt of needed care for anxious youth. For many families, traditional office-based care presents transportation obstacles, time demands that compete with work needs, childcare coordination challenges, and prohibitive costs and co-payments [39]. The relative unavailability of services in non-English languages causes linguistic disparities,[40] and institutional mistrust and stigma associated with visiting a mental health clinic place traditional office-based care out of reach for many families.[41,42] Moreover, for several years the COVID-19 pandemic and associated stay-at-home guidelines shut down the majority of office-based services.

2.4 Service barriers disproportionately affect youth from minoritized communities.

Thus, it is not surprising that anxious youth from such communities are particularly underserved. For example, anxious youth of color and in families with resource insecurity are significantly less likely to receive anxiety services than non-Hispanic White youth[43,44] and youth from resource-secure households.[44,45] Also, anxious youth in immigrant households and in non-English-speaking households use mental health services less than anxious children of U.S.-born caregivers and English-speaking households.[46]

2.5 Technology-Based Strategies Have Shown Promise for Improving Access to Care.

Technology-based strategies for extending the delivery of CBT to anxious youth have been supported in the literature[47–58] and show promise for meaningfully overcoming treatment barriers. Research documents rapidly rising rates of household Internet availability in the U.S., with 97% of people below the age of 65 years now reporting regular Internet use, and 85% of people below the age of 65 years having household Internet access.[59] Racial/ethnic- and income-related disparities in Internet access persist, particularly when considering household and mobile Internet access, although 91% of Black people and 86% of people earning less than $30,000/year nonetheless report regular Internet usage.[59] Work remains for continuing to expand Internet access, but these latest Internet use data speak to the considerable potential Internet-delivered CBT formats hold for broadening the reach of supported care. Two leading Internet-delivered approaches for extending CBT availability are (1) telehealth and hybrid care, and (2) guided online care.

Telehealth and Hybrid Care. Telehealth formats and hybrid options (i.e., mix of telehealth and office-based care) leverage synchronous telecommunications (typically videoconferencing) for the remote provision of live and interactive therapist-led care. Telehealth has been increasingly studied[47–50] as a means to overcome logistical challenges to traditional brick-and-mortar CBT for youth anxiety and stigma about attending a mental health facility. Research in controlled settings and specialty clinics finds that telehealth options for a range of child mental health challenges can produce gains comparable to traditional office-based CBT.[47–50,60–62] In some trials, telehealth has even outperformed traditional office-based care on key outcomes,[61] likely due to the improved ecological validity afforded in telehealth by treating families in their natural spaces. Furthermore, relative to traditional office-based care, telehealth is associated with significantly reduced caregiver-perceived barriers to care[61] and significantly improved session attendance, particularly for racial and ethnic minoritized youth.[63] After years of research, telehealth entered the clinical mainstream during the COVID-19 pandemic,[64–66] during which time it temporarily became the dominant mode of outpatient mental health care. In post-pandemic times, telehealth still plays a prominent (albeit understudied) role in youth mental health care.

Guided Online Care. Guided online care (i.e., self-administered/self-paced, with minimal therapist support) offers a computerized CBT delivery format that reduces therapist demands relative to both office-based care and telehealth, while also affording greater family flexibility, agency, and control. As such, guided online care addresses many of the same logistical care barriers as telehealth, but can also address person-power issues in the mental health workforce, inconsistencies in care quality across practice settings, cost issues, and, for some families, issues of mistrust about working directly with a healthcare professional. Accordingly, self-administered online CBT may in some cases be the preferred treatment mode. CBT lends itself well to standardization to reduce drift and digitization due to its highly structured nature, and digital delivery may be particularly well-suited to youth and younger families who avidly engage with media and technology. That said, attrition can be high in self-administered online care. Increasing studies find some level of minimal/low-intensity human support is often needed to accompany self-administered online CBT—i.e., guided online CBT—to sustain patient motivation, promote adherence, and prevent disengagement.[67,68] Several very strong self-paced, computerized CBT programs have been developed for the treatment of youth anxiety and controlled trials have shown many of these programs can produce sizeable treatment gains, particularly when administered with some level of guided support.[51–58]

2.6 Gaps Persist in Understanding How Various Pediatric Anxiety Treatment Formats Perform and Compare in Typical Care Settings.

Despite great promise in the use of technology-based strategies relying on varying levels of therapist involvement to expand the reach of CBT for pediatric anxiety, much remains to be learned about how such modernized CBT formats perform in typical care settings. Similarly, little

is known about what factors may facilitate versus challenge successful engagement with these modernized CBT formats in usual care settings, and whether specific subpopulations of anxious youth may differentially benefit from these options. With regard to telehealth and hybrid strategies for pediatric anxiety, most support has come from small-scaled trials conducted in tightly controlled contexts and anxiety specialty clinics with highly selected samples and research therapists. Such work cannot speak to telehealth effectiveness or hybrid treatment under typical care circumstances and is underpowered to examine predictors of differential telehealth response. With regard to guided online CBT for pediatric anxiety, research to date has been conducted with predominantly non-Hispanic White and English-speaking samples, and most of the trials have been implemented in anxiety-specialty clinics and/or research settings. Evaluating the effectiveness of guided online CBT in diverse populations under usual care conditions is critical for understanding the extent to which this format can truly expand the accessibility and acceptability of care and reach underserved populations. Further, clinical trials of guided online CBT have not included a therapist-led treatment comparison, rendering it hard to make informed comparisons across treatment formats and precluding an understanding of which CBT formats for pediatric anxiety work best for whom.

3 - Rationale/Significance

3.1 Problem Statement

Most children with anxiety do not receive treatment for many reasons, including lack of therapists, stigma, getting to appointments, and time-commitment. Online delivery of CBT can lead to meaningful improvements in child anxiety and could make CBT available for more families (Morgan et al., 2017). Providing these treatments in community pediatrics practices could help even more children, particularly lower income and minority families who may not seek care elsewhere. Despite increasing support and uptake of face-to-face and online formats of CBT, to date no study has directly compared face-to-face and online CBT delivery methods in pediatric settings with predominantly low income and minority families, nor has research evaluated whether these two formats may differentially work better for certain patients or scenarios.

The project outlined in this protocol responds to PCORI's (Patient Centered Outcomes Research Institute) Special Area of Emphasis on digital health interventions for treating anxiety in children and adolescents at risk of reduced access to care, including immigrant, racial/ethnic minority, and low-income patients. This protocol also addresses the AHRQ (Agency for Healthcare Research and Quality) future research needs for the integration of mental health/substance use treatment in primary care.

3.2 Purpose of Study/Potential Impact

This study addresses three critical yet unanswered questions related to improving the delivery of CBT and treatment outcomes for anxiety in pediatric health settings. Answering the following question offers the potential to meaningfully improve the quality of the evidence available to help children, families, and organizational stakeholders make informed decisions regarding clinical practice and implementation strategies for the treatment of childhood anxiety:

(1) What is the comparative effectiveness of implementing therapist-led (telehealth, office-based, or hybrid) versus guided online formats of CBT to treat youth anxiety identified in pediatric health care settings?

(2) Which factors might moderate outcomes across treatment formats and sequences? Which patient subgroups might benefit most from each of the treatment formats?

(3) What are the barriers and facilitators to delivering this care in pediatric health care settings and for the diverse patient populations served?

Both the effectiveness and implementation questions are relevant to advancing strategies for addressing anxiety in pediatric health care and optimizing patients' and families' access to, options for, and quality of anxiety treatment. In recent years there has been a surge of interest in online treatment delivery formats that offer more accessible, flexible, and efficient care with the potential to reach a greater portion of the population in need.

3.3.1 Potential Benefits

Families enrolled in the study would benefit from:

- Receiving evidence-based treatment for youth anxiety
- Parents or guardians receiving education on anxiety and how they can help manage their child's anxiety through an evidence-based program
- Receiving support from a trained professional over the phone (if they are randomized to the guided online format)
- Having access to a convenient evidence-based self-administered CBT program online (if randomized to the online format) that would not be offered outside of the study

Therapists and program staff enrolled in the study would benefit from:

- Assisting participating families with access to child behavioral health services
- Learning a new framework for delivering CBT
- Providing valuable information to primary care practices and integrated health networks about the potential benefits and barriers to implementing these interventions for children with anxiety
- Providing evidence-based information to support patient and provider decision making and patient centered care

3.3.2 Potential Risks

Potential risks to patient participants are psychological and the need to protect confidentiality:

- Because the research covers the topic of mental health and potential psychosocial stressors, participation may be emotionally distressing to individuals in the study.
- Although we will strive to maximize cultural sensitivity in delivery of the proposed intervention, it is possible that, among guardians, their explanatory models of their child's condition will be incompatible with our proposed interventions and even the assessments, which may upset some participants.

- Although data will be stored in a secure and confidential manner, and we will code all stored data and store it separate from any direct participant identifiers, accidental breaches of confidentiality are technically possible.

Potential risks for staff participants are the need to protect confidentiality:

- Although data will be stored in a secure and confidential manner, and we will code all stored data and store it separate from any direct participant identifiers, accidental breaches of confidentiality are technically possible.
- Because the research involves feedback about the study and the clinic's ability to implement mental health care, staff participants may be concerned or distressed about how this may impact their employment. Their responses will be kept confidential and will not be shared with their employer.

The primary risk for study participants is breach of confidentiality. We have taken measures to ensure the safety and security of all data and participant information which is outlined in the data storage/ security section of this protocol.

4 - Study Objectives and Aims

Building on the strong evidence supporting CBT for the treatment of mild-to-moderate pediatric anxiety, the present multisite trial was designed to examine the comparative effectiveness of modernized CBT delivery formats that have shown initial promise for expanding the reach of care. Specifically, the Kids FACE FEARS trial (Kids Formats of Anxiety Care Effectiveness Study For Extending the Acceptability and Reach of Services) is a type 1 hybrid effectiveness and implementation pragmatic study designed to compare Therapist-Led CBT (telehealth, office-based, or hybrid) versus Guided Online CBT (with minimal therapist support) in usual care settings for the treatment of pediatric anxiety.

Table 1, below, presents the specific aims and objectives of the Kids FACE FEARS trial.

Table 1. Specific Aims of the Kids FACE FEARS Trial

Aim	Domain	Objective
Aim I	Comparative Effectiveness	To compare the acute and longer-term effectiveness of Therapist-Led CBT (telehealth, office-based, or hybrid) versus Guided Online CBT (with minimal clinician involvement) for treating youth anxiety identified in pediatric healthcare.
Aim II	Heterogeneity of Treatment Effects	To determine whether key factors predict or moderate differential treatment engagement or response, in turn informing treatment personalization for various patient subgroups.
Aim III	Implementation Facilitators and Barriers	To explore quantitative and qualitative data to understand perspectives, preferences, background factors, clinical and treatment engagement variables, and organizational factors that impede or facilitate implementation of, and patient engagement with, the comparators in pediatric health settings.

Note: Kids FACE FEARS=Kids Formats of Anxiety Care Effectiveness study For Extending the Acceptability and Reach of Services

4.1 Primary Objective

The objective of Aim 1 (*Comparative Effectiveness*) is to compare the acute and long-term effectiveness of Therapist-Led CBT (telehealth, office-based, or hybrid) vs Guided Online CBT (with minimal clinician support) for treating youth anxiety identified in pediatric healthcare. It is hypothesized that youth in both conditions would show significant curvilinear improvements over time characterized by relatively steep improvements during the beginning and middle of the treatment phase, followed by a slowing down of improvements toward the end of treatment and then relative stability across the follow-up time interval. Comparative effectiveness analyses will

compare differences in outcome slopes across the two conditions. Aim 1 focuses on the following primary treatment outcomes across the comparators: family-rated anxiety severity, family-rated anxiety-related life impairment, independently rated treatment responder and anxiety remission status, family perceived effectiveness, and family satisfaction with care. Data on a range of secondary outcomes are also collected.

4.2 Secondary Objectives

The objective of Aim 2 (*Heterogeneity of Treatment Effects*) is to determine whether key factors predict or moderate differential treatment engagement or response, in turn informing treatment personalization for various patient subgroups. To understand heterogeneity in treatment response across youth, moderating factors examined include: demographic factors, clinical factors, caregiver and youth attitudes, and language of care (English versus Spanish). Additional factors are also assessed to afford further tests of predictors and moderators of treatment response.

Aim 3 (*Implementation Facilitators and Barriers*) is exploratory, with the objective to understand perspectives, preferences, background factors, clinical and treatment engagement variables, and organizational factors that facilitate or impede implementation of, and patient engagement with, the comparators in routine pediatric health settings.

5 – Engagement and Partnerships with Patients, Other Stakeholders, and Scientific Advisors

Throughout all stages of the Kids FACE FEARS trial, investigators are engaged in collaborations with patient, parent, and community stakeholders who have experience (themselves or loved ones) with mental health challenges such as anxiety, as well as with treatment providers, clinical supervisors, and program administrators who are responsible for providing care to families. Investigators also engage with a Study Advisory Committee comprised of members dedicated to improving access to evidence-based treatment, and a Data Safety and Monitoring Board to further ensure patient safety and protection. These mutual partnerships with stakeholder groups meaningfully inform each aspect of the study design, implementation, and dissemination, as described below.

Patient Family Advisory Council (PFAC). The Kids FACE FEARS Patient Family Advisory Council (PFAC) is made up of 22 members (16 parents and 7 adolescents) with lived experience (personal or family) with youth anxiety and its treatment. PFAC members were identified and recruited through patient advisory boards at participating clinical sites in all four study regions, extended patient networks of hospital systems, clinical networks of study team members, and through study team member connections with patients and families with anxiety in their communities. Throughout study design, implementation, and analysis, the PFAC will convene regularly in person and on group videoconferencing calls to ensure that patient/family perspectives are fully integrated into all aspects of the study and that research activities are aligned with patient/family needs. PFAC meetings will be held throughout the study. Separate meetings will be held in English and Spanish. For each set of meetings, separate one-hour sessions are held with an English-speaking Youth Council, an English-speaking Caregiver Council, and a Spanish-speaking Youth/Caregiver Council. Bilingual youth can chose whether to be in the English-speaking Youth Council or the Spanish-speaking Youth/Caregiver Council. Meetings will occur quarterly during the first three years of the study, bi-annually during the fourth year of the study, annually during the fifth year of the study, and twice during the data analysis/interpretation phase of the study. Each PFAC meeting is structured as followed: 1) an overview of the meeting agenda, 2) a review of study progress and updates (including study changes based on PFAC feedback), 3) a presentation of current study tasks/goals 4) introduction of specific questions/prompts for discussion, 5) division into breakout groups to facilitate small group discussion and brainstorming, and 6) full-group discussion and closure. Prior to the COVID-19 pandemic, PFAC meetings were held in a hybrid format, with all regions convening together on Zoom, and in-person break-out groups convening within study regions prior to a final all-region discussion on Zoom. After the pandemic began, all PFAC meetings are held entirely on Zoom, with virtual breakout rooms used for small group discussions. To further facilitate virtual engagement, brainstorming, and interaction among group members, study staff will utilize collaborative digital tools (e.g., Zoom reaction features, screensharing, a collaborative

digital whiteboard via Google Jamboard). PFAC members will help with study planning and provide input throughout about participant recruitment and project implementation. PFAC co-investigators will assist in creating research poster presentations for professional conferences and will be invited to collaborate on major scholarly papers for the project. PFAC members will also provide suggestions about ways to effectively disseminate findings to study participants and to the public.

Treatment Providers and Clinical Supervisors. Natural providers in participating pediatric health settings (i.e., clinicians not employed by the Kids FACE FEARS investigative team, and not working in anxiety specialty settings) serve as the treatment providers in the Kids FACE FEARS trial. These providers also provide stakeholder input and collaboration, along with clinical supervisors and clinic staff at the participating settings. Their participation and feedback helps the investigative team refine training and implementation efforts and contribute to an improved understanding of barriers and facilitators to implementing the treatment comparators in usual care settings. Therapists and clinical supervisors from across the four participating pediatric health networks will be trained by the study team to deliver best-practices CBT for youth anxiety. Clinicians and supervisors at the participating sites will engage in full-day training and then receive bi-weekly, small group consultation through videoconferencing calls led by a pediatric anxiety treatment expert (see Procedures) throughout the study. Therapists and clinical supervisors will provide quantitative and qualitative feedback about the training and consultation model and overall effectiveness via questionnaires about their CBT knowledge pre- and post-training, through quantitative ratings and qualitative feedback, questionnaires about their comfort with technology and the organizational climate of their professional setting, and through therapist session forms and posttreatment logs. Clinicians and supervisors provided further information about successes and challenges in delivering the CBT comparators during bi-monthly consultation calls led by an expert in child anxiety treatment. These calls will be used to clarify therapy skills, promote sustained learning and prevent drift, support therapists, and gain feedback from clinicians about their experiences implementing the treatment.

Study Advisory Committee (SAC). The Study Advisory Committee (SAC) consists of 14 nationally known researchers and other clinical professionals (e.g., psychiatrists, psychologists, pediatricians, clinical social workers, child health service researchers, primary care physicians, medical directors) committed to clinical research to improve access to evidence-based treatments for underserved youth. The SAC includes a scientific steering committee with considerable collective expertise in pediatric mental health, digital mental health, working with minoritized youth, leading large multisite randomized clinical trials, and overseeing prior PCORI-funded projects. The SAC will meet roughly twice annually with the investigators via videoconferencing across the planning, recruitment, implementation, and analysis phases of the study. These meetings will afford a structured opportunity to provide external advisory support

and input on project design and implementation, as well as navigation of various challenges as they arise, including those introduced by the COVID-19 pandemic.

Data Safety and Monitoring Board (DSMB). Data Safety and Monitoring Board (DSMB) members will have considerable collective experience in the conduct of clinical and developmental research with youth, the conduct of clinical trials, and working with diverse families. They will be involved to externally assess the protection of data and participant confidentiality, and help ensure the trial is conducted according to high scientific and ethical standards. The DSMB is responsible for safeguarding the interests of study participants, assessing the safety and efficacy of study procedures, and monitoring the overall conduct of the study. The DSMB will meet via videoconferencing about twice yearly to provide independent oversight of data management and integrity and participant safety. DSMB members will include a clinical child psychologist with experience conducting federally funded clinical trials and experience serving on university Institutional Review Boards (IRB) and DSMBs, and a child/developmental psychologist with extensive experience conducting applied research with diverse families.

6 - Study Design

6.1 General Design Overview

The KFF trial is a multisite, pragmatic, randomized clinical trial (RCT) comparing the effectiveness of Therapist-Led CBT (telehealth, office-based, or hybrid) versus Guided Online CBT (with minimal therapist support) for the treatment of elevated youth anxiety identified in pediatric health care settings. Families are enrolled from high-volume, urban pediatric health care sites affiliated with major medical centers in four U.S. cities: Baltimore, MD, Boston, MA, Miami, FL, and Seattle, WA. Universal screening of English- and Spanish-speaking youth receiving primary or secondary pediatric health care in these hospital networks will identify potentially eligible youth with elevated anxiety who, if interested, are referred to behavioral health teams in their hospital system for potential study participation. Elevated youth anxiety is required for eligibility; to maximize generalizability a formal anxiety disorder diagnosis is not required. Eligible and interested families are randomly assigned to one of the two treatment comparators and given up to 20 weeks to complete their allocated treatment. All services and assessments are provided in English and in Spanish, as needed. Major assessments are conducted at baseline, midtreatment, posttreatment, and roughly one-year follow-up.

To maximize generalizability, exclusion criteria are minimal compared to previous large-scale RCTs of youth anxiety treatment.[34] To observe treatment comparators under natural circumstances in general pediatric health care settings, study treatment is incorporated into the natural flow of care at each participating site (e.g., clinical care is not funded by the study grant, research therapists are not being used, anxiety specialty clinics are not involved in clinical care). Natural therapists at the participating clinical settings will complete training led by youth anxiety treatment experts, and then participate in biweekly consultation calls.

Institutional review boards (IRBs) at each participating site approved and oversaw the human subjects research aspects of the study, with Boston Medical Center's IRB serving as the primary ethics review board for the trial. The trial is pre-registered (ClinicalTrials.gov ID: NCT03707158).

6.1.1 Study Setting

This multisite comparative effectiveness trial is being conducted at high-volume, urban pediatric health care sites affiliated with four major medical centers (Johns Hopkins Hospital in Baltimore MD, Boston Medical Center in Boston MA, Nicklaus Children's Hospital in Miami FL, Seattle Children's Hospital in Seattle WA). These sites were selected as clinical performance partners due to their roles in serving large numbers of diverse pediatric patients and providing a high volume of services in English and in Spanish, their collective representativeness of under-resourced pediatric health settings that serve diverse populations from a range of socioeconomic backgrounds, and for the advantages offered in studying the treatment comparators in the context of academic hospital-community health center partnerships. For

example, Boston Medical Center is the largest safety net hospital in New England with a large affiliated network of community health centers. Nicklaus Children's Hospital is home to the largest pediatric teaching program in the Southeastern United States and the majority of its patient population is Hispanic/Latine, reflecting the demographics of the South FL community.

6.2 Outcomes

6.2.1 Primary Outcome Variables. The primary clinical outcomes assessed in the Kids FACE FEARS trial are focused on anxiety symptoms, anxiety-related impairment, treatment responder status, anxiety remission status, and patient-centered outcomes focused on perceived effectiveness and treatment satisfaction. Specifically, these include:

- Youth anxiety symptoms - measured via the PROMIS Pediatric Short Form Item Bank v2.0-Anxiety. The PROMIS pediatric self-report will be completed by children ages 8-18 and parent proxy reports will be complete by guardians for all children. Only parent proxy reports will be collected for children under the age of 8.
- Life interference - measured via the Child Anxiety Life Interference Scale; CALIS
- Treatment Responder Status – measured via the Pediatric Anxiety Rating Scale; PARS
- Family Perceived Effectiveness – measured via caregiver- and youth self-report
- Treatment Satisfaction – measured via caregiver- and youth self-report

6.2.2 Secondary and Exploratory Outcome Variables. Secondary clinical outcomes assessed in the Kids FACE FEARS trial focus on treatment engagement and barriers, broader youth psychopathology (i.e., internalizing problems, externalizing problems, and attention problems), youth sleep difficulties, caregiver internalizing symptoms (i.e., depression symptoms, anxiety symptoms, and stress symptoms), and therapist perceptions of treatment response. Specifically, these include:

- Treatment engagement and barriers – measured via administrative logs, therapist reports, and family reports of: Attendance, Homework engagement, Treatment completion, Child participatory engagement, Caregiver participatory engagement, Comprehension difficulties, Difficulties making time for treatment, Treatment discomfort, Technology treatment challenges, and Therapeutic alliance.
- Youth internalizing problems - measured via the Pediatric Symptom Checklist; PSC-17
- Youth externalizing problems - measured via the Pediatric Symptom Checklist; PSC-17
- Youth attention problems - measured via the Pediatric Symptom Checklist; PSC-17
- Youth sleep problems - measured via a sleep item generated for this study
- Caregiver depression symptoms – measured via the Depression, Anxiety, Stress Scale; DASS-21

- Caregiver anxiety symptoms – measured via the Depression, Anxiety, Stress Scale; DASS-21
- Caregiver stress symptoms – measured via the Depression, Anxiety, Stress Scale; DASS-21
- Therapist-perceived effectiveness – measured via items generated for this study

Other secondary outcomes incorporate a series of a moderator analyses to elucidate heterogeneity of treatment effects across formats among important subgroups of patients. On this front, we will examine: Patient characteristics, Family characteristics, Provider characteristics, and Organizational and system characteristics

6.3 Study Population

6.3.1 Number of Participants. Power analysis (accounting for an expected attrition and missing data) indicated we require 150 participants per group, for a total of 300 participants in the study.

6.3.2 Eligibility Criteria. The study eligibility and inclusion, and exclusion criteria for families include:

Inclusion/ Eligibility

- Elevated child/adolescent anxiety - Operationalized as T-Score on the PROMIS Pediatric Short Form-Anxiety Scale v2.0 $\geq$ 55 (Child eligible if *either* the Pediatric Self-Report *or* the Parent Proxy Report score was $\geq$ 55)
- Child aged 7-18 years (inclusive) at time of screening
- Child and caregiver(s) are fluent in English or Spanish
- If taking medication for emotional problems, child must be on a stable dose (Operationalized as no adjustments to prescription for $\geq$ 8 weeks)

Exclusion Criteria

- Severity requiring higher level of care, as defined by any of the following:
  - Suicidal thoughts or behaviors (STB) with *active* plan or STB(s) that required a higher level of care within the past 6 months (e.g., inpatient, partial hospitalization)
  - Anxiety-related absences $\geq$ 50% of school days over the past month (If summer, attendance during last month of previous school year considered)
  - Substance use that required emergency services or inpatient/partial hospitalization within past 3 months

    - Clinician determined child requires higher level of care than outpatient services
- History of diagnosed autism spectrum disorder or intellectual disability with severe challenges and needs for support (e.g., complete absence of verbal communication unrelated to anxiety)
- Currently engaged in CBT or planning to continue different therapy for anxiety during study treatment phase
- Child is a ward of the state

The decision to include families fluent in either English *or* Spanish was made to (a) improve the generalizability of trial findings, relative to existing research on the treatment of youth anxiety; (b) recruit a sample that would be more representative of the general U.S. population and the diverse range of anxious youth seen in clinical practice; and (c) provide treatment-related findings that would also be informative to the estimated 33.3% of mental health treatment facilities that provide services in Spanish.[81] Currently, it is estimated that over 41 million people in the U.S. speak Spanish, and with migration patterns, this number is rising. Many single-site trials evaluating treatment for youth anxiety have offered intervention in English and in Spanish,[50,82–85] but large multisite trials conducted to date on youth anxiety treatment have restricted eligibility to just English-speaking families. Accordingly, the Kids FACE FEARS trial offers a rare large-scale examination of treatment for pediatric anxiety that is more broadly generalizable to the >90% of U.S. households that speak either English or Spanish.

Several factors informed the decision to not consider formal DSM or ICD diagnoses as part of study inclusion or exclusion. Eligibility criteria were intentionally relaxed relative to previous large-scale trials[e.g.,34] to better approximate the full range of anxious youth in need of care. Inclusion criteria for this trial requires youth to have elevated anxiety levels, but does not require formal anxiety disorder diagnoses, given the high number of anxious individuals in need of care who miss diagnostic thresholds by DSM or ICD technicalities,[86,87] especially in medical populations.[88–90] Further, comorbid diagnoses do not preclude eligibility in the Kids FACE FEARS trial (as long as they do not acutely require a higher level of care such as inpatient or partial hospitalization), given research showing such requirements can exclude up to half of children seeking care from research trials.[91] By relaxing eligibility criteria in these ways, the Kids FACE FEARS trial can be thought to generalize broadly to the common range of anxious youth and their families who typically present for care, rather than to just “pure” diagnostic groups of youth with anxiety disorders who are represented in narrower efficacy trials. The decision to not consider DSM or ICD diagnoses as part of study eligibility is consistent with concerns about the poor reliability and differentiation of pediatric anxiety disorder diagnoses,[92–95] and associated trends in clinical science priorities moving away from formal diagnoses.[96,97] Moreover, there is evidence that clinicians rarely use structured diagnostic interviews outside of research contexts,[98] rendering findings based on structured diagnostic interviews poorly aligned for informing clinical practice. Finally, not including structured research-based diagnostic interviews

in the trial's assessment protocol addresses the need to minimize participant burdens and assessment demands in a pragmatic effectiveness trial. Reducing the assessment time that is focused on diagnostic nuances also affords opportunity to instead assess several important factors that have previously been neglected in large-scale clinical trials for the treatment of child anxiety (e.g., adverse childhood events, experiences of discrimination, mental health stigma; see Measures, below).

6.4 Therapist Participants

Existing therapists from across the four participating pediatric health networks will participate. Therapists will be natural providers in the pediatric health settings participating in the trial (i.e., clinical staff not employed by the research trial and not working in anxiety specialty settings). We estimate around 50-60 therapists will participate in the study. They will consent to be in the study as participants before their on-site training for the Cool Kids Program. The study eligibility and inclusion criteria for therapists and program staff include:

Inclusion/ Eligibility

- Currently employed as therapist or staff at participating pediatric health care sites
- Agreed to participate in study and collect data on their patient for study purposes

Exclusion

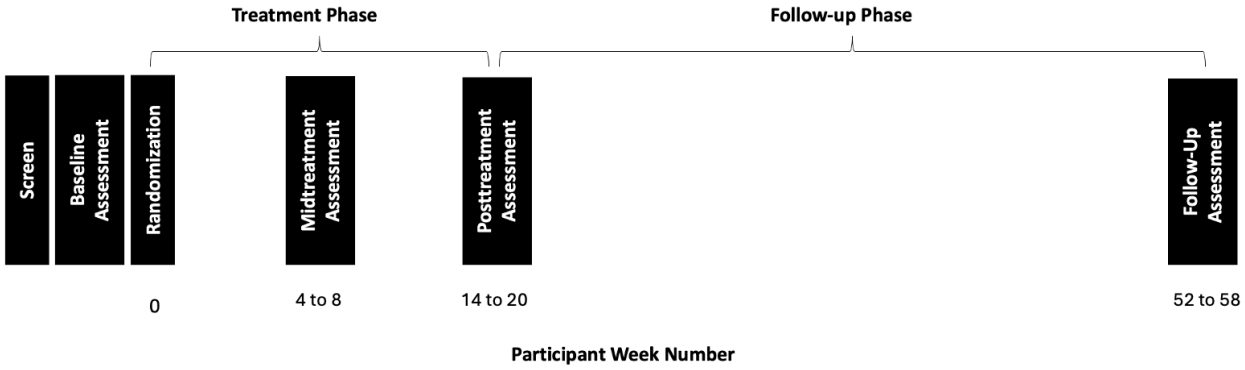
- Has not completed the Cool Kids program training

7 - Methods

7.1 Participation Flow

Figure 1 presents the study timeline for participating families. Following initial screening and consent, families complete baseline assessment (Week 0) and eligible participants are then randomized to one of the two treatment comparators. Participants are granted up to 20 weeks to complete their allocated treatment program. The decision to allow a 20-week treatment window was informed by PFAC and stakeholder input urging that an appropriate and realistic timeframe for treatment would be one that allows for periodic missed sessions, holiday breaks, health-related cancellations, and attendance-interfering life events. All randomized families are invited to complete a midtreatment assessment once they complete half of their allocated treatment. Families who do not complete half of their allocated treatment by the end of the second month of their treatment phase are invited to complete a midtreatment assessment at Week 8. All randomized families are invited to complete a posttreatment assessment once they fully complete their allocated treatment program. Families who do not complete their allocated treatment program by the end of the fifth month of their treatment phase are invited to complete a posttreatment assessment at Week 20. All randomized families are invited to complete a follow-up assessment at Week 52.

Figure 1.



Note: Week numbers reflect target number of weeks since baseline that participants in the Kids FACE FEARS Trial will complete assessments at each timepoint.

7.2 Description of Interventions/Comparators

We are testing two delivery strategies of CBT for youth anxiety disorders. CBT is the “gold standard” for the treatment of anxiety and is currently used as the standard of care by therapists at all our participating sites. This research does not change the current standard of care used by our sites – it expands the mode used to deliver standard of care by providing therapists training on the evidence-based Cool Kids framework (i.e. a standardized version of CBT).

Specifically, the Kids FACE FEARS trial tested two CBT delivery strategies for pediatric anxiety: (1) Therapist-Led CBT (telehealth, office-based, or hybrid), and (2) Guided Online CBT (with minimal therapist support).

Comparator 1: Therapist-Led CBT for Youth Anxiety (telehealth, office-based, or hybrid). An extensive body of controlled studies supports Therapist-Led CBT for anxious youth and their families, with therapist-led CBT conventionally considered a "gold standard" psychological treatment for anxious youth.[31–34] Therapist-Led CBT has traditionally entailed office-based care in which a therapist directly trains youth (and often caregivers) in anxiety management skills then guides children in planning and participating in graded exposure tasks in which they approach increasingly feared situations. In the landmark Child/Adolescent Anxiety Multimodal Study (CAMS) trial, roughly 60% of youth treated with therapist-led CBT classified as "treatment responders" by masked IEs.[34] In more recent years, telehealth formats of Therapist-Led CBT for youth anxiety have received considerable and comparable research support.[47–50]

Although a number of established and highly overlapping Therapist-Led CBTs for youth anxiety exist, the well-supported *Cool Kids* CBT suite for youth anxiety[99,100] was selected for several important reasons. First, *Cool Kids* includes all the "gold standard" CBT components for treating youth anxiety and has an extensive research base.[101–103] Second, *Cool Kids* is a time-limited and relatively brief suite of treatment programs delivered across roughly 3 months, which accommodated the PFAC and stakeholder advisor suggestion for relatively short-term treatment. Third, the *Cool Kids* suite of treatment programs comprehensively includes developmentally tailored versions for the full age range of youth included in the study (7-18 years). Fourth, the *Cool Kids* treatment suite has a documented history of successful implementation when rolled out on large-scale levels.[103,104] Fifth, a parallel self-administered online version of *Cool Kids* teaches youth the same anxiety management skills as the therapist-led version, and in a roughly comparable number of sessions/modules, thus allowing for well-matched and time-equitable comparisons. And finally, the *Cool Kids* therapist-led and online treatment programs are all available in English and in Spanish.

The standard *Therapist-Led Cool Kids Therapy for Anxiety (ages 7-12)*[99] is a structured, evidence-based, 10-session program for treating youth anxiety in middle childhood and entails ten 50-minute weekly sessions with children and families. Therapists teach youth and caregivers core CBT components including anxiety psychoeducation, cognitive/coping skills for thinking more realistically and adaptively, problem-solving skills, and graded exposures to anxiety provoking situations. Caregivers and youth are taught skills for managing anxiety and for reducing avoidant behaviors. Caregivers are included in all sessions (adjusted developmentally) and are taught parenting skills plus personal anxiety management. The program is supported by

a structured therapist manual and with developmentally tailored child and parent workbooks. *Cool Kids* is available in many languages, including English and Spanish, and has been adapted slightly for different age groups. The *Therapist-Led Chilled Therapy for Anxiety (ages 13-18 years)* is an adolescent version of *Cool Kids* and includes a workbook geared specifically for adolescents; in this version teens take a more central role in managing their anxiety, and caregivers do not participate in all of the sessions. This version also includes ten sessions.

Comparator 2: Guided Online CBT for Youth Anxiety (With Minimal Therapist Support). To expand the accessibility and reach of CBT for anxious youth, a suite of self-paced, online, multimedia, CBT-based programs for youth anxiety was developed to run parallel to the therapist-led *Cool Kids* program. This online suite of programs covers identical content in a largely self-administered format. Similar to Therapist-Led *Cool Kids*, the *Cool Kids Online* suite of programs is comprised of separate developmentally tailored online programs, two of which were used in the present trial, depending on the age of the child: (1) "Cool Kids Online" for ages 7-12 years, and (2) "Chilled Out" for youth ages 13-18. [54,105,106] These programs consist of 8 modules that are to be completed on a roughly weekly basis allowing for well-matched and time-equitable comparisons to the Therapist-Led CBT comparator. The online programs have already been used in numerous countries and are available in multiple languages, including Spanish. The programs include the same core CBT components as the Therapist-Led *Cool Kids* programs, feature interactive, engaging formats, and include video and audio clip examples of how to implement skills. In Cool Kids Online, caregivers take on the role of their child's coach, helping them put their skills into practice, and learn helpful ways of responding to their child's anxiety. In the Chilled Out adolescent online version, the teen takes primary responsibility for program completion, and there are features designed to specifically increase teen engagement—e.g., there are real teens featured in the videos, teens demonstrate skills for managing anxiety, and there is a "playlist" menu where teens can choose to re-visit content and cover skills at their own pace. The programs were originally developed in Australia. For both Cool Kids Online and Chilled Out, "Americanized" versions of the programs were used that include videos with diverse representation (e.g., American children, families, and experts; broader representation of individuals of color; removed Australian accents or vernacular).

To foster supportive accountability and engagement,[67,68] families in this condition receive brief phone check-in calls (i.e., < 15 minutes) from a therapist every other week. To ensure these brief calls do not drift into treatment sessions, therapists work from a conversation guideline to standardize calls (with space for flexibility as appropriate). Therapists should begin each check-in call with an explanation of the purpose of the call—i.e., to see how their use of the online modules is going, to find out whether the child/teen/caregiver has any questions, to support the family with the program, and to make a plan for continued practice. Therapists then check in briefly about each of the following components: (a) engagement with online program and activity completion ("Were you able to log into the online program? If not, what got in the way?"); (b)

identification of current difficulties/barriers, including technical or motivational challenges (“Did anything get in the way of completing activities or practice? Did you experience any difficulties as a parent with respect to your child/teen’s anxiety management?”); (c) brainstorming possible solutions to identified barriers (“Let’s see if we can problem-solve together and come up with some solutions to help you complete materials this week”); (d) review of anxiety and caregiver progress (“Has your/your child’s level of anxiety changed since beginning the program?); (e) technical questions about content (“Do you have any specific questions about the material that you learned in the modules you completed?”); (f) assignment/plan for next two weeks, providing encouragement and praise for even small successes; and (g) confirmation of the next call.

Of note, the comparators included across the two treatment delivery strategies cover identical therapeutic content, although the therapist-led CBT program entails slightly more sessions than there are modules in the self-administered CBT program in order to afford opportunities for alliance building. At the same time, participants in the self-administered online CBT program are able to revisit various modules multiple times. It is believed that the additional number of sessions in the therapist-led CBT program is roughly offset by the opportunity for those in the self-administered CBT program to revisit modules multiple times. In addition to the two comparators offering identical therapeutic content, participants across the two delivery strategies will be given the identical amount of time (i.e., up to 20 weeks) within which to complete their course of treatment, further ensuring equipoise across comparators.

7.3 Implementation of Cool Kids CBT in Pediatric Health Settings

In order to analyze component 1 of the study, therapists, program staff, and research assistants will be asked to complete assessments about organizational factors that serve as barriers or facilitators to implementing the comparators in the real-world context of pediatric primary care and pediatric health settings. Study personnel will have a team meeting with site staff to introduce them to the study and their roles as researchers and participants in the study. Therapists and program staff will be sent consent forms along with their pre-training assessments prior to their on-site Cool Kids CBT training. By completing the pre-training assessments, therapists are indicating that they have read the consent form, that all of their questions have been answered, and that they voluntarily agree to participate the study. Research staff will track which staff were sent consent forms and completed pre-training assessments, and will follow up individually with clinic staff as needed to ensure enrollment into the study before the site training day.

7.4 Evaluating Therapist-Led Cool Kids (office-based or telehealth) vs. Self-Administered Web-based CBT for Child Anxiety

Once therapists at sites are trained in delivering therapist-led Cool Kids CBT, all patients screened positive for elevated anxiety can be offered Cool Kids CBT as standard treatment at

the discretion of their therapist. Those who screen positive for elevated anxiety and choose to enroll in the study will be randomized to receive either the therapist-led Cool Kids (telehealth, office-based, or hybrid) CBT, or the guided online Cool Kids CBT. Participants in the study will be asked to complete assessments throughout their treatment and post-treatment for the purposes of this study. Short-term and longer-term outcomes will be analyzed in both arms to compare both forms of delivering CBT.

7.5 Method of Assignment/Randomization

Participants will be randomized by family. If the participant will be completing the program and enrolling in the study without parental involvement, they will be randomized individually. Each patient/family will receive a unique study ID at the time of referral to the study that is not connected to identifiable data. Before randomization, the referred patient/family will complete the following enrollment procedures: (1) each referred patient will complete a clinical intake at their referral site with a therapist, (2) each referred patient/ family with complete an assessment to determine eligibility for the study, (3) each referred patient/family will give study staff consent to participate in the study, (4) the participants will complete baseline assessment, and (5) the participants will complete the PARS assessment

Once a participant/family gives consent to enroll in the study, they will be provided with a unique ID number and this ID number will be connected to their identifiable data (access to identifiable data will be limited). The clinical intake can happen before or after consent is received, but the baseline assessment and PARS assessment must be completed after the patient gives consent to enroll in the study. Once all four steps of enrollment (consent, clinical intake, baseline assessment, and PARS) are completed, the participant/family will be randomized.

Anticipated participants were divided into 16 strata based on the 16 combinations of 4 regions (Boston, Miami, Baltimore, Seattle), 2 languages (English, Spanish), and 2 age groups (7-12, 13-18). For each strata, a randomized list of conditions (therapist-led treatment versus guided online treatment) was generated at Sealed Envelope using random blocks of size 4. Random blocks help maintain equally sized treatment groups while also reducing bias in random assignment by making it more difficult for researchers to (deliberately or not) predict the next condition. Random assignment lists have been archived with the Data Management team and with Dr. Coxe.

Randomization assignments are made centrally at the FIU data coordination site. Once a participating family’s baseline assessments are completed (see Measures), the randomization assignment software is programmed to send an automated push notification revealing their assigned condition simultaneously to the FIU data management team (for data recording purposes) and to the research coordinators and clinical team at the participant’s site (to orient the family to their assigned treatment condition).

Each site will create their own workflow for recruitment procedures and submit this to the lead site. Sites will also report their standard of care procedures for delivering the therapist-led program – whether it will be office-based, via telehealth, or a hybrid.

Because of the nature of the intervention, we will not be able to mask study participants, therapists, and RAs from treatment assignment. However, research staff who will be administering the PARS assessment will be masked to study condition.

7.6 Measures

All measures and interviews are to be available and administered in English or Spanish, depending on participant preference. Consistent with a recommended multi-informant assessment strategy, [112,113] measurement of outcomes includes caregiver-report questionnaires, youth-report questionnaires, therapist-report questionnaires, ratings of independent evaluators masked to each family's treatment condition, and administrative logs. To maximize generalizability and rigor while minimizing patient and clinic burdens, priority has been placed on supported measures that are brief and available free-of-cost in the public domain. Moreover, consistent with growing recognition that supported clinical interventions are intended to impact a range of domains of functioning (rather than a single narrow domain),[114,115] a set of outcomes were included to consider multiple aspects of treatment response, including symptom severity, impairment, and more patient-centered factors like perceived effectiveness, treatment satisfaction, and treatment engagement.

Although attempts should be made to collect data from both caregivers and youth across assessment points for all families, to minimize participant burdens and maximize engagement, only caregiver-reports are required to randomize children ages 7-12 years, and only youth self-reports are required to randomize adolescents ages 13-18 years. Furthermore, 7-year-old participants are not to be administered self-report questionnaires, due to concerns about the reliability and validity of self-reports of anxiety in children this age voiced by the trial's patient and family advisory council and scientific advisory panel, and corroborated by scientific literature. [116–118] Such youth should be administered self-report forms at later assessment points if they turn 8 during the trial. In addition, although youth self-reports of primary and secondary clinical outcomes are to be administered to all youth $\geq$ 8 years, a subset of youth self-report variables will only be administered to youth $\geq$ 13 years given: (a) recommendations from the trial's patient and family advisory council and the scientific advisory panel to minimize the assessment burdens outside of clinical outcomes for participating children $\leq$ 12 years, and (b) concerns from these advisory groups about younger children's abilities to accurately self-report on some of these variables (e.g., their own treatment histories, family treatment barriers; details below).

Measures included in the Kids FACE FEARS trial can be sorted into four groups: (i) Primary Clinical Outcomes. (ii) Secondary Clinical Outcomes; (iii) Treatment Variables; and (iv) Study Covariates, Predictors and Other Included Measures.

7.6.1 Primary clinical outcomes. Primary clinical outcomes assessed in the Kids FACE FEARS trial focused on anxiety symptoms, anxiety-related impairment, treatment responder status, anxiety remission status, and patient-centered outcomes focused on perceived effectiveness and treatment satisfaction. Table 3 presents a summary of the primary clinical outcomes assessed, which are described in detail below.

Table 3. Primary Clinical Outcomes in the Kids FACE FEARS Trial

			Assessment Point			
Domain	**Measure**	**Informant(s)**	**Baseline**	**Midtreatment**	**Posttreatment**	**1-Year Follow-Up**
Youth Anxiety Symptoms	PROMIS Pediatric Short Form-Anxiety (8a v2.0)	C, Y	X	X	X	X
Anxiety-Related Impairment	Child Anxiety Life Interference Scale (CALIS)	C, Y	X	X	X	X
Treatment Responder Status						
PARS Treatment Responder	Pediatric Anxiety Rating Scale (PARS)	IE	X		X	
Primary Patient-Centered Outcomes						
Family-Perceived Effectiveness	Perceived Effectiveness Scale	C			X	X
Family-Perceived Treatment Response	Clinical Global Impression Scale-Improvement (CGI)	C, Y		X	X	X
Treatment Satisfaction	Satisfaction Scale	CS, Y		X	X	

Note: Kids FACE FEARS= Kids Formats of Anxiety Care Effectiveness study For Extending the Acceptability and Reach of Services; C = Caregiver Report of Child; CS = Caregiver Self-Report; Y = Youth Self-Report (administered to youth $\geq$ 8 years); IE = Independent Evaluator Report (masked to treatment condition)

Anxiety symptoms. The *PROMIS Pediatric Short Form-Anxiety Scale (8a v2.0)* is being used to assess youth anxiety severity across time. Caregiver-reports will be collected via the parent-proxy form, and youth self-reports will be collected via the pediatric form for youth ages ≥ 8 years. Across psychometric studies, the measure has exhibited strong reliability, structure, and validity in the measurement of youth anxiety severity.[72–75] The PROMIS Pediatric Short Form-Anxiety Scale is also free, brief (8 items), and publicly accessible, which minimizes patient and clinic burdens and positions the measure for use in under-resourced settings and other typical care settings.[72] Raw total scores are converted to T-scores normed for age and sex.

Anxiety-related impairment. The *Child Anxiety Life Interference Scale* (*CALIS*)[119] is a measure of life interference and impairment associated with youth anxiety problems. Items are each rated on a five-point Likert-style scale (0= not at all, 4 = a great deal), and are summed to generate a total interference score. Parent and youth ≥ 8 years will complete separate CALIS forms to offer distinct accounts of caregiver-reported and youth self-reported anxiety-related life impairment. The parent form consists of 16 items (scoring range: 0-64) and the youth form consists of 9 items (scoring range: 0-36) The CALIS parent and youth forms have exhibited strong psychometric properties in previous research.[119,120]

Treatment responder status. The *Pediatric Anxiety Rating Scale* (*PARS*)[79] will be used to independently evaluate clinical significance across the treatment conditions and to benchmark study findings against previously conducted RCTs on youth anxiety.[34] The PARS is a well-supported, clinician-rated instrument for assessing the frequency and severity of anxiety symptoms associated with common anxiety disorders in children between the ages of 6 and 17 years.[79,121] It consists of a 50-item symptom checklist followed by seven global items each rated on a six-point (0-5) scale. Six of the global items are summed to generate a PARS Total Score (range: 0-30). PARS Total Score reductions of 35% or more from baseline to posttreatment are interpreted as reflecting "*PARS Treatment Response*."[121] For the present study, Independent Evaluators (IEs) masked to treatment condition conducted PARS interviews at baseline and at posttreatment with caregivers and youths together and then generated scores based on the pooled information.

Primary patient-centered outcomes. To assess *Caregiver-Perceived Effectiveness*, caregivers will be asked on a 7-point scale at midtreatment and again at posttreatment "How effective do you think the program [has been/was] in treating your child's anxiety?" [0=*very ineffective*; 3=*somewhat effective*; 6=*very effective*]. In addition, caregivers and youth ≥ 8 years will complete a patient-adapted version of the *Clinical Global Impression-Improvement Scale* (CGI-I)[122] to characterize their judgement of treatment-related improvement, relative to the child's baseline presentation. Consistent with the standard version of the CGI-I, scores of 1 ("*very much improved*") or 2 ("*much improved*") will be interpreted as reflecting "*Caregiver-Perceived Treatment Response*" (for caregiver-report) or "*Youth-Perceived Treatment Response*" (for

youth self-report). The caregiver- and youth-report versions of the CGI-I will be administered at midtreatment, posttreatment, and follow-up.

To assess *Treatment Satisfaction*, caregivers and youth ≥ 8 years will be administered a *Satisfaction Scale* that has them rate three items along 0-3 rating scales at midtreatment and again at posttreatment: “Overall, how satisfied [have you been/were you] with the services that [your family/you] received?” [0=*quite dissatisfied*; 3=*very satisfied*]; “Would you recommend this program to a friend if they [had a child with/had] anxiety?” [0=*no, definitely not*; 3=*yes, definitely*]; and “How pleased [have you been/were you] with how this program has helped [your child/you] with anxiety” [0=*quite displeased*; 3=*very pleased*]. These three items will be averaged for each informant to generate Caregiver Total Satisfaction Scores and Youth Total Satisfaction Scores. For dichotomous interpretation, mean scores ≥2 will be interpreted as “Satisfied” and mean scores <2 will be interpreted as “Dissatisfied.”

7.6.2 Secondary clinical outcomes. Secondary clinical outcomes assessed in the Kids FACE FEARS trial focus on broader youth psychopathology (i.e., internalizing problems, externalizing problems, and attention problems), youth sleep difficulties, caregiver internalizing symptoms (i.e., depression symptoms, anxiety symptoms, and stress symptoms), and therapist perceptions of treatment response. Table 4 presents a summary of the Secondary Clinical Outcomes assessed, which are described in detail below.

Table 4. Secondary Clinical Outcomes in the Kids FACE FEARS Trial

Domain	Measure	Informant(s)	Assessment Point				
			Baseline	After Each Session	Midtreatment	Posttreatment	1-Year Follow-Up
Broader Youth Psychopathology							
Internalizing problems	Pediatric Symptom Checklist (PSC-17)	C, Y	X		X	X	X
Externalizing problems	Pediatric Symptom Checklist (PSC-17)	C, Y	X		X	X	X
Attention problems	Pediatric Symptom Checklist (PSC-17)	C, Y	X		X	X	X
Youth Sleep Difficulties	Sleep Item	C, Y	X		X	X	X
Caregiver Internalizing Symptoms							
Depression symptoms	Depression, Anxiety, Stress Scale (DASS-21)	CS	X		X	X	X
Anxiety symptoms	Depression, Anxiety, Stress Scale (DASS-21)	CS	X		X	X	X
Stress symptoms	Depression, Anxiety, Stress Scale (DASS-21)	CS	X		X	X	X
Therapist Perceptions of Treatment Response							
Therapist-Perceived Effectiveness	Perceived Effectiveness Scale	T				X	

Therapist-Perceived Improvement	Clinical Global Impression Scale-Improvement	T	X	X

Note: Kids FACE FEARS= Kids Formats of Anxiety Care Effectiveness study For Extending the Acceptability and Reach of Services; C = Caregiver Report of Child; CS = Caregiver Self-Report; Y = Youth Self-Report (administered to youth ≥ 8 years); T = Therapist Report

Broader youth psychopathology. The *Pediatric Symptom Checklist* (PSC-17)[76] is a brief questionnaire developed to identify child and adolescent emotional and behavioral challenges in pediatric and primary care settings. The measure has exhibited strong validity and reliability in psychometric analyses across diverse samples of youth.[123–125] PSC-17 subscales separately assess internalizing problems, externalizing problems, and attention problems. For the present study, caregivers and youth ≥ 8 years will complete separate PSC reports, and all three subscales will be included.

Youth sleep difficulties. Caregivers will be asked to rate on a 5-point scale the frequency with which the following statement applies to their child: "In the past 7 days, my child has been having sleep-related difficulties (for example, difficulty falling asleep or sleeping through the night)" [0=*never*; 2=*sometimes*; 4=*always*]. Youth ≥ 8 years will be similarly asked to rate on a 5-point scale the frequency with which the following statement applies to them: "In the past 7 days, I have been having sleep-related difficulties (for example, difficulty falling asleep or sleeping through the night)" [0=*never*; 2=*sometimes*; 4=*always*].

Caregiver internalizing symptoms. The *Depression, Anxiety, and Stress Scales* (DASS-21)[126,127] is an adult self-report of negative emotional states that has demonstrated strong psychometric properties.[127,128] Respondents rate their experiences across 21 items using a 4-point severity/frequency scale ranging from 0 (*never*) to 3 (*always*). DASS-21 subscales separately assess symptoms of depression, anxiety, and stress. All three subscales were used in the present study.

Therapist perceptions of treatment response. To assess *Therapist-Perceived Effectiveness*, therapists will be asked on a 7-point scale at posttreatment: "How effective do you think the program was for treating this child?" [0=*very ineffective*; 3=*somewhat effective*; 6=*very effective*]. In addition, after each treatment session (for Therapist-Led CBT cases) or check-in call session (for Guided Online CBT cases), therapists will complete the *CGI-I*[122,129] to characterize their session-by-session judgement of the extent of treatment-related improvement, relative to the child's baseline presentation. Therapists will again complete a CGI-I at posttreatment.

7.6.3 Treatment variables. Treatment variables assessed in the Kids FACE FEARS trial focus on treatment preferences and expectancies, the scope and content of each session and check-in call, treatment fit and flexibility, treatment engagement and barriers, and therapeutic alliance. Table 5 presents a summary of the treatment variables assessed, which are described in detail below.

Table 5. Treatment Variables in the Kids FACE FEARS Trial

Domain	Measure	Informant(s)	Assessment Point				
			Baseline	After First Session	After Each Session	Midtreatment	Posttreatment
Treatment Preferences and Expectancies							
Treatment Preference	Treatment Preferences & Expectancies Survey	CS, Y	X				
Anticipated Treatment Comfort	Treatment Preferences & Expectancies Survey	CS, Y	X				
Anticipated Treatment Comprehension Difficulties	Treatment Preferences & Expectancies Survey	CS, Y	X				
Anticipated Treatment Scheduling Difficulties	Treatment Preferences & Expectancies Survey	CS, Y	X				
Therapist-Anticipated Treatment Effectiveness	Early Treatment Expectations Form	T		X			
Therapist-Anticipated Participatory Engagement	Early Treatment Expectations Form	T		X			
Therapist-Anticipated Therapeutic Alliance	Early Treatment Expectations Form	T		X			
Therapist Case-Specific Self-Efficacy	Early Treatment Expectations Form	T		X			
Scope and content of treatment sessions/check-in calls	Session Summary Form	T			X		
Treatment Fit and Flexibility	Session Summary Form	T			X		
Treatment Engagement and Barriers							
Attendance	Administrative Data	A			X		
Homework engagement	Session Summary Form	T			X		

Treatment completion	Administrative Data	T			X
Child participatory engagement	Session Summary Form	T	X		
Caregiver participatory engagement	Session Summary Form	T	X		
Comprehension difficulties	Treatment Barriers Survey	CS, Y		X	X
Difficulties making time for treatment	Treatment Barriers Survey	CS, Y		X	X
Treatment discomfort	Treatment Barriers Survey	CS, Y		X	X
Technology treatment challenges (family report)	Technological Experiences And Reactions Scale	CS, Y		X	X
Technology treatment challenges (therapist report)	Technological Experiences And Reactions Scale	T	X		
Therapeutic alliance (family report)	Perceptions of Therapeutic Alliance Scale	C/CS, Y		X	X
Therapeutic alliance (therapist report)	Perceptions of Therapeutic Alliance Scale	T			X

Note: Kids FACE FEARS= Kids Formats of Anxiety Care Effectiveness study For Extending the Acceptability and Reach of Services; C = Caregiver Report of Child; CS = Caregiver Self-Report; Y = Youth Self-Report (administered to youth $\geq$ 13 years); T = Therapist Report; A = Administrative Data

Treatment preferences and expectancies. Prior to randomization, caregivers and youth ≥ 13 years will each complete a *Treatment Preferences and Expectancies Survey* designed for the present study. Respondents will indicate whether they would prefer to receive Therapist-Led CBT (coded: 0) or Guided Online CBT (coded: 2), or whether they have no preference between the two conditions (coded: 1) [*Treatment Preference*]. Respondents will also rate each of the two treatments on *Anticipated Treatment Comfort*, *Anticipated Treatment Comprehension Difficulties*, and *Anticipated Treatment Scheduling Difficulties* on 0-6 scales.

Data will also be collected on therapist's early treatment expectations for each family. Specifically, after the first clinical encounter with an assigned family (i.e., first session for Therapist-Led CBT families; first check-in call for Guided Online CBT families), therapists will complete an *Early Treatment Expectations Form* developed for the present study. This form has therapists indicate their level of agreement with the following item on a scale from 0 (*very ineffective*) to 6 (*very effective*): "Thinking about the treatment course ahead, how effective do you think the child's assigned treatment condition will be in treating this child's anxiety?" (*anticipated treatment effectiveness*). To measure therapist's *Anticipated Effectiveness of the Non-Assigned Treatment*, therapists will also use the same scale to indicate their level of agreement with the following statement: "If instead of [Therapist-Led CBT/Guided Online CBT], this family had been assigned to Guided Online CBT/Therapist-Led CBT], how effective do you think *that* treatment would be in treating this child's anxiety?" (*Anticipated Effectiveness of Non-Assigned Treatment*).

The *Early Treatment Expectations Form* will also assess therapists' early expectations about treatment engagement for each family. Specifically, after their first clinical encounter with an assigned family, therapists will be asked to respond to the following items, along a scale from 0 (*to a small extent*) to 4 (*to a very great extent*): "Thinking about the treatment course ahead, to what extent do you expect this child will actively participate in their assigned course of treatment?" (*Anticipated Child Participatory Engagement*); and "Thinking about the treatment course ahead, to what extent do you expect this child's caregiver(s) will actively participate in their assigned course of treatment?" (*Anticipated Caregiver Participatory Engagement*).

Furthermore, the *Early Treatment Expectations Form* also assesses therapists' early expectations about treatment alliance for each family. Specifically, after their first clinical encounter with an assigned family, therapists will be asked to respond to the following items, along a scale from 0 (*never*) to 6 (*always*): "Across treatment, I think this child and I will work well together" (*Anticipated Therapist-Child Collaboration*); and "Across treatment, I think this child's caregiver(s) and I will work well together" (*Anticipated Therapist-Caregiver Collaboration*). Therapists will also use the same scale to rate the extent to which they predict they will enjoy working with the child (*Anticipated Therapist-Child Bond*); the extent to which they predict the child will enjoy working with them (*Anticipated Child-Therapist Bond*); the extent

to which they predict they will enjoy working with the child's caregiver(s) (*Anticipated Therapist-Caregiver Bond*); and the extent to which they predict the child's caregiver(s) will enjoy working with them (*Anticipated Caregiver Therapist Bond*).

Finally, the *Early Treatment Expectations Form* will be used to assess *Therapist Case-Specific Self-Efficacy* with regard to implementing the assigned treatment. Specifically, after their first encounter with a family, depending on the family's treatment assignment, the therapist will be asked to rate how well they predict they will be able to conduct [Therapist-Led CBT/Guided Online CBT], along a 0 (*very limited*) to 4 (*very high*) scale.

Scope and content of treatment sessions and check-in calls. After each treatment session (for Therapist-Led CBT cases) or check-in call session (for Guided Online CBT cases), therapists will complete a *Session Summary Form* that was developed for the present study. On this form, therapists will indicate who participated in the session (e.g., youth, caregiver, other), the language in which the session was held (English, Spanish, or both), whether the session began on time (and if not, how late it began), the length of the session, and the format of the session (e.g., in-office, phone, videoconference). Therapists in each condition will also check off all of the content and topics that were covered in the session they just held, from a list of options: psychoeducation; detective/realistic thinking; fear hierarchies; future exposure practice; in-session exposure practice; rewards and reinforcement; parenting issues related to youth anxiety; additional coping skills (e.g., problem-solving, social skills, assertiveness, relaxation techniques); non-CBT strategies (e.g., interpreting the meaning of symptoms, interpreting the meaning of child's play or artwork); discussion of issues not directly related to anxiety (e.g., major family transitions, conflicts other than co-occurring non-anxiety problems); review of previous homework; assignment of new homework; and/or addressing barriers to treatment/homework. For Therapist-Led CBT cases, therapists will also indicate the session number(s) in the protocol that were covered in that session.

Treatment fit and flexibility. As part of the *Session Summary Form* completed by the therapist after each treatment session (for Therapist-Led CBT cases) or check-in call session (for Guided Online CBT cases), therapists will indicate their level of agreement with the following statement on a scale from 0 (*not at all*) to 6 (*extensively*): "To what extent was the content covered this [session/check-in call] a fit to this child's clinical presentation and individual needs?" To assess needs for treatment flexibility, therapists will also indicate after each session their level of agreement with the following statement on a scale from 0 (*not at all*) to 6 (*extensively*): "How much did you need to tailor or adapt the content or structure of this session because of the child's clinical presentation and individual needs?" Moreover, as part of the *Session Summary Form*, therapists will select the reason(s) they may have covered content outside of the treatment protocol in the session they just held from a list of options (if relevant): (a) had to address a clinical emergency that made them concerned about immediate safety, (b) needed to

address a topic of the week that did not directly relate to the focus of the treatment protocol (e.g., family conflict, school trouble), (c) had to address a co-occurring/co-presenting issue other than child anxiety (e.g., ADHD, medical problem), (d) needed to engage in an alliance-building activity, (e) needed to address treatment resistance, (f) other (describe).

Treatment engagement and barriers. Therapists will complete weekly logs reporting whether study families on their caseloads attended their scheduled sessions or support calls and whether they completed the homework assigned in their previous session or support call. These data will be used to characterize *Treatment Attendance* and *Homework Engagement*. *Treatment Completion* is defined for Therapist-Led CBT as attending 10 treatment sessions, and for Guided Online CBT Care as attending 4 support calls. For Guided Online CBT families, administrative backend data will also be collected from the central server to further assess user/usage analytics.

To assess session-by-session participatory engagement, as part of the *Session Summary Form* completed by the therapist after each treatment session (for Therapist-Led CBT cases) or check-in call session (for Guided Online CBT cases), therapists will indicate their level of agreement with the following statement on a scale from 0 (*not at all*) to 6 (*extensively*): "To what extent did you feel that this child was engaged in today's [session/check-in call]. For example, did the child appear motivated and committed to improving, and was the child actively participating in the [session/call]" (*Child Participatory Engagement*). When appropriate, a parallel item will be asked of therapists regarding the caregiver's engagement in that session (*Caregiver Participatory Engagement*). At posttreatment, therapists will respond to modified versions of these items to report on participatory engagement across the entire course of treatment.

To assess *Comprehension Difficulties*, caregivers and youth $\geq$ 13 years across both conditions will be asked at midtreatment and again at posttreatment "How hard has the intervention been for [your family/you] to understand?" [0=*never hard*; 3=*sometimes hard*; 6=*very hard*]. To assess *Difficulties Making Time for Treatment* caregivers and youth $\geq$ 13 years will be asked at midtreatment and again at posttreatment "How hard has it been for [your family/you] to [make your schedule work for treatment sessions/find time to work on and complete the computer-based treatment modules online]?" [0=*never a problem*; 3=*sometimes a problem*; 6=*often a problem*]. To assess *Treatment Discomfort*, caregivers and youth $\geq$ 13 years will be asked at midtreatment and again at posttreatment "How comfortable [has your family/have you] felt when [attending treatment sessions/completing the computer-based treatment modules online]?" [0=*very comfortable*; 3=*sometimes comfortable*; 6=*very uncomfortable*].

The *Technological Experiences And Reactions Scale* (*TEARS*)[130] will be administered to specifically assess *Technology-Based Treatment Challenges*. The TEARS is a brief

questionnaire that measures disruptions and patient frustrations with telehealth sessions and digital mental health. Psychometric research has demonstrated the reliability and validity of the measure. At midtreatment and again at posttreatment, Therapist-Led CBT participants (most of which completed sessions via telehealth) and Guided Online CBT participants will use the TEARS to rate the extent to which technology issues and time spent addressing technology-related issues took away from the quality of the intervention, frustrated them, and/or interfered with treatment understanding. For families in either condition, therapists will also complete the therapist-report TEARS at the conclusion of each session/check-in call and again at posttreatment. In addition to the TEARS, therapists and families will report basic information on how families were logging in and engaging with the treatment, and the devices they were using.

Therapeutic alliance. A caregiver *Perceptions of Therapeutic Alliance Scale* will aske caregivers at midtreatment and again at posttreatment to respond to the following items, along a scale from 0 (*never*) to 6 (*always*): “I think the therapist and I [work/worked] well together to help with my child’s anxiety” (*Caregiver-Therapist Collaboration*); “I feel like I [like/liked] the therapist” (*Caregiver-Therapist Bond*); “I feel like the therapist [likes/liked] me” (*Therapist-Caregiver Bond*); “I feel like my child [likes/liked] the therapist” (*Child-Therapist Bond*); and “I feel like the therapist [likes/liked] my child” (*Therapist-Child Bond*).

A youth *Perceptions of Therapeutic Alliance Scale* will ask youth ≥ 13 years at midtreatment and again at posttreatment to respond to the following items, along a scale from 0 (*never*) to 6 (*always*): “I think the therapist and I [work/worked] well together to help with my anxiety” (*Child-Therapist Collaboration*); “I feel like I [like/liked] the therapist” (*Child-Therapist bond*); and “I feel like the therapist [likes/liked] me” (*Therapist-Child Bond*).

A Therapist *Perceptions of Therapeutic Alliance Scale* will ask therapists at posttreatment to respond to the following items, along a scale from 0 (*never*) to 6 (*always*): “Looking back on treatment, I think this child and I worked well together to help with their anxiety” (*Child-Therapist Collaboration*); “Looking back on treatment, I feel like I liked this child” (*Therapist-Child Bond*); and “Looking back on treatment, I feel like I liked the child’s caregivers” (*Therapist-Caregiver Bond*).

7.6.4 Study covariates, predictors and other included measures. A number of study covariates, predictors, and other included measures will be assessed in the Kids FACE FEARS trial. These measures focus on demographic information, youth health and education, adverse childhood experiences, experiences with discrimination, mental health stigma, caregiver beliefs about youth anxiety and overprotection, technological literacy, openness to technology-based supports, therapist attitudes and knowledge about youth anxiety and treatment, therapist self-efficacy, and organizational climate of the treatment setting. Table 6 presents a summary of

these Study Covariates, Predictors, and Other Included Measures (which are described in detail, below).

Table 6. Covariates, Predictors, and Other Variables Assessed in the Kids FACE FEARS Trial

Domain	Measure	Informant(s)	Assessment Point			
			Baseline	Midtreatment	Posttreatment	1-Year Follow-Up
Demographic information	Demographics and Background Form	C/CS, Y[a]	X			
Youth health and Education	Demographics and Background Form	C, Y[a]	X			
Adverse Childhood Experiences	CYW ACE-Q; Expanded ACE-Q	C, Y[b]	X	X	X	X
Experiences with Discrimination	Everyday Discrimination Scale (EDS)-Short Version	CS, Y[a]	X			
Mental Health Stigma	Parental Attitudes Toward Psychological Services Inventory—Stigmatization Scale	CS	X			
Beliefs about Youth Anxiety & Overprotection	Parental Attitudes, Beliefs, and Understanding of Anxiety (PABUA)—Overprotection Scale	CS	X	X	X	X
Technological Literacy	Technological Ease and Computer Habits Inventory (TECHI)	CS, Y[b], T	X			
Openness to Technology-Based Supports	Beliefs and Attitudes about Technology as a Child Health Resource (BATCH-R)	CS	X		X	
Therapist Attitudes and Knowledge						
About evidence-based treatments	Evidence-Based Practice Attitudes Scale (EBPAS)	T	X[c,d]			
About exposure therapy	Therapist Beliefs about Exposure Therapy Scale (TBES)	T	X[c,d]			

About child anxiety and CBT	Knowledge Test	T	X[c,d]
Therapist Self-Efficacy			
CBT/Anxiety Self-Efficacy	Therapist Self-Efficacy Scale-CBT for Youth Anxiety	T	X[c,d]
Common Factors Self-Efficacy	Therapist Self-Efficacy Scale-CBT for Youth Anxiety	T	X[c]
Patient Responsivity Self-Efficacy	Therapist Self-Efficacy Scale-CBT for Youth Anxiety	T	X[c]
Organizational Climate of Treatment Setting			
Adequacy of Resources	TCU Organizational Readiness for Change Scale	T	X[c]
Organizational Climate	TCU Organizational Readiness for Change Scale	T	X[c]

Note: Kids FACE FEARS= Kids Formats of Anxiety Care Effectiveness study For Extending the Acceptability and Reach of Services; C = Caregiver Report of Child; CS = Caregiver Self-Report; Y = Youth Self-Report

[a] Administered to youth $\geq$ 11 years

[b] Administered to youth $\geq$ 13 years

[c] Measure administered to therapists prior their onboarding and training

[d] Measure administered again to therapists after their training

Demographic information. Caregivers and youth ≥ 11 years will provide data on caregiver and youth age, gender, race, ethnicity, nativity (U.S.- or foreign-born), family and household living structure, languages spoken, and language(s) preference, among a number of other demographic pieces of information. Caregivers will also provide information on their child's grade level, as well as their own highest level of education and literacy comfort. Families will be classified as experiencing *baseline resource insecurity* if the caregiver indicates at baseline that the family experienced any of the following circumstances over the prior 12 months: (a) unhoused or living in a shelter; (b) unable to pay the rent or mortgage on time; (c) the food they purchased did not last and they did not have money to get more; (d) there was concern their food would run out before they got money to buy more; and/or (e) the gas or electric company threatened to shut off or refuse gas or electricity to their residence for not paying bills.

Youth health and education. Caregivers will provide information on the child's developmental history, medical history, previously diagnosed mental health problems, mental health treatment history, academic performance and attendance, and school accommodations.

Adverse childhood experiences. The Center for Youth Wellness (CYW) *Adverse Childhood Experiences Questionnaire* (CYW ACE-Q)[131] will be used to assess stressful life experiences that can impact child adjustment and development. From a list of 19 specific adversities, caregivers and youth ≥ 13 years will each report on the total number of challenging circumstances that participating children and adolescents have endured or encountered. This list includes 10 items from the original conceptualization of adverse childhood experiences (e.g., physical, emotion, and sexual abuse; physical and emotional neglect; household dysfunction; living with family members who misuse substances; living with family members with mental illness), as well as a broadened set of 9 additional experiences that can similarly cause prolonged stress that were not included in the original ACES conceptualization (e.g., death of a caregiver, exposure to neighborhood violence; immigration- or deportation-related separation from caregiver; identity-based discrimination; abuse or threats from a romantic partner). Two more additional items were also added to assess whether the child had directly experienced a natural disaster (e.g., earthquake, tornado, wildfire, hurricane) or a manmade disaster (e.g., terrorist attack, mass shooting, plane crash, industrial fire/explosion, bridge collapse). Respondents will review the list of items, tally the number of these experiences that the child has endured, and report that total number. Accordingly, the quantity of experienced ACES will be assessed, but information will not be collected for the research record that clarifies which specific ACES were experienced by the child. Per guidelines for the CYW ACE-Q, scores between 1 and 3 indicate "moderate exposure" to ACES and scores ≥ 4 are considered "high" and indicate "considerable exposure" to ACES.

Experiences with discrimination. The *Everyday Discrimination Scale-Short Version* (EDS)[132] will be used to measure the frequency with which youth and caregivers are subjected to routine experiences of unfair treatment. The EDS Short Version is a briefer 5-item adaptation of the original 9-item EDS[133] that has been found to show strong reliability and reliability. Respondents indicate how often they experience situations such as being treated with less respect than other people, having people act afraid of them, having people act as if they are not smart, and being threatened or harassed. The frequency of each item is rated on a scale ranging from 0 (*never*) to 5 (*almost everyday*). For responses ≥ 2, follow-up questions ask respondents to indicate what they think is the main reason for these experiences (e.g., their ancestry, gender, race, age, religion, weight, sexual orientation, education or income level). The scale has been used extensively in the mental health field. Higher scores represent more incidences of everyday discrimination as compared to lower scores.

Mental health stigma. The *Parental Attitudes Toward Psychological Services Inventory* (PATPSI)[134] Stigmatization scale will be administered to assess the extent to which caregivers are concerned about how others negatively perceive people who have emotional or behavioral health challenges or who seek psychological services. Using a scale ranging from 0 (*strongly disagree*) to 5 (*strongly agree*), respondents will rate their level of agreement with eight items (e.g., “I would not want others to know if my child had a psychological or behavioral problem”; “Having been mentally ill carries with it feelings of shame”). The measure has exhibited strong psychometric properties, including a sound factor structure and great reliability and validity.[134]

Caregiver beliefs about youth anxiety and overprotection. The *Parental Attitudes, Beliefs, and Understanding of Anxiety* (PABUA) – Overprotection Scale[135] is a supported self-report measure that evaluates caregiver attitudes and beliefs about their child’s anxiety, and the extent to which they believe they must protect their child from anxiety and distress. Items assess caregiver beliefs about appropriate levels of autonomy-granting, whether caregivers believe they should let their anxious child avoid anxiety-provoking situations, and issues of general enmeshment in the caregiver-child relationship. Psychometric research has found the measure and scale to exhibit strong convergent validity, divergent validity, and internal consistency.[135]

Technological literacy. Caregiver and youth *technological literacy* at baseline will be assessed via the *Technological Ease and Computer Habits Inventory* (TECHI)[136] which consists of 17 items assessing the extent/frequency of technological usage in everyday life, as well as competency and patience with technology. Items are rated on 0-5 scales, and the TECHI Total Score ranges from 0-85 (with higher scores indicating greater technological usage, competency, and patience). The TECHI has demonstrated strong psychometric

properties for measuring technological literacy in the context of technology-based mental health treatment.[136]

To assess therapist technological literacy going into the project, therapists will also complete the TECHI prior to full onboarding and training for the trial.

Openness to technology-based supports. The *Beliefs and Attitudes about Technology as a Child Health Resource* (BATCH-R)[137] is a brief supported self-report that assesses caregiver attitudes (e.g., comfort, trust) toward technology's role in mental health supports and services, parenting information and resources, and professional guidance. The Openness to Technology-Based Mental Health Supports and Treatment scale has caregivers rate from 0 (*strongly disagree*) to 5 (*strongly agree*) their level of agreement with eight items (e.g., "Online computer-based mental health programs can be helpful for treating childhood anxiety"; "I am open to seeking out information online about my child's health and development"; "I trust the information I receive online about parenting"). The measure has exhibited strong psychometric properties, including a sound factor structure and great reliability and validity.[137]

Therapist attitudes toward evidence-based treatments. The *Evidence-Based Practice Attitudes Scale* (*EBPAS*)[138] assesses mental health provider attitudes toward evidence-based practices and adopting new interventions. Fifteen EBPAS items assess the extent to which the therapist: (a) would adopt a new practice if it made sense and was used by trusted colleagues (*Appeal* subscale); (b) would adopt a new practice if it was required by their agency (*Requirements* subscale), (c) is open to trying new treatments (*Openness* subscale), and (d) believes research-based interventions are not clinically useful (*Divergence* subscale). Respondents rate their agreement with items on a scale from 0 (*not at all*) to 4 (*to a great extent*), resulting in four subscale scores and an EBPAS Total Score reflecting overall positive disposition toward adopting evidence-based treatments and protocols. Therapists will complete the EBPAS prior to completing their training, and again after completing training.

Therapist openness to exposure therapy. The *Therapist Beliefs about Exposure Therapy Scale* (*TBES*)[139] is a therapist self-report questionnaire that measures negative attitudes they may hold about exposure therapy (e.g., "Compared to other psychotherapies, exposure therapy leads to higher dropout rates"). Respondents rate their agreement with each of 21 beliefs about exposure therapy along a 5-point scale (0=*disagree strongly*; 4=*agree strongly*). Items are summed, resulting in a TBES Total Score (range: 0-84), with higher scores reflecting more negative views of exposure therapy. Therapists will complete the TBES prior to completing their training and again after completing training.

Therapist knowledge about child anxiety and CBT. An 8-item *Knowledge Test* was created to assess therapists' familiarity with basic research findings about child anxiety (e.g., fear is a natural emotion; physical sensations of anxiety cannot harm a child; differences between fear and anxiety) and its evidence-based treatment (e.g., the three-component model of CBT; the value of exposures). Therapists will complete this knowledge test prior to completing their training and again after completing training.

Therapist self-efficacy. Therapists will complete the *Therapist Self-Efficacy Scale-CBT for Anxiety in Youth* (TSES-CAY),[140] a 16-item survey that measures the extent to which therapists perceive they are capable of competently conducting CBT for youth anxiety. Items from a therapist self-efficacy scale for the treatment of adult depression[141] were adapted to assess therapist perceptions of their abilities treating anxiety in children and adolescents. TSES-CAY factor analysis has identified a three-factor structure: (a) *CBT/Anxiety-Specific Self-Efficacy* (which measures perceived ability to conceptualize client problems using the CBT model, maintain the structure of CBT, teach CBT skills, putting anxious patients in anxiety-provoking situations, and instruct patients to practice skills outside of session); (b) *Common Factors Self-Efficacy* (which measures perceived ability to build therapeutic alliance, empathize with children/families, etc); and (c) *Patient Responsivity Self-Efficacy* (which measures perceived ability to adapt to patient/family needs, work collaboratively with patients/families, and address treatment barriers as they arise). Therapists will complete all three scales of the TSES-CAY prior to completing their training. After completing their training, therapists will again complete the TSES-CAY CBT/Anxiety-Specific Self-Efficacy scale.

Organizational climate of treatment setting. The *Texas Christian Association Organizational Readiness for Change scale* (*TCU ORC*)[142] will be used to assess organizational attributes and motivational factors of the clinical settings participating in the trial that can impact the overall success of treatment implementation. Prior to training and onboarding for the trial, therapists, supervisors, administrative directors, and staff across the clinics participating in the trial will complete the TCU ORC subscales that assess Adequacy of Resources (including Offices, Staffing, Training, Equipment, Internet, and Supervision) and Organizational Climate (including Mission, Cohesion, Autonomy, Communication, Stress, and Change). The TCU ORC has exhibited strong psychometric properties, and observed ORC subscale scores can be compared for interpretation against 25th percentile scores, 50th percentile scores, and 75th percentile scores reported from national data.[143]

7.7 Therapist Training and Ongoing Consultation

Existing therapists and clinical supervisors from across the four participating pediatric health networks will be trained by the study team to deliver CBT for youth anxiety. Consistent with best practices for promoting quality implementation of evidence-based treatment,[107–110] a

multi-component strategy is to be used that involves training workshops for therapists and supervisors, followed by asynchronous online resources and ongoing small group consultation of therapists and supervisors. The same therapists are to participate in care across both treatment comparators.

7.7.1 Training workshop. Prior to treating patients on the Kids FACE FEARS trial, therapists and supervisors will participate in one full-day (8 hour) training or two half-day (4-hour) trainings. These trainings will be led by members of the Training, Fidelity and Sustainability Core (e.g., Dr. Donna Pincus, Dr. Alyssa Farley, Dr. Jami Furr, Dr. Kelsey Hudson, Dr. Rachel Merson, and Annie Dantowitz, LICSW). Those attending these trainings should be natural providers and supervisors in the pediatric health settings participating in the trial (i.e., clinical staff not employed by the research trial and not working in anxiety specialty settings). Trainings can be provided in-person or on Zoom. All clinicians and supervisors will be provided with a full set of Cool Kids treatment workbooks prior to the start of the training. Trainings will incorporate didactic components and active teaching approaches (e.g., live role-plays, demonstrations of core skills, small break-out groups, interactive video presentations, opportunities for therapists to actively practice using specific CBT skills to treat child anxiety).

Trainings are to start with an introduction to the trial, followed by: (a) overviews of the core principles of CBT for youth anxiety, (b) detailed, step-by-step instructions in how to deliver the core skills in the Cool Kids and Chilled therapy protocols (e.g., psychoeducation, cognitive restructuring, exposure, and parenting anxious behaviors), and (c) additional coping skills such as problem solving, social skills building, and progressive muscle relaxation. Therapists and supervisors are taught about the adaptive and unhelpful aspects of anxiety, factors that maintain youth anxiety, and evidence-based strategies for offsetting these factors. Trainings will also emphasize the importance of caregiver involvement in treatment (as appropriate, and when feasible), between-session practice, and treatment fidelity within flexibility.[69,111] Moreover, therapists and supervisors will be provided guidance on addressing common treatment barriers, such as lack of between-session practice or poor treatment attendance, and how to problem-solve and support families through various challenges that can emerge during treatment.

These trainings will also include a demonstration of the guided online programs (including illustrative video clips and how to log in and access the online materials) and will incorporate direct instruction on how to conduct check-in calls for the guided online treatment condition. Therapists and supervisors will be provided with a check-in call conversation guidelines/scripts to follow (see description of Comparator 2, above), and will be taught how to navigate common questions.

After each training, therapists and supervisors will complete post-training knowledge quizzes. Any therapist who scores <80% on the post-training knowledge quiz will receive individualized follow-up training and support, and will then be retested with an alternate form of the knowledge quiz, and will be required to meet the 80% training criterion prior to treating patients in the study.

7.7.2 Asynchronous online resources. After each training, therapists and supervisors will be provided resources to support their delivery of the treatment comparators, including session outlines, training recordings and booster supports as needed. In response to requests from therapists and supervisors, a website with helpful resources has been developed to further support therapists as they implement treatment. This website includes treatment demonstration videos, treatment module summaries, and therapist training slides. A guided refresher course was created and is included on the website that includes audio and video training demonstration videos and interactive training activities.

7.7.3 Consultation and support. Providers (therapists and supervisors) at the study performance sites will participate in regularly held group consultation videoconferencing calls led by experts in the treatment of pediatric anxiety. These consultation calls will be held in addition to any routine supervision that may be naturally afforded to providers in their local hospital or clinical network.

All participants who attend a training workshop will be assigned to a recurring consultation call group. Therapist consultation calls will be held biweekly (i.e., twice monthly). These calls are designed to support therapists on the project, to prevent therapist drift, and to afford education and scaffolding to providers. Approximately 4-6 therapists are to be assigned to each call group. The remote format enables consultation call groups to contain a mix of therapists from across study sites and regions. Calls will each be one hour, and will be used to clarify and role-play therapy skills, to answer any questions about the two treatment formats, and to support therapists as they implemente the treatments. Site supervisors will also participate in a separate, once-monthly supervisor group consultation call, also led by an expert in pediatric anxiety treatment.

Each consultation call will be structured to formally review a specific rotating skill or topic, including: psychoeducation, fear hierarchies and exposures, cognitive strategies, cultural considerations, parenting factors, check-in calls, homework compliance, general coping skills, treatment flexibility, COVID-related anxiety, school anxiety, developmental considerations, and technology-related issues. Each call will also include a “Therapist Spotlight,” in which a rotating therapist will have an opportunity to receive more individualized attention and in-depth consultation about one of their patients. These Therapist Spotlights give call leaders the opportunity to clarify and correct any potential

problems with treatment delivery, and to provide individualized follow-up training and support to therapists as needed. Therapist spotlights also provide opportunities for therapists to provide peer input to one another and to learn from one another's experience and perspectives.

7.8 Safety, Reaction Management, and Clinical Deterioration

All study participants will be working with trained therapists who can assist participants if they were to become upset. If a participant becomes upset during the process of being interviewed and/or while completing assessment measures with an RA (Research Assistant), the RA will ask if the participant/ family would like to check-in with their doctor or one of the clinicians with behavioral health training at the site. Participants will also be provided with the phone numbers of their site research staff who they can contact if they become upset while completing the assessments online. The research staff will connect them with an available clinician in these situations. The study facility will be appropriate to children, as these facilities will be pediatric healthcare sites. We will make sure that all psycho-educational materials, treatment plans are written in a straightforward manner, at the appropriate literacy level. We will use translators/language line as needed to further ensure guardians fully understand study procedures and communicate concerns about their child's care.

As all site staff and the investigators are mandated reporters, families will be informed that any disclosure of abuse, risk to a child or elder will need to be reported to the appropriate state protection agency. Endorsement of suicidality, risk to self or others will require emergency evaluation for safety and disposition by the clinical staff and RAs will have a contact at each site for reporting such disclosures and to activate the clinical protocol for these types of events. RAs will also contact the study PIs and report the event to the lead site and for inclusion in reports to the DSMB.

7.8.1 Safety policy

The study intervention does not pose an additional risk to pregnant women and so pregnant women (guardians or youth participants) can be enrolled in the study.

Therapist concern for patient mental health severity and/or safety:

If the child's therapist has concerns over the safety of the child or their current severity of illness, the therapist will report their concerns to the site clinical supervisor and a decision regarding the needed level of care (e.g., inpatient, acute care) will be made based on a

clinical determination. The team will then report this to the study PIs to discuss if the child should be removed from the study.

Research assistant concern for patient mental health severity and/or safety:

If the PROMIS Short Form for Anxiety shows an increase of 5 points on the T-score metric at an assessment point (or the equivalent of 0.5 standard deviation which is a clinically meaningful difference) (Norman, Sloan, & Wyrwich, 2003), the local RA will notify the participant's therapist. Their therapist will discuss with the clinical supervisor and site PI if the participant should be removed from the study and referred to a different model of care or level of treatment.

If the DASS-21 completed by guardians shows severe or extremely severe in any dimension of the assessment (depression, anxiety, stress) or if the guardian marks a score of 2 or 3 on item 21 ("I feel that life is meaningless") at an assessment point, the RA will notify the family's therapist (Lovibond & Lovibond, 1995). Their therapist will discuss the appropriate course of action with the site supervisor for clinical determination to ensure the safety and well-being of the child and guardian. The clinical team will again discuss with the PI if family should be removed from the study.

Examples of situations where family/ child may need to be removed from the study include: emergence of a psychotic disorder, need for prolonged residential placement, youth detention, suicidal behavior, parental/ guardian psychiatric hospitalization. Clinical decision making will be the first principle for addressing family treatment needs for any worsening mental health severity, safety and functioning.

REDCap will automatically send an email to the local RA at each site whenever a score is flagged on either measures.

Telehealth and Zoom Videoconferencing

In order to protect patients during pandemics, such as COVID-19, patients and participants will have to option to complete study visits via Zoom Video Communications software. This will be provided as an option for study visits/ procedures including consent procedures, PARS baseline assessments, and technical orientation. Zoom Video Communications is a remote conferencing services company that provides remote conferencing services, that combines video conferencing, screen sharing services, online meetings, chat, and mobile collaboration, with both audio and video communication options. Participants can use zoom via their phone, computer, or tablet/Ipad. Study visits will not be recorded.

If the participant's preference is for videoconference, the RA will send the participant a link to a Zoom meeting, along with a link to the Zoom Privacy Policy. The RA will also send instructions on how to use Zoom, including guidance on best practices for sharing as little personal information with Zoom as possible. These best practices will be: (1) suggesting that the participant only enter their first name instead of their full name, and (2) if they don't want to give their email, that they should feel free to use name@noemail.com<mailto:name@noemail.com> as their email address. The link to join the Zoom meeting with only be accessible by the RA conducting the visit and the patient or participant. The RA will complete the video conference in a private room, and the meeting will not be recorded. If a participant is not comfortable with using the Zoom software, they will always have the option to call-in to the meeting via phone, or meet in-person.

7.8.2 Removal of Participants. All instances of study dropout will be documented using a Premature Termination form on REDCap including the reason for dropout, who decided that the participant would drop out (i.e., parent or guardian, therapist, study staff, adolescent patient), and whether the dropout resulted from burden of intervention, study assessment, or both. Withdrawn participants will be encouraged to continue to participate in study assessments throughout the 1-year follow-up period in order to optimize the intention-to-treat assessment design. Participants may withdraw voluntarily at any time for any reason.

There are two types of participant withdrawal: "treatment withdrawal" and "study withdrawal."

1. **Treatment withdrawal** is when a participant drops out of treatment (either because they are no longer interested or because a clinician or study investigator feels that treatment is no longer appropriate), but still provides the research team with posttreatment data by completing assessments at post treatment and Week 52.

2. **Study withdrawal** is when a participant (or a provider on behalf of the participant) explicitly communicates that they are no longer interested in being a part of the study at all – including future assessments and compensation. Cases of "treatment withdrawal" are not automatically considered to be "study withdrawal" unless the participant specifically states that they never want to be contacted again by the study, or if a clinician or study investigator deems that any future contact would be inappropriate.

Participants may be removed if:

- If the participant's provider or therapists feels the study is negatively impacting the participant's health or wellbeing resulting in increasing severity of illness that is clinical assessed as such by the therapist/ provider team. Such cases will be

assessed clinically, and an appropriate treatment plan will be determined and then discussed with the PI for determination of whether patient should be removed from study.

- If there is an increase in the participant's anxiety levels based on the PROMIS Pediatric Short Form for Anxiety and or other worsening of mental health status that leads to change in the treatment plan/ level of care determination by clinical team.
- If the participant becomes suicidal and presents with clinically determined safety risk to self or others.

If staff or therapists participating in the study leave the participating clinical site, they will be asked to complete 1 follow up assessment before leaving. Once they leave employment at the site, they will be removed from the study.

7.8.3 Data Safety Monitoring Plan. The study PIs, Donna Pincus and Jonathan Comer, will be responsible for monitoring the study and will do so in the following way:

(1) They will continuously assess protection of data and participant confidentiality. If any breach in the protection of participant data is identified or breach of confidentiality, it will be reported as an adverse event to the lead site and be assessed to determine if the event relates to the study and requires any protocol changes or study-wide action to ensure the protection of patient data.

(2) They will meet with site PIs on a monthly basis to review study progress and elicit any concerns. They will be charged with minimizing any risk involved with participation, monitoring the risks and benefits during implementation of the project on a timely basis, and ensuring that the research is conducted according to high scientific and ethical standards.

The principal investigators will also report the findings to the PCORI program staff. PCORI will be informed of any actions taken by the IRB as a result of their continuing review.

In addition, a **Data Safety and Monitoring Board (DSMB)** will meet twice annually to provide independent oversight of data management and integrity, and participant safety.

Data Safety and Monitoring Board Co-Chairs: Martha Tompson, PhD is Associate Professor of Psychology at Boston University and Director of the Family Development and Treatment Program; she is a renowned expert in the family-based treatment of pediatric mood and anxiety problems, and has extensive experience leading randomized clinical trials. Shannon Pruden, PhD is Professor of Psychology at Florida International University and a leading expert on child development and individual differences. The Co-Chairs will

meet twice annually to independently review and evaluate study data for participant safety, study conduct, progress, and efficacy, and make recommendations for modifications if needed.

7.8.4 Adverse Events Definition and Reporting. Potential Adverse events are defined as potential physical, emotional, legal or financial risk. We do not foresee any physical, legal, or financial risk for any of the study participants.

The following definitions will be used in the assessment of safety:

Adverse Event (AE) is any abnormal or harmful behaviors, increasing severity of symptoms that are identified by the therapist, suicidal behaviors or attempts, breach in the protection of participant data or breach of confidentiality whether or not considered related to the participants' participation in the research.

Serious Adverse Event (SAE) is any adverse event that

(1) results in death;
(2) is life-threatening;
(3) results in inpatient hospitalization or prolongation of existing hospitalization;
(4) results in a persistent or significant disability/incapacity;
(5) based upon appropriate medical judgment, may jeopardize the participant's health and well-being and requires hospitalization, other mental health or medical stabilization, child protection services or other higher level of care.

Life-threatening means that the event places the participant at immediate risk of death from the event as it occurred.

Unanticipated Problem is defined as an event, experience or outcome that meets **all three** of the following criteria:

- is unexpected; AND
- is related or possibly related to participation in the research; AND
- suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Unexpected means the nature, severity, or frequency of the event is not consistent with either:

- the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or
- the expected natural progression of any underlying disease, disorder, or condition of the participant(s) experiencing the adverse event and the participant's predisposing risk factor profile for the adverse event.

7.8.5 Adverse Event Reporting Plan

Reporting Adverse Events to IRB:

If adverse events arise;

1. Study staff will inform their site PI and document the adverse event using an adverse event form and adverse event log (provided by lead site).
2. The site PI will determine if the adverse event meets the definition of a serious adverse event or an unanticipated problem, or only meets the criteria of an adverse event.
3. The site PI will report the event to their institution's IRB per their institution's guidelines for reporting.

At BMC, adverse events that are not unanticipated problems will be reported at the time of continuing review by the IRB. No other adverse events/serious adverse events are anticipated — any that arise and meet the definition of an unanticipated problem will be reported to the IRB within two business days of learning of the event if it is life-threatening. Other unanticipated problems will be reported within 7 days.

Reporting Adverse Event to Lead Site (BMC):

All adverse events must be reported to the lead site using an adverse event form.

For all adverse events,

1. The adverse event form and log should be emailed to the study PIs (Drs. Comer and Pincus) and the lead site manager at least 2 days prior to the biweekly study PIs meeting (which will include all site PIs).
2. Site PIs must disclose adverse events at the biweekly meeting for the purposes of informing all site PIs and discussing any potential trends that need to be addressed across the study.
3. The lead site will review all adverse events on a monthly basis to identify if any adverse event needs to be re-defined as a serious adverse event or unanticipated problem based on study-wide data and assess if any actions need to be taken as a result.

If the event meets the definition of a **serious adverse event**, an adverse event form should be emailed to the study PIs (Drs. Comer and Pincus) and the lead site manager **within 2 business days**.

If the event meets the definition of an **unanticipated problem**, an adverse event form should be emailed to the study PIs (Drs. Comer and Pincus) and the lead site manager **within 24 hours**.

7.9 Screening for Anxiety and Study Enrollment

All participating primary and secondary pediatric care clinics use either the 8-item PROMIS Anxiety Short Form v2[72–75], the Pediatric Symptom Checklist (PSC-17),[76] Generalized Anxiety Disorder (GAD-7),[77] and/or the Patient Health Questionnaire (PHQ-9)[78] to initially screen for elevated anxiety in their patients. These screenings are part of standard practice at the participating sites. Sites will not be required to receive consent to screen because the screen is part of standard of care at either the primary care or behavioral health level. For clinics only using the PHQ-9 (which provides a depression score) for initial screening of potential internalizing problems, elevations are to be followed-up with administration of a validated anxiety assessment. These screenings are part of their standard practice so every child is screened for anxiety related symptoms at every visit. Youth in participating primary and secondary pediatric care settings who show elevated anxiety scores are referred to integrated or co-located behavioral health teams in their hospital for information about the Kids FACE FEARS trial. Families at the participating primary and secondary pediatric care clinics who voice concerns about youth anxiety (regardless of screener scores) are also to be referred to integrated or co-located behavioral health teams in their hospital for information about the trial and potential eligibility evaluation. All sites have the option to refer patients to the study directly. HIPAA waivers have been secured to access (but not store) screening data for the purposes of identifying and contacting potential study participants. Such referral and permission are documented through each pediatric health setting's internal mechanism(s) for referring families to ancillary services and case management. The

overall goal is to align referral and consent as closely as possible with existing workflows to reduce staff/family burden and to support sustainability. Primary and secondary pediatric care providers and staff should be educated about the study to increase project awareness and facilitate referrals. Sites are not required to receive consent to screen because screening is part of standard care. When a family is referred to the study, a Kids FACE FEARS staff member contacts them to inform them about the study, answer any questions, review eligibility (see Eligibility), and enroll them if interested and eligible. Once the patient is referred to a behavioral clinician, the clinician will use the 8-item PROMIS Anxiety Short Form v2 as a secondary screening measure as part of standard practice.

Research staff at some sites will also routinely review behavioral health and psychiatric clinic referral queues in the electronic medical record (a list of patients referred to behavioral health/psychiatry by providers at primary care and affiliated pediatric practices) to check for referrals to anxiety treatment. The research staff at sites will follow up with the patient's referring providers, or clinical staff responsible for reviewing and triaging referrals, to provide more information about the study and request permission to follow up directly with patients about the study. Once permission is received, staff should follow the same screening procedures outlined under the "direct referral" pathway in the MOP.

Different sites may have varying referral mechanisms. However, all sites will obtain permission from the guardian or 18-year-old, or their clinical provider, prior to contacting study staff about the eligible child.

A positive PROMIS 8a Anxiety v2 Short Form screen is defined as a T-score above 55 which is:

A raw score of 17 or above on the pediatric parent proxy
Or
A raw score of 19 or above on the pediatric self-report

A positive screen using the PSC-17 is defined as:

An internalizing score of 5 or above
Or
Responding to item 15 ("worries a lot") with "sometimes" or "often"

Participant recruitment will be very closely monitored on a monthly basis. If the enrollment and randomization rate across the study falls short for any consecutive two-month period (i.e., <90% of the targeted goal for each two-month period) investigators will evaluate the underperformance, and may shift allocation of funds as necessary to sites that are meeting

recruitment numbers to ensure milestones are met.

7.10 Enrollment

7.10.1. Eligibility Determination

Below are the steps completed for each participant before they are deemed eligible for the study:

1. The participant is identified as potentially eligible (step 1 of eligibility) by clinician or through standard of care screening (refer to Section “Screening for Anxiety and Study Enrollment”).
2. The participant is invited to participate in the study by their pediatric clinician and referred to the study.
3. The local RA reaches out to the participant to initiate consent and enrollment procedures.
4. The local RA completes the eligibility assessment screening form on REDCap to determine if they meet inclusion criteria and do not meet any exclusion criteria (step 2 of eligibility).
5. The participant completes their baseline assessment and has their final eligibility screening (step 3 of eligibility).
6. The participant is deemed eligible.

<u>There are 3 steps for screening in this study to confirm eligibility:</u>

Eligibility 1 – Standard of Care

<u>Screening in pediatric health site for potentially eligible patients:</u>

The screening procedure for the first step of eligibility is a standard of care procedure already being implemented at all participating sites. All sites participating in the study will either screen in waiting rooms using the (1) PROMIS or (2) other standardized behavioral health screening to refer to the study, or (3) refer directly to the study based on clinical judgment. For all 3 avenues of referral, the patient will have an initial screening using the PROMIS scale before referral to the study. These patients will be identified as potentially eligible and invited to the study by their pediatric clinician.

Eligibility 2 – Eligibility Screening Form

Screening after referral to the study:

This screening form will be completed by RAs with patients after they have been referred to the study to determine if they meet the study's inclusion criteria and do not meet any exclusion criteria. If it is identified that the patient requires a higher level of care, the safety protocol will be initiated and a clinician will follow-up to decide if this treatment is appropriate for this child and if they can be enrolled in the study.

Eligibility 3 – Research Assessment

Screening to determine final eligibility of study participants:

Final determination of eligibility will be based on the participant's PROMIS score from their baseline assessment. After a participant gives consent to participate in the study and completes the eligibility assessment, they will complete baseline assessment which includes the PROMIS measure. If either the parent-proxy or self-report score at baseline is positive, they will be deemed eligible for the study.

A positive PROMIS 8a Anxiety v2 Short Form screen is defined as a T-score above 55 which is:

A raw score of 17 or above on the pediatric parent proxy

Or

A raw score of 19 or above on the pediatric self-report

Randomization Determination

Once a patient is referred to the study, the following procedures will be initiated to enroll the participant, confirm eligibility, and randomize the participant. In order to be randomized to the study, the RA must confirm that the following procedures have been completed with the participant:

a. Eligibility Screening Procedures
b. Informed Consent Procedures
c. Baseline Assessment Procedures
d. PARS Baseline Procedures
e. Clinical Intake Procedures

Once these procedures are complete, randomization procedures are automatically initiated.

Each site will provide a workflow for their recruitment procedures that includes eligibility assessment and informed consent procedures, baseline assessment, PARS assessment, and clinical intake. This workflow will be shared with the lead site and any changes will be reported within a week of implementing the updated workflow.

7.10.2 Eligibility Screening Procedures. Once a referral is sent to the on-site research team for eligible families who are interested in participating and have a positive PROMIS score (eligibility 1), the research staff will complete an eligibility screening to determine if they meet inclusion criteria. The research staff member will first read the brief screening consent script and get permission to screen the patient. Once they have received permission to screen, they will complete the screening form on REDCap. This data will be collected on REDCap with no identifying patient information but the research staff at the clinic will hold the screen ID for eligible and interested patients to link the screening form to the patient. Sites will request a HIPAA waiver to access screening data to identify and contact potential study participants. If the participant meets inclusion criteria and does not meet any exclusion criteria, the research staff member will continue to informed consent procedures.

7.10.3 Informed Consent Procedures. Consent can be done in person, on the phone, or via videoconference using Zoom software. Research staff will meet in-person with the family to complete informed consent while in the clinic when both research staff and family are able to do so, or families will be consented by phone or videoconference using Zoom later (i.e., because family could not stay in clinic to provide informed consent or research staff were not present on site).

Research staff will attain assent for patients under the age of 18. Sites will follow their local IRBs policy for attaining assent for minors. Sites will also follow their institution’s policy for re-consenting child participants in the study who turn 18 while in the study.

For patients who choose to designate a coach who is not their parent, the coach will be consented over the phone. On site clinical staff will not be involved in the research consent process as that is the responsibility of the PIs with the help of designated research staff.

If consent procedures are done in-person, site staff will also request a HIPAA agreement during the time of consent to access patient’s diagnostic history coded in their medical record at clinical assessment. If consent procedures are done over the phone, the site coordinators will request a HIPAA agreement over the phone and collect the participant’s signature via REDCap. If the site’s IRB requires a signed paper HIPAA agreement, site coordinators will work with clinic staff to find a time to meet with the participant in person to request a HIPAA agreement, or

All sites will have site-specific consent forms approved by their local IRB. These forms will be uploaded to REDCap to capture consent electronically. If local IRBs require paper consent forms, sites will be able to document that consent was attained on REDCap so the lead site can track enrollment centrally.

BMC will request an alteration of consent for children turning 18 years old while enrolled in the study. BMC RAs will call children who turn 18 and read them a short script describing what the study and what they have given assent for previously.

The procedures for attaining consent are outlined in the Manual of Procedures in the Informed Consent section. These procedures include consent for guardians and adult patients, assent for minors, and consent for coaches.

7.11 Baseline Assessment Procedures

As part of enrollment procedures, the participant must complete the baseline assessment. Baseline assessment will be completed by the participant with an RA in person or over the phone after consenting to be in the study. If participants are unable to complete the assessment at that time, they will be emailed a REDCap link to complete the assessment at another time.

Research staff will call the participant at least every week for a month after the participant has given consent to remind them to complete the assessment, or to complete their baseline assessment with them over the phone. If the patient does not receive the call, research staff will leave a message using the message script. Research staff should stop follow-up calls after 1 month if the participant still has not completed baseline assessment.

For a child under the age of 13, it is necessary to have the completed parent baseline assessment for randomization. For a child ages 13 or over, it is necessary to have the completed child baseline assessment for randomization. The local RA should aim to facilitate the completion of both parent and child baseline assessments. In each family, if one subject has completed baseline but the other has not (i.e. the parent completed baseline but the child did not), continue to follow up with the family for 2 weeks to have the other complete baseline assessment. After 2 weeks, even if the other subject has not completed their baseline assessment, proceed with randomization of the family only if the necessary assessment has been completed (parent baseline for children <13 and child baseline for children ≥13).

If the participant completes the assessment and their PROMIS score in the baseline assessment is negative, they are no longer be eligible for the study. The RA will notify the

participant of their ineligibility, and a clinician will follow-up with them to discuss other treatments.

7.11.1 PARS Baseline Procedures. As part of baseline assessment and enrollment procedures, the participant must complete the PARS assessment with a trained clinical therapist, post-doc associate, graduate student, or a research staff member. This assessment must be completed after the participant has given consent to participate in the study. Sites may designate a clinician or research staff member to administer PARS at the site, or choose to have a central trained assessor at BU or FIU complete PARS with the participant. The PARS assessment can be administered in-person at the site, over the phone, or via videoconference using Zoom.

7.12 Clinical Intake Procedures

As part of the enrollment procedures, the participant must complete a clinical intake with a clinical therapist to determine the patient's clinical condition and if outpatient CBT is an appropriate level of care for the patient. Participants will complete the designated program based on their age (Cool Kids for 7-12 year olds, and Chilled for 13-18 year olds).

7.13 Randomization Procedures

Once a participant has completed all 5 procedures necessary to be randomized, the local RA will complete a randomization form in REDCap to document and confirm that all procedures have been completed. Once all procedures have been documented, the form can be submitted, and the random assignment will be released. Randomization assignments are made centrally at the FIU data coordination site. Families are randomly assigned to one of the two treatment conditions by randomization software programmed to stratify assignments by Site (Baltimore, Boston, Miami, or Seattle), Language of Treatment (English or Spanish), and Age (7-12 years or 13-18 years). An automated push notification is sent that reveals the family's assigned condition simultaneously to the FIU data management team (for data recording purposes) and to the research coordinators and clinical team at the participant's site (to orient the family to their assigned treatment condition). The local RA will report the result to their clinical team and to the participant.

7.14 Assigned Diagnoses Form

In order to complete an Assigned Diagnoses Form, the clinic site must have a signed HIPAA authorization agreement from the participant. The participant can refuse to give HIPAA authorization and still continue to be in the study.

The local RA will review the HIPAA authorization agreement with participants once they have given consent to enroll in the study. If the participant agrees, a link to the REDCap HIPAA authorization form will be emailed to them for their signature. If the site IRB does not allow collection of their signature via REDCap, the local RA will work with the clinic team to identify a day to review a HIPAA authorization agreement form with the participant in person. If the participant agrees, the form needs to be signed by the participant and stored in a secure filing cabinet. Once an RA confirms on REDCap that a HIPAA authorization agreement has been signed by the participant, the assigned diagnoses form will be available in the participant's REDCap record to be completed by the therapist or RA.

A local RA will access diagnostic information via the participant's medical record to complete the assigned diagnoses form on REDCap or the participant's therapist will complete the form as part of their session 1 log. If the form has been completed by an RA on REDCap, the therapist will go into their session form for the first visits, click submit at the bottom and will move onto the Assigned Diagnoses Form. They will see that the form has already been completed and can just click submit. If the form had not been completed by an RA, the therapist will click on the link to complete their log for the first visit and will be redirected to the Assigned Diagnoses form where they can fill out the form.

7.15 Study Visits, Therapeutic Contacts, and Assessments

7.15.1 Study Visits and Therapeutic Contacts. Participants will have different points of contact with therapists and different modes of follow-up according to which study arm they are assigned to. The scheduling and coordination effort for therapy delivery and check-ins for the self-paced online version will be conducted at individual sites.

7.15.1.1 Therapist Contacts During the Treatment Phase for Guided Online CBT Participants. Before the beginning of treatment in the guided online CBT arm, the following points of engagement must occur:

1. The therapist providing supportive accountability for the case must reach out to the patient over the phone or online to introduce themselves to boost patient engagement.
2. A technical orientation on the self-paced online program must take place with the participant. The technical orientation will be conducted using tools provided by the lead site. This orientation will go over how to navigate the program and who to contact with technical issues. This orientation can be conducted in-person, over the phone or via videoconference using Zoom software. The participant will always be

given the option to either attend the orientation in-person, on the phone, or via videoconferencing.
3. Participating families in this condition are given up to 20 weeks (i.e., the treatment phase) to complete their treatment program.
4. The therapist will work with the participant (and/or their family) to schedule check-in calls every 2 weeks. Throughout the duration of the program, these check-in calls will be held with the family or caregiver for children ages 7-12, and will be held with the child for children ages 13-18.
5. The participating family is guided to complete one self-administered module of the program each week. Families are encouraged to revisit and review completed modules as frequently as they wish.
6. The therapist will call the guardian and/or child every 2 weeks to check-in and provide supportive accountability. For each scheduled check-in/supportive accountability call, therapists should make at least 3 attempts to contact the family.
7. Therapists are to complete will complete a brief session log on REDCap after every check-in/supportive accountability call.

7.15.1.2 Therapist Contacts During the Treatment Phase for Therapist-led CBT Participants

1. Participating families in this condition are given up to 20 weeks (i.e., the treatment phase) to complete their treatment program.
2. Each therapy session should be scheduled for 50-60 minutes. Therapists are advised to schedule families for roughly one therapy session per week.
3. Therapists can schedule multiple sessions a given week to help “catch up” if cancellations, missed appointments, holidays, or schedule breaks places them behind schedule.
4. Therapists are to complete will complete a brief session log on REDCap after after every treatment session.

*All clinics will work with their team to establish a workflow that is conducive to the procedures established above. This workflow will be shared with the lead site and any changes will be reported within a week of implementing the updated workflow.

7.15.1.3 Therapist Session Logs

Therapists will be required to complete a session log on REDCap after every session with study participants. The session log will include a checklist to record the skills/content covered in that session. At the point of randomization, FIU will generate a link that is specific to the participant and send this link to the site RA. The RA will send the link to the

participant's therapist with the name of the participant. The therapist is responsible for keeping this link and accessing it to fill out the log after every session.

7.15.2 Midtreatment, Posttreatment, and Follow-up Assessment Procedures

Florida International University (FIU) will be responsible for emailing a link to participants to complete the midtreatment, posttreatment, and follow-up assessments. Specifically, all randomized families are invited to complete a midtreatment assessment (consisting of caregiver- and youth self-report questionnaires) once they complete half of their allocated treatment. Families who do not complete half of their allocated treatment by the end of the second month of their treatment phase are invited to complete a midtreatment assessment at Week 8. All randomized families are then invited to complete a posttreatment assessment (consisting of caregiver- and youth self-report questionnaires) once they fully complete their allocated treatment program. Families who do not complete their allocated treatment program by the end of the fifth month of their treatment phase are invited to complete a posttreatment assessment at Week 20. All randomized families are then invited to complete a follow-up assessment at Week 52 (consisting of caregiver- and youth self-report questionnaires). Families will be emailed 2-4 weeks ahead of their follow-up assessment target date (i.e., 2-4 weeks before week 52).

BMC and FIU RAs will assist all sites in conducting follow-up calls to participants in order to increase assessment completion rates. A reminder email will be sent to the participating family by FIU to complete their assessment every 4 days for at least 2 weeks (or until the assessment is complete). FIU RAs will run weekly reports off REDCap to see which participants have not completed their assessments and inform local RAs of which of their participants have outstanding data. If a participant has not completed their assessment after 2 weeks, the RA from the participant's site will call the participant in an attempt to complete the assessment over the phone. For posttreatment assessments, RAs should stop reminder contacts to participants when the participant 8 weeks after the assessment is initially emailed to them. At this point, the posttreatment assessment point is considered missing. For follow-up assessments, RAs should stop reminder contacts to participants 8 weeks after the assessment is initially emailed to them.

7.15.3 Posttreatment PARS

PARS assessments will be completed at posttreatment for each family by central assessors at FIU, BU, or BMC who are masked to treatment assignment.

7.15.4 Retention and Study Compensation

Based on similar studies conducted in usual care settings that do not provide free study treatment, we expect roughly 30-50% attrition by the final follow-up timepoint, and roughly 10% of data points to be missing with each collected timepoint. REDCap surveys will be configured to minimize missing values (e.g., requiring participants to complete each item, or explicitly indicate “refuse to answer” before proceeding to the next item; providing real time alerts to the data management team when items or entire forms are missing). Data will additionally be checked on a weekly basis by a research supervisor, and patterns of missingness will be identified and corrected in real time throughout the study. To further reduce instances of missing data, we have kept the number of study forms to a minimum in order to minimize the burden to participants, and participants will be provided compensation for their time completing study forms. Finally, participants will be compensated for the burdens of completing study assessments (see below).

Given the aim to evaluate treatment engagement and performance under typical circumstances, families are not compensated for participating in treatment. To ensure generalizability and observe the treatment comparators under natural conditions, treatment is not funded by the study nor offered for free. Rather, treatment is to be paid for via the natural channels of payment in the participating health centers (e.g., insurance and co-payments). In contrast, families are compensated for participation in study assessments that are not part of the treatment comparators under study. Specifically, families will receive the following compensations for completing various study assessment components:

a. $50 for baseline assessment (staggered payments: $25 following baseline questionnaires and $25 following baseline PARS completion)
b. $25 for midtreatment assessment
c. $50 for posttreatment assessment
    i. $30 additional compensation for completing posttreatment PARS assessment
d. $100 for completing follow-up assessment

*Coaches (who are not guardians) will not receive compensation for the assessments they complete. Compensation will only be provided to the youth and guardian informants. One ClinCard that will be loaded with the above payments will be given to each family for each child enrolled in the study.

Automatic email reminders and weekly emails and phone calls from Kids FACE FEARS staff members should be used to increase participation in study assessments. Families who do not complete the baseline assessment are not randomized. Families who do not complete

their assigned treatment are still invited to complete all subsequent evaluations (i.e., midtreatment, posttreatment, and follow-up evaluations).

FIU will run weekly reports to see which participants have completed their assessment and send this report to BMC. The lead site RA will load the appropriate compensation amount onto the participant's ClinCard as each of the assessment points is complete.

7.16 Statistical Considerations

Study results will be reported according to CONSORT guidelines.

7.16.1 Sample size determination. Power analysis to determine the appropriate sample size for the trial had to take into account data clustering and repeated measurements. Study data were clustered in multiple ways, resulting in non-independent observations and inflated type I error. First, there were multiple observations per child due to the repeated measures design with four major assessment points. Second, there was additional clustering due to multiple children from each site. The intraclass correlation (ICC) is a quantitative estimate of clustering and allows for adjustment for non-independence. Study investigators estimated an ICC of .5, meaning it was anticipated that 50% of the variation in the observations would be due to differences between individuals and between sites (the remaining 50% of the variation was assumed to be due to individuals varying in their responses over time). The design effect (DE) reflects the extent to which standard errors are deflated if clustering is ignored. The DE is equal to 1 + (m – 1) × ICC, where m is the number of repeated measures. Accordingly, with 4 time points and an assumed ICC of .5, the design effect was calculated to be 2.5. Any sample size estimate must be multiplied by 2.5 in order to obtain a sample size appropriate for the observed clustering while maintaining nominal alpha and power levels.

The required study sample size was calculated via conventional methods for repeated measures / mixed models analysis. Required sample size is a function of the alpha (type I error rate) and beta (1 – power) values. Required size per group is: $n = 2 * (Z_{1-\alpha} + Z_{1-\beta})^2$. Before adjusting for the DE, these computations found n=60 was required in each group for an alpha=.05 (assuming family-wise error rates=.05 across the study to account for multiple comparisons) and power=.8 (corresponding to beta=.2). After adjusting for the DE of 2.5, this power analysis indicated n=150 was required per group (60 × 2.5), for a total of N = 300.

The needed sample size of N = 300 (outlined above) was based on the primary comparative effectiveness tests of this study (Aim I). That said, a sensitivity analysis was also conducted to evaluate the magnitude of effects that could be detected in moderation analyses

examining heterogeneity of treatment effects (Aim II). These analyses were conducted with G*power using the repeated measures analysis of variance (ANOVA) test. Repeated measures ANOVA is similar to a mixed model in some respects, but simpler and uniformly less powerful[80] using the repeated measures ANOVA, therefore, offers a conservative estimate of the effects able to be detected with each mixed model. With N = 300, alpha = .05, power = .8, two treatment conditions, four measurements, and a correlation between repeated measures of .5, the trial was powered to detect moderation effects as small as Cohen's *d* = 0.068. This is 7% of a SD difference and a very small effect.

7.16.2 Handling of Missing Data

7.16.2.1 Prevention and monitoring. All study data will be collected via electronic capture and communication directly with the study team. Based on similar studies conducted by our group and in related research in similar settings, we expect roughly 10% of data points to be missing. REDCap surveys will be configured to minimize missing values (e.g., requiring participants to complete each item, or explicitly indicate "refuse to answer" before proceeding to the next item; providing real time alerts to the data management team when items or entire forms are missing). Data will additionally be checked on a weekly basis by a research supervisor, and patterns of missingness will be identified and corrected in real time throughout the study. To further reduce instances of missing data, we have kept the number of study forms to a minimum in order to minimize the burden to participants, and participants will be provided compensation for their time completing study forms. Finally, participants will be compensated for the burdens of completing study assessments at a rate of $50 for baseline assessments (including PARS) and, $25 for midtreatment assessments, $50 for posttreatment assessments (including PARS), $100 for week 52 assessments and $30 for completion of PARS at posttreatment (note: compensation will not be provided for completion of measures that will be included as part of routine care). Coaches will not receive compensation for the assessments they complete.

7.16.2.2 Statistical handling of missing data. All analyses will consist of intention-to-treat models drawing on all available data. To account for missing data, we will employ multiple imputation. Recommended procedures for single and multilevel multiple imputation will be conducted using BLIMP software, using fully conditional specification multiple imputation (FCS-MI). For each model, 50 datasets with imputed values will be created using other model covariates as predictors of missingness. Model convergence will be assessed across 8 Markov Chain Monte Carlo (MCM) processes and verified for potential scale reduction (PSR) factor<1.05. Main analyses will be conducted on the imputed dataset and the results will be pulled for final estimates (using R 4.4.1 mitml for imputation pooling per Rubin's rules, and lme4 for multilevel models, or lm and glm for linear and logistic regression models).

7.16.2.3 Reporting dropout and missing data. All instances of study dropout will be documented, including the reason for dropout, who decided that the participant would drop out (i.e., parent or guardian, therapist, study staff, adolescent patient), and whether the dropout resulted from burden of intervention, study assessment, or both. Withdrawn participants will be encouraged to continue to participate in study assessments throughout the follow-up period in order to optimize intention-to-treat models. A CONSORT diagraph will account for all participants across the study.

7.16.2.4 Loss to Follow-up and Withdrawal from Treatment. This study will be using an intent-to-treat analysis so once a participant is randomized, they will always be included in analysis. If participants do not complete their entire treatment program (or withdraw from treatment) or take longer than 20 weeks, all post and follow-up assessments will still be sent to them at the indicated time points and local RAs will still perform follow-up procedures to assist with data collection.

7.16.3 Covariates

Covariates for each model will include site, language of care, youth age, youth gender, youth race, youth ethnicity, and family resource insecurity (see Measures)

7.16.4 Primary analyses: Comparative effectiveness analyses. For primary analyses on continuous outcomes that were measured across the 4 major timepoints (e.g., caregiver- and youth-reports on the PROMIS Anxiety Scale, CALIS), mixed models of change[144] will be run separately for each outcome. Mixed models are preferred for longitudinal designs because they allow for individual estimates of change and have robust power in the presence of missing data and attrition.[145,146] Covariates for each model will include site, language of care, youth age, youth gender, youth race, youth ethnicity, and family resource insecurity (see Measures), and any other baseline variables found to significantly differ across participants in the two conditions. The random effects of intercept (reflecting individual variation in mean outcome level) will be assessed. The fixed effects of Treatment Condition, Time, and the Treatment × Time interaction will be analyzed in the prediction of change. We will examine non-linear models of change (i.e., log transformations of Time), which afford examination of symptom trajectories across time that are not gradual and incremental (e.g., steep improvements during initial weeks of treatment, followed by a slowing down of improvements toward the end of treatment, and then relative stability across the follow-up time interval). To aid interpretation of the meaningfulness of between-group differences, Cohen's *d*'s will be computed for each continuous outcome on model means at post and follow-up.

For primary analyses on the dichotomous categorical outcomes PARS Treatment Responder Status at posttreatment, baseline PARS scores will be examined for each participant to determine their individual thresholds for classification as Treatment Responders (i.e., 35% PARS score reduction). These thresholds will be used to classify each participant's statuses as posttreatment. Logistic regression models will examine Treatment Condition (along with the study covariates) as a predictor of Treatment Responder Status and Remission Status at post. For primary analyses on continuous outcomes of Treatment Satisfaction at post, linear regression models will examine Treatment Condition (with the study covariates) as a predictor of caregiver- and youth-reported posttreatment satisfaction.

7.16.5 Heterogeneity of treatment effects. For Aim II analyses (heterogeneity of treatment effects) predictor and moderator terms will be added to the models predicting youth anxiety severity that were outlined above. For study covariates being considered as predictors/moderators (e.g., language of care, youth age, youth gender, youth race, youth ethnicity, and family resource security), this will entail only adding interaction terms, as the main effects of these variables will already be in the models. For the additional variables considered as treatment moderators that are not already included as model covariates (e.g., caregiver nativity) this will entail adding main effects and interaction terms to the models. For each model examining heterogeneity of treatment effects, the relevant terms of interest will be the 2-way interaction of Variable × Time (reflecting whether the variable uniformly predicted change across the two treatments) and the 3-way interaction of Variable × Treatment Condition × Time (reflecting whether the variable moderated treatment effects; i.e., whether the variable predicted differential response across the treatments). As with the Aim I comparative effectiveness analyses, log transformations of Time will be entered to consider non-linear models of change. Significant interactions will be followed up with post-hoc probing on subgroups to clarify the nature and direction of interaction, and results will be plotted for visual depiction.

7.16.6 Facilitators and barriers. Descriptive statistics will be run for models exploring facilitators and barriers to care and implementation (Aim III). These models will include the same covariates as outlined for Aim I and Aim II analyses. Treatment Condition will be added as a predictor in models comparing whether facilitators and barriers differ between the two treatment comparators.

7.16.7 Interim Analysis. Interim descriptive data will be summarized each year for the investigative team. Our team will conduct analyses as required for the reporting of findings in peer-reviewed manuscripts and at conferences, and will assist with editing and writing manuscripts.

8 – Ethical Considerations

8.1 Ethical Considerations

Recruitment and retention strategies: This study is designed as a pragmatic trial. To maximize external validity, CBT for child anxiety will be integrated into routine clinic workflows and all children ages 7-18 years, with exception of those meeting minimal exclusion criteria described below, will be eligible.

Retention strategies for CBT trial, data collection and follow-up assessments: Families will provide primary and additional contact information and will be provided with reminders for appointments and assessments. Modest patient incentives ($25-50) over the course of study participation at each data point will be provided for completing assessments.

Exclusion Criteria: The intervention is suitable for patients ages 7-18 with elevated anxiety under consideration for outpatient psychological treatment. In this pragmatic trial, study entry criteria is very inclusive, so most anxious children with other problems are not excluded. However, children will not be able to participate if they are acutely at risk, if they require a higher level of care, or if they have developmental delays or intellectual impairments with very severe challenges (e.g., complete absence of verbal communication unrelated to anxiety).

Involvement of vulnerable populations: The study will recruit children between 7-18 years and a parent or legal guardian. It will not involve prisoners or institutionalized individuals. The study could involve four populations considered to be vulnerable: pregnant women, children, and non-English speakers. As detailed elsewhere, we will obtain informed consent, child assent where applicable based on the child's age, protect confidentiality, prevent undue influence and coercion, and protect against risks of the study.

- Pregnant women: Although the study will not specifically target pregnant women, given that the study enrolls young children and their families, it is possible that a participant could be pregnant. Such women will not be excluded. Women of childbearing potential will be entitled the same protections as listed above. We foresee no extra risk for a woman of childbearing potential relative to other participants.
- Children: This research targets youth with elevated anxiety. Parents between the ages of 16-21 who are the legal guardians of the child referred for assessment, will not be excluded based on age; thus it is possible that we will enroll parents who are under 21. Young parents often face additional barriers accessing health services for

their children. For this reason and because according to state law in the study jurisdictions, we plan to enroll parents in this age group. We have enrolled such parents in previous studies, which were reviewed and approved by the IRBs at each of our institutions and without any adverse events. Therefore, we are confident that protocols for the proposed research will be ethical, lawful and will be approved by the participating institutions' IRB.

- Non-English speakers: We include non-English speakers (Spanish speakers) in order to address the need for research and an evidence base for effective treatments in this population. All materials, modules, and general resources presented to participants will be available in Spanish. We will have Spanish speaking RAs conducting screening and assessments who will also be available to answer any questions participants have. Additionally, many of our therapists are Spanish speakers. We are confident that our study will have enough resources and staff available to Spanish speakers to ensure the ethical conduct of research.
- Children and Parents Involved with DCF: Children who are wards of the state will be excluded. Children who are involved with DCF will still require us to obtain informed consent from the legal guardian and permission from DCF prior to study enrollment. A caregiver confirmed to be safe by DCF must be available to voluntarily participate along with the youth as already outlined in the protocol for all youth/ family participants. We will not include study participants who are mandated to treatment. We will follow all applicable laws for including children and parents who are involved with DCF.

Research Sites: The settings for the proposed project are Academic Medical Centers and Community Health Centers. We will collect data from all of these sources via de-identified, coded data in REDCap.

Material to be collected. The study will not make any use of biological specimens. Investigators will gather data from the following sources: (1) Patient and family reported measures; (2) Semi-structured interviews; (3) Provider fidelity measures; (4) therapist engagement logs; (5) administrative data and patient records.

Access to individually identifiable private information. All research staff will complete CITI Human Subjects Training and Child Protection Training. Only study staff completing training in HIPAA regulations and human subjects protections will have access to study data. For all sources of data, with the exception of the interviews, all identifying information will be removed and names replaced by ID codes. Furthermore, identifying information will not be shared with others outside this study. Names and contact information for each participant will be stored in REDCap separate from project data. Project data will only be linked to the patient's record ID. For the interviews, only names, phone numbers, and site information will be available to the qualitative team to contact participants and conduct interviews.

Transcripts from interviews will be identified by ID codes and identifying personal information will be masked. Cross-reference listing of this contact information for the subset of interviewees will be kept in password-protected encrypted files on secure servers.

Data collection, management, and protection. Research Electronic Data Capture (REDCap) located at Boston Medical Center will securely collect research data from across all four study regions, and Boston Medical Center will be responsible for overseeing the integrity and security of the data. REDCap is a scalable, web-based electronic data capture system that allows the investigative team to build online surveys and databases and input remote data over a secure web connection (a SSL certificate is required). REDCap features *authentication*, *auto-logout setting*, *data logging* (audit trails for tracking data manipulation and export procedures), *user privileges* (each user only has access to granted projects; privileges are granular on the project level, e.g., being able to export, enter, add or modify database metadata, to build/run reports, to modify user privileges, to view logs, etc). REDCap can be used to collect data for 21 CFR Part 11, FISMA, and HIPAA-compliant environments, and is specifically geared to support online or offline data capture for research and operations. The Data Services Group of the FIU Center for Children and Families (CCF) will have continuous 24/7 access to the data as well as project administration rights in order to fully execute their duties of data management, monitoring, and analysis.

Planning, configuration and end-user support for REDCap will be provided by BU and the Data Services Group of the CCF. To help protect and secure the data stored in REDCap's database, the software application employs several methods to protect against malicious users who may attempt to identify and exploit any security vulnerabilities in the system. Access to the REDCap data entry website will be based on permissions granted by username and password which will be managed by the Boston University Clinical and Translational Sciences Institute for the Medical Campus Office of Information Technology. Only authorized study members will be able to enter or view data. The login information (username) of the person submitting the information, the date and time submitted, and other navigational information will be automatically obtained and stored in the database. Information posted on forms will be electronically encrypted using secure socket layering (SSL) encryption technology so that only the intended recipient can decode the data. Data will reside on a secure, password protected server at Boston Medical Center (BMC) to which only designated individuals have access, thus providing a secure environment for all project data. The database will be automatically backed up on a nightly basis. Files stored on BMC servers will be protected by electronic 'firewalls' that restrict access to designated users. Restrictions and permissions to update the database will be controlled through the REDCap web application.

Non-BMC sites will be able to access the REDCap system after submitting an end user agreement. A Boston University REDCap account will be created for them and the BMC team will be responsible for giving users a customized level of project access. In particular, the Data Services Group of the FIU Center for Children and Families (CCF) will have accounts created for them and will have continuous 24/7 access to the data as well as project administration rights in order to fully execute their duties of data management, monitoring, and analysis.

8.2 Ethical considerations and Institutional Review Board (IRB) Review

This study is to be conducted according to applicable US federal regulations and institutional policies (which are based in federal regulations, guidance, and Good Clinical Practice guidelines). This protocol and any amendments will be submitted to the Boston Medical Center and Boston University Medical Campus IRB, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator. A copy of the initial IRB approval letter will be provided to the sponsor.

All participants for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The consent form will be submitted with the protocol for review and approval by the IRB. The consent of a subject, using the IRB-approved consent form, must be obtained before that subject is submitted to any study procedure. Consent will be documented as required by the IRB.

This protocol was made in accordance with Boston University/ Boston Medical Center IRB policies and will be reviewed by the institution’s IRB. The study's clinical sites in Boston will be overseen by Boston Medical Center's IRB. Regional sites will submit separate IRB applications using the study protocol and site specific forms to their respective institutional IRBs for approval according to their institutional policies. Oversight of clinical sites outside of Boston will be conducted by their respective IRBs. IRB oversight is by the respective IRBs with overall oversight from the study PIs as well as regional co-PIs.

8.2.1 Potential Risks. We do not foresee any physical, legal, or financial risk for any of the study participants in Aims I, II, or III.

Potential risks are psychological and the need to protect confidentiality

- Because the research covers the topic of mental health and potential psychosocial stressors participation may be emotionally distressing to individuals in the study.
- Although we will strive to maximize cultural sensitivity in delivery of the proposed intervention, it is possible that, among parents, their explanatory models of their

child's condition will be incompatible with our proposed interventions and even assessments, which may upset some participants.

- A potential risk to participants is potential loss of confidentiality. Although data will be stored in a secure and confidential manner, and we will de-identified all stored data, accidental breaches of confidentiality are technically possible.

8.2.2 Adequacy of Protection Against Risk

Recruitment and Informed Consent. We will obtain parental permission and child assent for all enrolled families. Youth 18 years of age will provide their own informed consent. A written description of the study and other informational materials (in English, Spanish, and at appropriate literacy level) will be made available to all families to assist them in the informed consent process. For eligible families who are interested in participating, research staff will complete eligibility assessment and consent procedures. This could be done at the time of a positive screen in the clinic, later on the phone, or later in person depending on the preference and availability of the parent/patient. To mitigate risks, subjects will be given multiple opportunities to decline participation. They will be advised of their right to refuse participation in all or any part of the research. Families who decline to participate will still be offered usual clinical services at the participating clinical setting. All participants will be assigned a numerical code and only project personnel will have access to a file linking names/contact information and ID codes. Research data will not include identifying information and will be encrypted and electronically stored on a password-protected study server.

To provide additional protections, we will assure that the investigative team has the appropriate expertise to deal with children and parents. Study facilities will be appropriate to children, as these facilities will be either families' homes or pediatric healthcare sites. We will make sure that all psycho-educational materials, treatment plans are written in a straightforward manner, at the appropriate literacy level. We will use translators/language line as needed to further ensure parents fully understand study procedures and communicate concerns about their child's care. As all site staff and the investigators are mandated reporters, families will be informed that any disclosure of abuse, risk to a child or elder will need to be reported to the appropriate state protection agency. Endorsement of suicidality, risk to self or others will require emergency evaluation for safety and disposition by the clinical staff and RAs will have a contact at each site for reporting such disclosures and in order to activate the clinical protocol for these types of events.

8.2.3 Potential Benefits of the Proposed Research to Human Subjects and Others.

The potential long-term benefits of participating in this study outweigh the risks. All eligible

children who demonstrate anxiety symptoms during screening will receive evidence-based services that match or exceed those currently provided at the participating sites.

8.2.4 Importance of the Knowledge to Be Gained. This pragmatic comparative effectiveness trial will generate high-quality experimental data that can directly inform best practices in the CBT treatment of pediatric anxiety. The plan to test two models of CBT delivery (therapist-led vs. guided online care) in pediatric healthcare settings in which low-income, ethnically diverse children receive routine health care services will provide valuable information to pediatric care practices and integrated health networks about the potential benefits and barriers to implementing this type of intervention for children with anxiety. The results can provide rigorous evidence-based information to support patient and provider decision-making and patient-centered care.

8.3 Participants Confidentiality

All research staff will complete CITI Human Subjects Research Training and HIPAA Training. Only study staff completing training in HIPAA regulations and human subject's protections will have access to study data. Boston University Medical Campus' Research Electronic Data Capture (REDCap) system will securely collect and manage research data from across all four study regions. For all sources of data, all identifying information will be linked to ID codes. Boston Medical Center and the participant's site will have access to the participant's name and contact information. Identifying information shared across sites will be limited to sites that need some information for their role in the study. Sites will hold the master code for their participants and only coded data will be shared with other sites.

FIU will have limited access to identifiable patient information. They will only have access to patient participant names, emails, and phone numbers which will be linked to a record ID in a file that will be stored separately from any clinical data. Assessments will be sent to participants via email by the FIU research team. The FIU research team will have access to only record ID numbers, phone numbers, and emails in order to; (1) create login usernames for participants randomized to the web-based treatment which will be linked to their study ID number; (2) send assessments to participants via email and; (3) conduct follow-up calls for assessment completion across sites. PARS administrators at FIU will have access to participant's names and contact information in order to contact participants to complete PARS over the phone. FIU will have continuous access to the data and will be able to run weekly reports to see when participants have completed mid-treatment sessions/modules and post-treatment sessions/modules. In order to provide all sites with data collection support, the regional site PI, Jonathan Comer, and his project manager will have access to all data including identifiable data.

BMC will be responsible for; (1) setting up participant's ClinCards and loading compensation amounts onto the card and; (2) managing and providing assistance to sites and; (3) conducting follow-up calls for assessment completion across sites. BMC will run weekly reports to identify participants who have completed assessments to provide compensation to participants. In order to set up ClinCards, BMC will need access to the patient's participant number and contact information including name, address, date of birth. In order to provide technical assistance to participants and sites, the BMC team will also need access to participant emails, phone numbers, and login information. All other participant data shared with BMC will be coded.

The Cool Kids Online IT Support team will only have access to participants' name, email addresses, and Cool Kids login information. This team will consist of study assistants led by PI - Dr. Jonathan Comer – who will reply to emails from participants regarding technical concerns with the Cool Kids Online program. Participants will be able to send emails to an encrypted BU email account regarding their technical issue. The support team will have access to this account and will be able to directly reply to participants.

Our consulting team at Macquarie University will be providing technical support to the Cool Kids IT Online Support team with the Cool Kids online system. The Macquarie team's involvement with the study will be strictly for technical support and troubleshooting any glitches in the Cool Kids Online system where the Cool Kids IT Support team needs support. The team will only have access to participant's email addresses and login information.

Access to data involving therapist/staff participants will be very limited. To maintain confidentiality, all identifying information will be linked to ID codes. Only BMC will hold the master code for these participants and only coded data will be shared with other sites, including their own site. FIU will only have access to therapist/staff participant emails which will be linked to a record ID in a file that will be stored separately from any clinical data. Assessments (except baseline assessment) will be sent to participants via email by the FIU research team. FIU will have continuous access to the data and will be able to run weekly reports to see when participants have to complete assessments.

8.4 Data Quality Assurance

BMC will be responsible for overseeing the security and integrity of the data. At the outset of the study, personnel who will be using the systems for direct data capture will attend in-person or remote training (depending on geographical proximity). Study team members outside of the South Florida area will attend web-based training. The goal of the training is to ensure uniformity of procedures among personnel, to achieve the ultimate aim of ensuring high quality protocol implementation and data collection. Subsequent training for new staff and booster sessions for existing staff will be conducted via webinar. The FIU CCF data

team will also provide quality control procedures for data collection and data entry. The quality control measures that we shall implement include detailed and unambiguous specifications for completion of each of the data collection forms. The FIU CCF data team will also oversee and monitor randomization assignments and sequences.

The CCF data team will provide regular status updates regarding data collection. They will also provide regular statistical summaries to the investigative team that include reports on enrollment as well as the current status of each study participant.

8.5 Data Collection

All PROs will be collected over the phone or electronically (i.e., no separate office-visits will be required for the collection of study data).

Consent, eligibility assessment, and baseline assessment will be completed on a tablet (through the electronic, HIPAA compliant REDCap). However, different clinics may choose to slightly alter the process in order for it to fit their current workflows (i.e. conducting paper and pencil screening). In all clinics, paper screening forms will be available for patients/guardians upon request if they prefer and the data entered into REDCap by study staff. All data will be entered by study staff into the REDCap database and the paper forms will be securely stored in a locked cabinet.

The team at Macquarie University will collect non-clinical data related to participant use of the online program from the back end of the online Cool Kids program. This data includes participant’s login information, login times, content accessed at each login, module completion time, and their IP address. The study team will also have access to back end data from the online Cool Kids program that will be used for analysis including usage of program, clicks, and participant answers to questions.

Due to the pragmatic nature of the trial, we have designed the data collection protocol to be concurrent and as integrated as possible with clinical encounters and participant progression through the Cool Kids therapist-led and self-administered online versions.

8.5.1 Access to Data

Only study staff completing training in HIPAA regulations and human subject’s protections will have access to study data. After data collection is complete, the FIU CCF data team will work to create a data sharing file that comprises the following components and accompanying annotation: the protocol, REDCap user's manual, annotated copies of all forms used in the study, the schedule of assessments, the data dictionary providing data

attributes and descriptive statistics for each variable, the study database tables representing the captured and cleaned data, the analytic data tables and the programming statements responsible for any data recoding or subsetting, data summaries of each data table including descriptive statistics for validation of value integrity, and written description of the study conduct and noteworthy details anticipated to potentially affect data interpretation.

8.5.2 Data Storage/Security

BUMC's Research Electronic Data Capture (REDCap) system will securely collect and manage research data from across all four study regions. REDCap is a scalable, web-based electronic data capture system that allows the investigative team to build online surveys and databases and input remote data over a secure web connection (a SSL certificate is required). REDCap features authentication, auto-logout setting, data logging (audit trails for tracking data manipulation and export procedures), user privileges (each user only has access to granted projects; privileges are granular on the project level, e.g., being able to export, enter, add or modify database metadata, to build/run reports, to modify user privileges, to view logs, etc.). REDCap can be used to collect data for 21 CFR Part 11, FISMA (Federal Information Security Management Act), and HIPAA (Health Insurance Portability and Accountability Act)-compliant environments, and is specifically geared to support online or offline data capture for research and operations.

To help protect and secure the data stored in REDCap's database, the software application employs several methods to protect against malicious users who may attempt to identify and exploit any security vulnerabilities in the system. Access to the REDCap data entry website will be based on permissions granted by username and password which will be managed by the Boston University Clinical and Translational Sciences Institute for the Medical Campus Office of Information Technology. Only authorized study members will be able to enter or view data. The login information (username) of the person submitting the information, the date and time submitted, and other navigational information will be automatically obtained and stored in the database. Information posted on forms will be electronically encrypted using secure socket layering (SSL) encryption technology so that only the intended recipient can decode the data. Data will reside on a secure, password protected server at Boston University Medical Center (BUMC) to which only designated individuals have access, thus providing a secure environment for all project data. The database will be automatically backed up on a nightly basis. Files stored on BUMC servers will be protected by electronic 'firewalls' that restrict access to designated users. Restrictions and permissions to update the database will be controlled through the REDCap web application.

Non-BUMC sites will be able to access the REDCap system after submitting an end user agreement. A Boston University REDCap account will be created for them and the BMC

team will be responsible for giving users a customized level of project access. Planning, configuration and end-user support for REDCap (https://redcap.bumc.bu.edu/) will be provided by the Data Services Group of the CCF. The Data Services Group of the FIU Center for Children and Families (CCF) will have accounts created for them and will have continuous access to the data as well as project administration rights in order to fully execute their duties of data management, monitoring, and analysis. All data will be stored at BUMC.

All paper records will be stored in locked storage spaces (cabinets or drawers) at the participant's clinic site. Only study staff will have access to the key to get into these storage spaces. Participant forms will be stored in a single folder that is labeled with their respective study ID number.

8.6 Study Records

Study records will include consent forms and patient data. We will gather data from the following sources: (1) Patient and family reported clinical measures; (2) Provider fidelity measures; (3) therapist engagement logs.

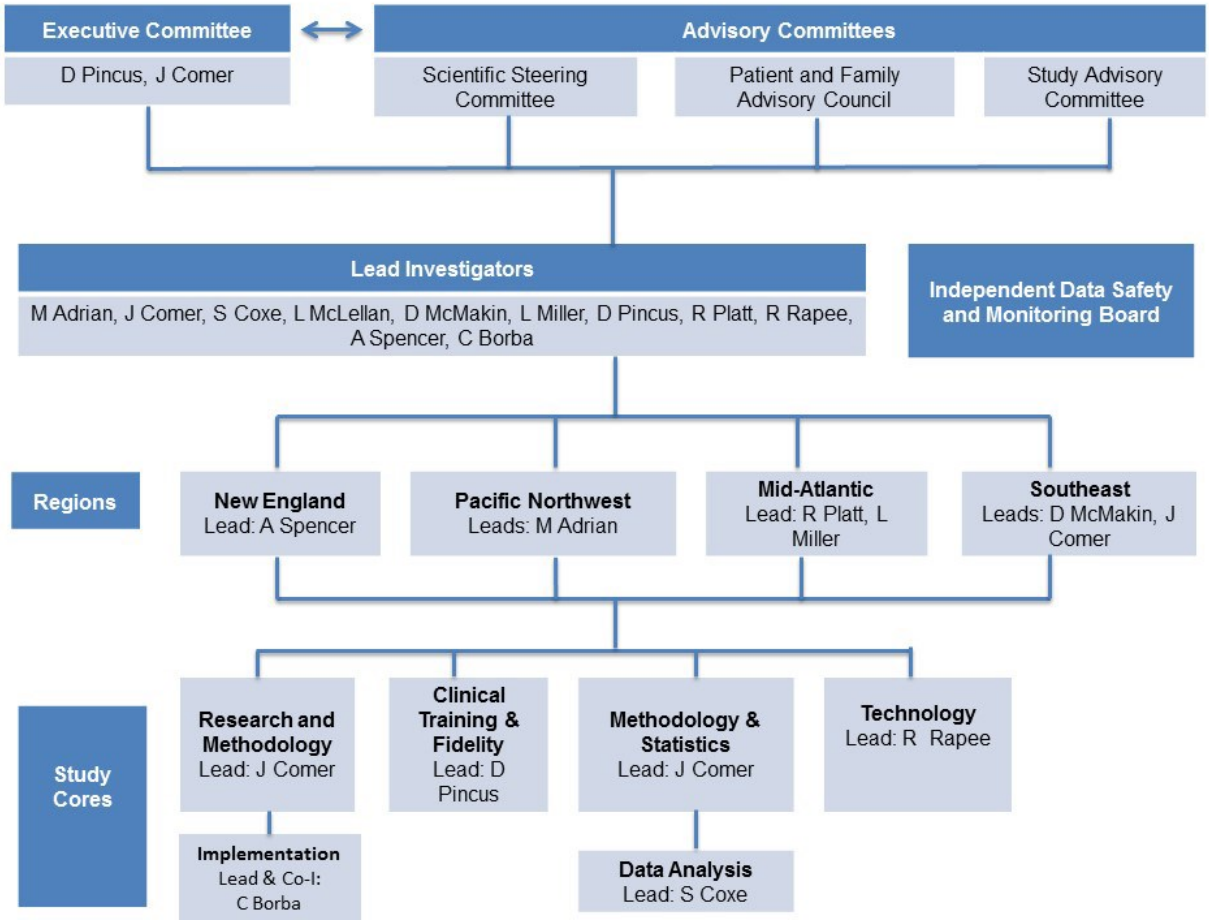
8.6.1 Retention of Records. Per Boston Medical Center policy, all study records will be retained for seven years after completion of the study. The full data package will be deposited in a PCORI-designated data repository for 7 years. The Full Data Package includes the Analyzable Data Set, Full Protocol, metadata, data dictionary, full statistical analysis plan (including all amendments and all documentation for additional work processes), and analytic code from a PCORI-funded research project. The package will be made available to third-party requests when PCORI makes the Final Research Report available on the PCORI website.

9 – Research Team and Project Coordination

The KIDS FACE FEARS project brings together an interdisciplinary team of researchers, and patient and stakeholder partners from across the country. The research team includes clinical psychologists, pediatricians and health services researchers with leading expertise in child behavioral health, technology and child anxiety disorders. Our team also includes patient and family partners as co-investigators. Members of the research team have prior experience working together successfully, and will have resources available (financial and institutional support) to ensure the projects' success. The proposed project will be conducted in Research and Community Environments (Boston University; Boston Medical Center; Florida International University; Seattle Children's Hospital; John's Hopkins University) are all institutions with extensive experience and well-resourced research environments to support a proposal of this scope and affiliated community primary care partners serving diverse populations, urban and rural, with experience in community-academic partnerships.

The Kids FACE FEARS project is overseen by the **KFF Executive Committee** (made up of Dual PIs **Jonathan Comer, Ph.D.** and **Donna Pincus, Ph.D.**), in consultation with the Scientific Steering Committee, the Patient and Family Advisory Council (PFAC), and the Study Advisory Committee. The Executive Committee coordinates with the **Lead Investigators** (made up of the primary Kids FACE FEARS investigators from each participating region and clinic, plus key investigators with specific content expertise in biostatistics and/or technology-based care) to implement all aspects of the study. One-to-two lead investigators serve as **Regional Lead(s)** for each of the four Kids FACE FEARS study regions. These Regional Leads coordinate and oversee all study activities in their respective regions. Four "scientific cores" were designed for the Kids FACE FEARS project, as well: the **Research and Methodology Core** is responsible for the study design and overall research conduct; the **Clinical Training & Fidelity Core** is responsible for all staff training and intervention delivery fidelity; the **Methodology and Statistics Core** is responsible for overseeing statistical planning and oversight, randomization and allocation concealment, data collection and integrity, and statistical analysis; and the **Technology Core**, assists with the technology aspects of the project and in particular the Web-based Cool Kids program.

Figure 2, below, provides and organizational overview of study:



Principal Investigators: **Donna Pincus, Ph.D.** and **Jonathan S. Comer, Ph.D.** (Dual-PIs) make up the Executive Committee and will direct the research team; they have an existing productive working relationship and will work synergistically to achieve project aims. Donna Pincus, PhD is a licensed clinical psychologist, an internationally known child anxiety expert, and the Director of the Child Anxiety Treatment Program at Boston University, Dr. Pincus' research focuses on the development of evidence-based treatments for youth with anxiety disorders. Dr. Comer is a Professor of Psychology and Psychiatry at Florida International University, where he is Director of the Mental Health Interventions and Novel Therapeutics (MINT) Program—an interdisciplinary clinical-research center devoted to leveraging technology to expand the reach and scope of children's mental health care. He is a leading expert in the treatment of pediatric anxiety, telehealth and digital mental health, and clinical trial methodology. Together, Dr. Comer and Dr. Pincus lead the Kids FACE FEARS Executive Committee.

The Executive Committee will resolve any issues related to planning, design, implementation, and financing. They are responsible for managing the overall project operations and project cores. They will work closely with the Study Cores, communicating

about methodology and aims and providing data about the project implementation. In addition, they will assist with the interpretation of outcomes and evaluation, and dissemination. The PIs will also regularly monitor risks to project goals and patient safety, and regularly report and problem solve with the Scientific Steering Committee. Both PIs will work closely with all clinical sites, consultants, subcontractors, and all project cores to monitor the progress of the project in regards to implementation, fidelity, and recruitment. Dr. Comer will have primary responsibility for overseeing the methodology, design, study implementation, and statistical aspects of the clinical trial. Dr. Pincus will have primary responsibility for the dissemination, training, treatment fidelity, and sustainability components of the Kids FACE FEARS project, and will serve the main point of contact with PCORI.

Earlier in the study's development and implementation, **Lisa Fortuna, M.D., MPH** (a leading child psychiatrist, health services, and disparities research) served as a Principal Investigator on this project as well, overseeing the coordination and launch of the project. Dr. Fortuna was the original chair of the study's Executive Committee, until she stepped down from the project when she left the project's prime institution (BMC) to accepted a department chair position at another institution.

Methodology Lead. **Jonathan Comer, Ph.D.** is a Professor of Psychology and Psychiatry at Florida International University, where he is Director of the Mental Health Interventions and Novel Therapeutics (MINT) Program—an interdisciplinary clinical-research center devoted to leveraging technology to expand the reach and scope of children's mental health care.

Qualitative Lead. **Christina P.C. Borba, PhD, MPH** is Director of Research for the Department of Psychiatry at Boston Medical Center. Dr. Borba has extensive experience in mixed methods research, teaching and training, and development and management of randomized clinical trials. Dr. Borba's current research focuses on mental health problems and cultural psychiatry in low-resourced settings in the US and abroad. She has expertise in mixed methods research and has participated in dissemination efforts for PCORI and NIMH studies.

Earlier in the study's development and implementation, **Michelle Porche, Ed.D.** (a developmental psychologist with extensive experience working with community partners in behavioral health services research, and in conducting mental health disparities research) served as the qualitative lead for the study. Dr. Porche was a member of the original Executive Committee for this study and served as the lead in launching the "Americanized" version of the guided online CBT program used in the study. Dr. Porche stepped down from the project when she left Boston University to accept a faculty position at another institution.

Biostatistics. **Stefany Coxe, Ph.D.** is an expert in quantitative methods for the social sciences and prevention science, having overseen data analysis for a number of large clinical trials, and serves as the lead biostatistician for the trial. **Anthony Dick, Ph.D.** serves in additional biostatistical capacities.

Regional Leads. We purposefully selected research sites with diverse patient populations in four different regions of the US to enhance generalizability of findings.

Regional Lead	Experience
New England Regional Lead: **Andrea Spencer, MD**	Associate Director of Behavioral Health Integration in Pediatrics at BMC; behavioral health integration/clinical trial methods
Pacific North West Regional Lead: **Molly Adrian, Ph.D.**	Pediatric mood and anxiety disorders; randomized clinical trials; technology-based treatment delivery; behavioral health integration in pediatric health settings
Mid-Atlantic Regional Lead: **Rheanna Platt, MD, MPH and Leslie Miller, MD**	Dr. Platt has experience implementing interventions among Spanish-speaking populations and Dr. Miller has experience with randomized trial of psychotherapy implementation at Bayview community psychiatry and delivery of psychotherapy at several college counseling centers.
Southeast Regional Lead: **Jonathan S. Comer, PhD; Dana McMakin, PhD**	International expert on pediatric anxiety treatment, clinical trials, use of technology, design and methodology, pragmatic trials (Comer). Mental health interventions for adolescent mood and anxiety disorders; translational research to inform intervention science (McMakin).

The research team will report to the Study Advisory Committee (SAC), made up of a multidisciplinary team of stakeholders. Members of each of the advisory groups have been engaged in all aspects of planning this proposal and will continue to play a key role in project implementation, analysis, interpretation/dissemination of findings. *Scientific Steering Committee (SSC) Chairs.* **Margarita Alegría, PhD** is the Chief of the Disparities Research Unit at Massachusetts General Hospital, and a Professor in the Department of Psychiatry at Harvard Medical School. She has published extensively on improving health care service delivery for diverse populations, and ways to bring the community's perspective into the design of health services. She is currently PI of four National Institutes of Health (NIH)-funded research studies as well as a PCORI project. **Ron Rapee, Ph.D.,** internationally known child anxiety expert developer of the *Cool Kids* Suite of online and face-to-face CBT protocols is Distinguished Professor and ARC Laureate of Psychology at Macquarie University in Sydney, Australia. His recent work has focused on public dissemination and access to empirically validated programs and so his participation in the scientific advisory

board meetings will be helpful in advising the large scale study of Cool Kids. *Study Advisory Committee (SAC) Co-Chairs.* **Tumaini Rucker Coker, MD, MBA** is Director of Research for the Center for Diversity and Health Equity at Seattle's Children's Hospital. She has extensive experience with programs that build the capacity of hospitals and community to respond to the mental health needs of children. **Rebecca Brigham, LICSW** is supervisor of the Pediatric Integrated Behavioral Health (IBH) social work team at Boston Medical Center where she provides programmatic support, clinical supervision, and training in evidence-based practices. In year 3 of the study, the SSC and SAC meetings will be combined for continued engagement in all aspects of project implementation as a multidisciplinary team.

Other Key Personnel and Consultants: **Lauren McLellan, Ph.D.,** co-developer of the *Cool Kids* Suite of online CBT protocols, is Director of Online Programs in the Centre for Emotional Health at Macquarie University, and an expert in the development and evaluation of technology-based strategies for improving the reach of youth anxiety treatment. Drs. Rapee and McLellan have extensive experience collaborating and conducting large clinical trials using both Cool Kids comparators. Their research has included the wide dissemination and implementation of Cool Kids nationally in Australia and Norway.

Data Safety and Monitoring Board Co-Chairs. **Martha Tompson, PhD** is Associate Professor of Psychology at Boston University and Director of the Family Development and Treatment Program; she is a renowned expert in the family-based treatment of pediatric mood and anxiety problems, and has extensive experience leading randomized clinical trials. **Shannon Pruden, PhD** is Professor of Psychology at Florida International University and a leading expert on child development and individual differences.

Kids FACE FEARS Advisory Groups		
Scientific Steering Committee (SSC) MEETS TWICE ANNUALLY (2 hour meetings)	Address methodological issues, recruitment and retention, analysis, and advise on dissemination of results.	**Chair:** Margarita Alegría, PhD; Michael Silverstein, MD, MPH; Barry Zuckerman, MD. Ron Rapee, PhD; Lauren McLellan, PhD; Ricardo Munoz, PhD
Study Advisory Committee (SAC) MEETS QUARTERLY (2 hour meetings)	Ensure stakeholder perspectives inform study conduct. The SAB holds primary responsibility for all decisions regarding publications, communications, and dissemination of results.	**Chairs**: Rebecca Brigham, LICSW and Tumanini Rucker Coker, MD, MBA David Henderson, MD; Megan Bair-Merritt, MD, MSCE; Robert Vinci, MD; Alexander Fiks, MD, MSCE; Iman Sharif, MD; Jonathan Woodson, MD; Eileen Costello, MD; Jonathan Welch, MD, and Gwen Wurm, M.D.
Patient and Family Advisory Council (PFAC)	Ensure research activities are aligned with patients' needs	**Patient and Parent Co-Investigators**: Melissa Ripley,

MEETS QUARTERLY (2 hour meetings)	and that patients' perspectives are fully integrated in all aspects of the study.	Karen Pierre-Louis, Gary McCreary, and Tomas Munarriz Parent Advisory Councils from all four regions
Data Safety Monitoring Board (DSMB) MEETS TWICE ANNUALLY (1 hour meetings)	Independently review and evaluate study data for participant safety, study conduct, progress, and efficacy, and make recommendations for modifications if needed	**Chairs**: Martha Tompson, PhD and Shannon Pruden, Ph.D.

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