Study Protocol

Official Title: BRITEPath, Component 3 of iCHART (Integrated Care to Help At-Risk Teens)

ClinicalTrials.gov ID (NCT number): NCT04000399

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PROTOCOL TITLE:

The Center for Enhancing Treatment & Utilization for Depression and Emergent Suicidality Phase 1b-Study 3-BRITEPath

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VERSION NUMBER/DATE:

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REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?

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1.0 Study Summary

Study Title	BRITEPath-ETUDES Phase 1b
Study Design	Stepped wedge randomization; We will evaluate BRITEPath's feasibility and efficacy compared to treatment as usual care (TAU) across sites.
Primary Objective	We will create and rapidly iterate user interfaces to develop the three components of BRITEPath: (1.) Guide2BRITE, an electronic guide for mental health clinicians providing step-by-step instructions in the onboarding of the safety plan, emotion regulation, and distress tolerance skills for (2.) the BRITE app, a personalized and interactive safety plan and self-monitoring tool for the adolescent; and (3.) the clinician dashboard, BRITEBoard, to track adolescents' app use, distress, and treatment progress as well as to promote communication and collaboration among mental health and primary care providers.
Secondary Objective(s)	We will test BRITEPath's impact compared to TAU utilizing a stepped wedge design and a RE-AIM framework. BRITEPath focuses on novel approaches to support treatment and management of adolescent depression and suicidality in pediatric primary care and community mental health settings.
Research Intervention(s)/ Investigational Agent(s)	Mobile App based intervention
IND/IDE #	n/a
Study Population	12-26 yo patients seeking mental health treatment
Sample Size	50
Study Duration for individual participants	12 weeks
Study Specific Abbreviations/ Definitions	BRITEPath=BP Guide2BRITE=G2B BRITE=app used on participant Mental health=MH Behavioral health=BH

2.0 Objectives*

Suicide and suicidal behavior are leading causes of adolescent mortality and morbidity. Suicide ideation is one of the strongest predictors of imminent suicide or suicide attempt. Among common psychiatric disorders, depression has the strongest association with suicide ideation and attempt, but anxiety, substance abuse, and disruptive disorders also elevate risk. Therefore, to identify adolescents at high suicidal risk, it makes sense to screen for depression AND for suicidal ideation, regardless of diagnosis. There is some evidence, mostly in adults, that brief interventions can reduce risk for suicidal behavior, whether through improved connection with services, increased sense of connection and social support, or via systematic follow-up, and while some brief interventions aimed at safety planning have been advanced, there are no brief interventions for adolescents. Furthermore, insufficient resources are available to guide clinicians in suicide risk assessment and management. In fact, a review of the literature for suicide prevention apps shows that of 123 available smartphone apps, none are geared to providing guidance for clinicians treating adolescents. This lack of resources is especially problematic because as primary care clinics implement depression screening for adolescents and enhance collaborative mental health (MH) care as recommended by the United States Preventive Services Task Force (USPSTF), more youth with depression AND those with acute suicide risk will be identified. Adolescents receiving treatment from an embedded MH provider may also result in the identification of even more adolescents with acute suicide risk. Enhancing mental health screening and providing embedded mental health treatment in primary care may have the unintended negative consequence of increasing emergency referrals and hospitalizations, which reflect the absence of current suicide risk management practices in primary care. Emergency department (ED) referrals for further evaluation are among those least favored by suicidal patients and may inadvertently decrease patients' motivation to access and engage in follow-up treatment. Thus, there is urgent need to equip primary care with the capacity to assess and stabilize depressed and suicidal adolescents, in order to avoid unnecessary ED referrals and hospitalizations and ultimately, to reduce suicidal behavior upon follow-up.

We will develop an app-based intervention, BRITEPath that enhances the capacity of pediatric primary care to effectively manage depressed and suicidal adolescents by referral to embedded MH services. BRITEPath includes three components delivered by MH clinicians, including (1.) an electronic on-boarding procedure tool that supports MH clinicians, Guide2Brite; (2.) the adolescents' safety planning app, BRITE; and (3.) the clinician dashboard, BRITEBoard, to facilitate treatment planning and communication with other primary care providers.

2.2 The aims and hypotheses related to this specific protocol and submission are below for Phase 1b. Aims of the previous phase are in a University of Pittsburgh OSIRIS IRB protocol submission (#PRO18050281) entitled ETUDES Phase 1a-qualitative. Aims of later phases described briefly will be submitted in subsequent protocols.

We will test the feasibility of using BRITEPath in community & pediatric practices using a stepped wedge design. We hypothesize that participants, parents, and clinicians will find the intervention usable and feasible to deploy. We will assess the impact of BRITEPath alone (compared to its impact as part of iCHART in later phases of the ETUDES Center, by obtaining follow-up phone assessments on suicidality, depression, and functional status at 4 and 12 weeks after intake.

Aim 1b (Phase 1b, Feasibility). We will pilot BRITEPath in sites using a stepped wedge design (50 adolescents aged 12-26 yo). Hypothesis 1b: The use of BRITEPath will decrease depressive symptoms, distress, and suicidality (any self-injurious ideation, urges, or behavior) as well as improve overall functioning compared to TAU.

Criterion for success: 75% of adolescents who receive BRITEPath will use it, and 75% of MH clinicians will use Guide2BRITE and BRITEBoard.

3.0 Background*

Drs. Stepp (PI) and Brent (Co-PI) are have expertise with all aspects of the proposed study: developing psychosocial interventions targeting suicide, partnering with private companies to create smartphone apps to monitor suicide and other high risk behaviors in daily life as well as analyzing the intensive longitudinal data resulting from such research protocols, conducting randomized controlled trials of psychosocial interventions for suicidal adolescents, and evaluating long-term outcomes from longitudinal studies of high risk adolescents and families with excellent retention.

In a previous study, Dr. Brent and colleagues developed a brief, inpatient- based, novel intervention with an accompanying safety planning app (BRITE) for psychiatrically hospitalized, suicidal adolescents. In a pilot RCT with 66 adolescents, this app-supported intervention cut the incidence of recurrent suicide attempts by half (Incidence rate ration [IRR] for attempts=0.47, 95%CI 0.12-1.56, p=0.18), with a stronger effect in the 80% of adolescents with a previous history of a suicide attempt (IRR=0.23, 95% CI, 0.05-1.09). The app was accessed an average of 29 times over a 6-month period, 45.5% accessed the safety plan, and the more frequently the app was used, the greater the decline in suicidal ideation and increase in reasons for living (rho=0.36, p's=0.08). Participants rated BRITE high on usability using the Post-Study Satisfaction and Usability Questionnaire (lower score indicates greater satisfaction, range 10-70, mean scores 17.6-18.4). Moreover, clinicians who implanted the interventions wanted the app to guide them in formulating the safety plan and populating the app for use by the adolescent. These data provide preliminary support for the clinical utility of an app-supported intervention to reduce suicide risk in adolescents. An important next step is to further develop BRITE for use in pediatric care clinics by

developing a virtual treatment manual designed to guide clinicians in delivering the intervention and a clinician dashboard to monitor symptoms and treatment progress.

4.0 Study Endpoints*

At anytime, the primary investigators may discontinue a participant's participation in this study. The PI may decide to remove a participant off this study if their health or safety may be at risk; if they have not been following study instructions or because of a study administrative decision by the PI.

5.0 Study Intervention/Investigational Agent

Overview of the BRITEPath intervention

There are three components of the BRITEPath intervention, each of which will be described: 1) BRITE, 2) GUIDE2BRITE and 3) BRITEBoard. All participants assigned to the intervention components will receive each of these 3 components.

BRITE

BRITE is a tool for self-monitoring and self-management that is not targeting any specific diagnosis or medical condition. BRITE includes monitoring of distress on a daily basis paired with content targeting skill targeting emotion regulation, distress tolerance, social support, and reasons for living. Content will take the form of clinician-recommended videos, photos, and websites, as well as personalized content that has salience to the adolescent that they may add onto their app. In this way, the app is customizable to uniquely meet the adolescents' needs and preferences. Adolescents will be encouraged to use the skills on the app on a daily basis. Additionally, the BRITE app will include an electronic version of a safety plan that will be developed in collaboration with the youth's therapist. Safety plans, which contain coping strategies, social supports, and crisis contacts are used as a standard of care in the treatment of suicidal youth. Finally, on each screen of the app, there is a link to crisis contacts that will be programmed onto the app with the assistance of their therapist.

GUIDE2BRITE

Embedded mental health providers, who will treat youth who have access to the BRITE app, will use GUIDE2BRITE to facilitate the process of orienting youth to the app. GUIDE2BRITE will be an interactive website that leads the clinician through the process of developing a safety plan and identifying appropriate content for the BRITE app with their adolescent patient. During this process, providers will orient patients on the purpose and function of the app, demonstrating and practicing skills they will use as part of the app-based intervention. Guide2BRITE supports clinicians in the delivery of an intervention designed to: (a) identify likely triggers of suicidal and self-harm urges; assess lethality and restricting access to means; (b) teach skills via modeling and role-play to cope with suicidal and self-harm urges and (c) identify professional resources to access in a crisis should others means of coping fail. A mock-up that

shows the integration between BRITE and GUIDE2BRITE is provided within question 2.

BRITEBOARD
BRITEBOARD is a web-based portal that tracks participants use of the app, e.g. tracking distress ratings and times in which they added/removed content, as well as changes in patient outcomes over time, e.g. depression ratings collected as part of the study. In order to facilitate effective communication within the participant's clinical team, information on this portal will be shared among the adolescents' providers within their practice, including the embedded therapist, their primary care provider, and other providers within the office that are designated as part of the adolescents' care team.

6.0 Procedures Involved*

We will develop an app-based intervention, BRITEPath that enhances the capacity of pediatric primary care to effectively manage depressed and suicidal adolescents by referral to embedded MH services. BRITEPath includes three components delivered by MH clinicians, (as described previously in this protocol) including (1.) an electronic on-boarding procedure to that supports MH clinicians, Guide2Brite; (2.) the adolescents' safety planning app, BRITE; and (3.) the clinician dashboard, BRITEBoard, to facilitate treatment planning and communication with other primary care providers. Increasing pediatric primary care's ability to effectively intervene with these mental health problems is likely to lead to reductions in 1) adolescent distress, 2) suicidal and self-harm urges, thoughts, and behaviors, depressive symptoms, and 3) improvements in functioning. Although primary care practices following USPTF recommendations to integrate depression screening and embed MH clinicians into routine care will also inevitability increase detection of depressed and suicidal youth, no effective intervention for the pediatric primary care setting exists to treat and manage these mental health problems. We propose to address this gap in services by developing and pilot testing a novel app-based intervention, BRITEPath, optimized for delivery by embedded MH clinicians to adolescents with depression and suicidality in pediatric primary care.

BRITEPath will include several highly innovative features that are responsive to the needs of both the MH clinician and the adolescent, including (1) brevity of BRITE onboarding (30 minutes); (2) low provider training costs (4 hours); (3) immediate service delivery upon initiation of treatment for depression or suicidality; and (4) provision of services in pediatric primary care clinics where the majority of adolescents are served. Furthermore, the Guide2BRITE component is innovative because, to our knowledge, it is the only safety planning app aimed at helping clinicians deliver an empirically-supported intervention. Guide2BRITE could serve as a paradigm for electronic guides for managing a wide array of mental health problems and emergencies.

This study has the potential to improve treatment outcomes by assisting MH clinicians in creating an individualized safety plan, monitoring symptoms and skills use, and facilitating shared decision making between clinicians and with

parents and patients. The simplicity and flexibility of BRITEPath would allow for its dissemination to reach beyond specialty MH clinics and is consistent with the NIMH 2015 Strategic Plan emphasizing the need for individualized strategies to improve patient outcomes.

It is impractical for MH clinicians to offer BRITEPath only sometimes and to some patients and not others. Although a cluster randomized trial could address this issue, this design is not feasible for a pilot study. Thus, we will utilize a stepped wedge design in which all practices start with Treatment As Usual (TAU) initially and are randomly chosen to transition to BRITEPath at different times. All clinics will be initially monitored for at least two months during TAU for the main outcomes of fidelity to delivery of the intervention. This will be followed by a staggered adoption of BRITEPath. At each time period, a new clinic will begin implementing the intervention. Block randomization determines the order each clinic begins BRITEPath. Each time period (approximately 3 months), a web-based system will be used to assign the next clinic to begin using BRITEPath.

We recognize the limitations of the proposed stepped wedge study design for evaluating the effectiveness of BRITEPath, once a practice enters their intervention phase, assignment to BRITEPath cannot be concealed. This concern is somewhat mitigated by blind follow-up assessors. Alternative study designs (e.g., randomized control trial) pose significant implementation challenges. Clinicians may be hesitant to deliver TAU once the BRITEPath intervention is known, which could lead to study condition contamination (e.g.,BRITEPath strategies introduced into TAU condition) and nonrandom patient assignment to condition (e.g., more high acuity patients referred to BRITEPath). In a stepped wedge design these feasibility concerns are addressed by the eventual assignment of all participating practices to the intervention condition and BRITEPath can be offered to all patients moving forward. Additionally, these designs are consistent with our broader goal of enhancing participant and community stakeholder engagement with the ETUDES Center. Results from this pilot trial will allow us to estimate the effect size of the BRITEPath intervention compared to TAU for reducing suicide risk in pediatric primary care. If our initial results show promise, these effect size estimates would be used to design a larger and adequately powered randomized control trial of BRITEPath.

SCREENING

Trained research staff or site staff will determine appropriate potential participants to refer and either refer via email, phone, or in person when staff person is on site. Site staff will review medical record or be made aware of the potential participant's chief complaint at presentation to the clinical setting to determine eligibility. At the time of identifying an eligible participant, trained research staff will complete verbal eligibility screen (with parent if a minor participant is involved or with adult participant). Upon eligibility, trained research site staff will enter participant contact information and date of birth into University of Pittsburgh secure webapp saved behind a firewall. This will create an "ID" which

will communicate with the electronic Guide2Brite to create a profile for the participant in the secure BRITEPath web app.

STUDY INTERVENTION

Following informed consent discussion in the site's clinical setting, trained research clinical staff will implement BRITEPath intervention (described above), help participant download app, and schedule a follow up visit with the participant. Pittsburgh/ETUDES Center research staff will follow up with site clinicians or a designated primary care provider if safety issues emerge during the research phone calls following management of imminent safety/risk.

PITTSBURGH/ETUDES CENTER RESEARCH PHONE CALLS & EMR DATA

During 3 follow research phone calls the measures the research study will collect include: sociodemographic questions, the CSSRS scale & suicide scales, quality of life ratings, treatment history, barriers to treatment, readiness for treatment, attitudes toward seeking psychological help, anxiety & mania adaptive scales via the K-CAT mental health adaptive screen, substance use, depression history, treatment preferences, and if there's a family history of bipolar disorder that impacts the youth's risk for mental health problems. A waiver of HIPAA authorization to collect permission verbally over the phone will be used to access and collect medical record data. Electronic medical record information will be used to supplement treatment and service utilization and uptake of the BRITEPath intervention via the RE-AIM framework described in statistical analysis. Parents will respond to questions about their child, not themselves and youth will answer about themselves. Phone calls will take about 30-60 minutes. Once a participant is completed with the research study follow up period, they will NOT lose access to the BRITE app. They will have access to it as long as they keep it installed on their device.

Only medical information that is necessary to conduct the study intervention will be collected. This will include diagnostic records, referral information, dates, times, outcomes of patient appointments, notes pertaining to patient appointments, who in the EMR prescribed/referred patients to use the intervention, PHQ-9 responses & scores, Service utilization (# visits-PCP, Mental Health specialty, ER, hospitalizations); pharmacotherapy; medical/psychiatric comorbidity; insurance coverage, matching referrals provided by PCP to expert opinion, Use of technical components of interventions & webportals, # of providers engaging in training/intervention, % representation at practice site, # practices who deliver intervention, and any other information needed for cost analysis purposes.

As with the informed consent & assent, it is not practical for researchers to conduct any ETUDES research activities, including the HIPAA authorization for BRITEPath on site due to the time and work flow constraints that emerged from formative qualitative data collection prior to this trial. The providers identified the time constraint of about 5 minutes of patient interaction that would be allowed for

researchers to implement eligibility screening only. Thus the BRITEPath intervention, including informed consent and obtaining any necessary HIPAA authorization, was developed based on pilot focus groups and Phase 1a focus groups & interviews to be implemented without impacting the clinical work flows.

Further, the vast majority of participants recruited across sites are not near the research offices in Pittsburgh. It would put undue burden on the research participants to complete in-person consent, baseline, & follow up assessment visits to ask them to come to instead of using verbal consent in their "real world" setting (especially due to telehealth activities since the COVID-19 pandemic).

A cost analysis is a core piece of the practicality of implementing the BRITEPath intervention within the real world setting of pediatric primary care, thus access to the electronic medical record is required. The intervention being tested as part of the study requires an understanding of the diagnosis, health service utilization, comorbidity, insurance coverage, medication usage, and any other information needed to conduct a cost analysis. The intervention results will include a cost analysis of the service utilization and outcomes of diseases and comorbidity. The results will require information on how many individuals used the intervention and the impact on their service utilization and disease.

Note-full set of data collection measures will be provided upon request. A data use agreement will be developed with site in the event that site investigators plan to collaborate on publications and will have access to de-identified data to conduct analyses. Both the site and Pittsburgh will have access to identifiable data as they are managing participant information/patient records to recruit subjects.

PROCEDURES FOR MANAGING SUICIDAL RISK AT Multi-SITE Location

In the event that an adolescent is not able to commit to a safety plan or if the clinician feels concerned that the patient is at high imminent risk, the clinician will follow their standard care procedures. Standard care involves careful assessment to identify the presence of imminent risk. If the clinician and their supporting clinical team determine the adolescent is in imminent risk, they will communicate the level of risk to the parent/guardian. Additionally, Drs. Brent, Goldstein, or Stepp will also be available as needed. Depending on the level of clinical severity, the MH clinician has the option to call the phone crisis network either for phone support or to request a mobile crisis team, or to refer the adolescent directly to a local psychiatric emergency to be assessed for inpatient hospitalization.

7.0 Data and Specimen Banking*

During the data cleaning period at the end and following conclusion of the study, the data will be thoroughly searched for any identifiers, so that data storage on a long-term basis, will be stripped of identifiers.

Identifiable data collected by the study will be contained in secure, firewall-protected servers managed by Pitt/CSSD-NOC and will only be accessible by the research team.

We assure that the private information gathered as part of this study will not be reused or disclosed to any other person or entity, except when required by law, for authorized oversight of the study, or for other research for which the IRB has granted a waiver of written HIPAA authorization.

At the request of another researcher, we will provide de-identified data sets only via encrypted documents. The research statistical coordinator and data manager will keep a log of data shared.

Sharing Data with Kaiser Permanente:
Data from the CASA, Child and Adolescent Services Assessment and E-HR will be collected in order to meet the study aims of conducting cost analyses on ETUDES center research pilot studies, including BRITEPath. We are sending a limited set.

Data we are sharing includes responses from the Child and Adolescent Services Assessment (CASA) that is administered to both parent and child participants at baseline and all follow up visits. A limited data set of the CASA will be shared including all service utilization fields except names of facilities/providers. We also recode any date into "days since baseline." The investigators will collect electronic health record data including:
1) Service Utilization: # Visits (PCP, MH specialty, ER, hospitalizations); pharmacotherapy; medical/psychiatric comorbidity; Insurance coverage;
2) Personalized referral: Match to Screening Wizard & expert opinion;
3) Application utilization: Use of technical components of interventions & web portals (Text2Conect, BritePath);
4) Provider uptake: # Providers engaging in training/intervention % Representation at practice site; and
5) Practice uptake: # Practices who deliver intervention.

8.0 Sharing of Results with Subjects*

Upon publication of primary outcome paper, participants will be informed through a preferred contact method of the publication. No subjects will be identified without explicit and written consent in any publications that come from this project.

9.0 Study Timelines*

The duration of an individual subject's participation in the study is 12 weeks.

The duration anticipated to enroll all study subjects will be from 8/2019-2/2020.

The estimated date for the investigators to complete this study (complete primary analyses) is 4/2022.

10.0 Inclusion and Exclusion Criteria*

Individuals will be screened for eligibility via phone or after presenting to the site's clinical setting with an eligibility script and inclusion/exclusion questions. Reponses to the questions will be entered into a secure study database managed by the University of Pittsburgh housed on a secure, encrypted server behind University firewall. Individual logins will be provided to research/site staff associated with this project.

Inclusion Criteria:

-Youth aged 12-26 yo

-Own a device (e.g. smartphone, ipod, tablet) with capability to download BRITE app

-Biological or adoptive parent is willing to provide informed consent for teen to participate

-Youth speaks and understands English

-Positive PHQ score or provider determines patient has depressive symptoms based on clinical interaction and refers youth to the study (in cases when PHQ is not available OR provider/parent have concern that youth/patient has a mood or behavioral problem

-Family agrees to see a MH staff at the site

Exclusion Criteria:

-Non English speaking

-No parent willing to provide informed consent for minors

-No cell phone capability of downloading BRITE app

-Is currently experiencing mania or psychosis symptoms that would prevent participant from understanding/participating

-Evidence of an intellectual or developmental disorder (IDD)

-Life threatening medical condition that requires immediate treatment (included emergent suicidality, homicidality, abuse/neglect, or other mental or physical condition)

-Other cognitive or medical condition preventing youth from understanding study and/or participating.

-Adults unable to consent

-Pregnant women-not specifically included or excluded as intervention and research procedures conducted will not inquire if a woman is pregnant.

-Prisoners excluded

11.0 Vulnerable Populations*

Children ages 12-17 will be recruited through their parents and not directly advertised to with study information. Legal guardians with proper court paperwork, biological and/or adoptive parents will provide permission for their child to participate. The child will receive study information via email/mail and over the phone to aid in their understanding of the study procedures and trained clinical assessors will explain the procedures using language appropriate for their age/grade level. See consent process for additional details.

12.0 Local Number of Subjects

We expect to recruit about 10 subjects locally at each site onboarded to BRITEPath study as eligible and completed informed consent, and intervention with site clinicians.

13.0 Recruitment Methods

Participants will be screened through site staff and clinicians under the direction of the site investigators. Clinicians taking part in the research project will scan intakes via telehealth (or in person when the COVID-19 pandemic allows for in person procedures) appointments for eligibility by reviewing electronic medical record information and chief complaint for presenting to appointment. At time of appointment, trained clinician/research site staff will discuss BRITEPath study option and complete eligibility screening questions.

Flyers and informed consent fact sheets used to discuss procedures and risks/benefits may be emailed or mailed for the patient to view at any time.

Participants are provided with the BRITE app during this appointment following completion of the intervention. Upon responding to follow up phone calls made by Pittsburgh/ETUDES Center research staff, the participants will be paid up to $180 on a visa gift card type card and mailed to participants' address.

Baseline visit phone call after intervention completed at sitel: $40

Week 4 Follow Up call: $60

Week 12 Follow Up call: $80

14.0 Withdrawal of Subjects*

Youth and young adult participants and parents may be formally withdrawn by the PI's if they develop a condition that meets criteria for exclusion or if they show evidence of clinical deterioration that may require further hospitalization during the course of study participation. Participants who are at risk for suicide attempts may need to be psychiatrically hospitalized, and this may occur at any time during the course of the study. Participants will be referred to their primary care physician and further for hospitalization if their condition is unstable as manifested by suicidal ideation with the inability to voice that they can keep themselves safe, psychosis, current intoxication, mania, rapid cycling, or mixed state. With permission, the study team may consult an

outpatient clinician and/or the primary care physician responsible for the treatment of the youth if it is the clinical opinion of the study team that an emergency evaluation or referral for hospitalization is indicated. Participants will be encouraged to contact their PCP or outpatient provider with any concerns reported to the study team during phone assessments. In cases of severe adverse effects, patients may be instructed to go to the nearest emergency department. Adverse events will be reported to the IRB in accordance with current procedures.

Research participants may also choose to voluntarily withdraw and should provide written notice to the PI of their decision. Data collected up until the point of receiving this notice will still be included in the research study. Participants may choose not to authorize HIPAA verbally for the researchers to collect medical record information and still participate in the remainder of study activities.

15.0 Risks to Subjects*

Protection against risk will begin with careful clinical management and education of patients and families. Informed consent will be obtained at the enrollment phone visit and include specific details of all risks, including consequences of psychiatric illnesses.

Baseline & Follow Up Assessments conducted by Pittsburgh/ETUDES Center

The risks due to phone interview assessments and self-reported questionnaires are: 1) discussion of potentially upsetting information, 2) loss of confidentiality, and 3) assessment burden. The interviewers will all be trained and skilled interviewers who can assess and monitor the reaction to questioning about sensitive topics; interviewees will be given the option of not responding or ending the interview. The assessment has been streamlined to limit assessment burden by using only a few measures per outcome domain. Each phone assessment should take about 30-60 minutes. Participants will be appropriately compensated for their time. Another potential risk is the disclosure of abuse. We are very familiar with assessment, management, and reporting of child maltreatment as this is considered part of standard clinical care in psychiatry and pediatric primary care. These incidents are common during trials, and we have standard for both managing and reporting these incidents. In all cases, state law is followed. Risk management procedures involved referral if symptoms do not improve or worsen and procedures to protect confidentiality are in place, as well as annual review of study progress by a Data Safety Monitoring Board. Risk management procedures are in place to involve communication between study staff and primary care physicians if there are indicators of clinical deterioration (e.g. suicidal thoughts emerge in youth interview and youth cannot contract for safety), to protect confidentiality. Every effort will be made to schedule assessments at times that are suitable for participants and families (after school or work) as needed in order to minimize negative impact on other important work, school, or social activities.

Audio recording

Measures will be taken to upload recordings to a secure network drive monitored by the University of Pittsburgh IT department and erased from the recording devise.

BRITE Intervention:

Risk management procedures involve referral if symptoms worsen or patients do not make significant gains and procedures to protect confidentiality are in place. Parents will be advised to monitor their youth's phone/device to avoid their access of explicit or unwanted material, as they typically would with any device intended for their child's personal use. Additionally, study PI & CO-I will be available to consult with clinical staff about the intervention in cases where the intervention may not be providing any gain to the patient or if symptoms worsen. If a mental health staff identifies that their patient is at imminent risk for suicidal behavior, they will follow their usual standard of care in managing these symptoms. The BRITEPath intervention will in no way interfere with the usual standard of care practices of managing imminent risk in pediatric primary care.

The app is meant to measure distress, not suicidality, so there is no time in which it will trigger response from providers in real-time or outside of work hours. The app will direct patients to deploy their safety plan if they are in crisis, which includes numbers for 24-hour crisis hotlines. The contents of the participant's safety plan will be available, even when the participant does not have access to wifi/data. Some portions of the app, e.g. portions that link to websites or youtube videos, will not be available without internet connection. Warnings are programmed within the app to notify participants when a poor connection is in place that may limit their access to certain parts of the app.

Minimizing Risk of Suicidal Behavior

Since participants may be eligible who exhibit current suicidal ideation, the biggest risk for these participants is their risk for suicidal ideation, behavior, or even suicide. In relation to assessment, there is now clear evidence that asking about suicidal ideation and behavior will not increase the risk for such behavior. Further, through repeated assessments of psychopathology, suicidal ideation, and behavior, we provide an additional safety net for the participants and their families beyond that which would occur in clinical care. As noted above, the research team will be appropriately trained in clinical management of adolescent suicidal ideation and behavior. Both the Pittsburgh research team and local site will manage suicidal risk using suicide prevention procedures established by the American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameters on Suicidal Behavior. These include risk assessment, identification/modification of precipitants, and safety planning. Suicide risk will be managed within the primary care setting for youth in both the TAU and intervention group.

The ETUDES Center will generate "protocol alerts" for the Pittsburgh/ETUDES clinical assessors to assist with the detection and management of suicidality among adolescents. If suicidal ideation or behavior is endorsed at follow-up phone visits, trained clinical interviewers will engage in assessment of the adolescent's risk of attempt. A safety plan will be developed with youth expressing any suicidal ideation, if he or she does not already have one. The parent will be notified and the clinical interviewer will make a decision as to whether the patient is at imminent risk or not. Assuming that the patient can commit to a safety plan and the parent is agreeable, we already have obtained consent to notify the pediatrician and we will obtain permission to contact their therapist if they are in treatment. If the patient cannot commit to a safety plan and/or the clinical interviewer is concerned that the patient is at high imminent risk, this will be discussed with the parent, and the clinician will set up a conference call with a crisis hot line to further evaluate the patient. If the patient refuses or hangs up, then the crisis team will be contacted who will help determine further action. Outside of Allegheny County/Pittsburgh, PA, the crisis line is the National Suicide Prevention Lifeline, which can provide on-phone support, and can access emergency visits to the home based on local resources. If the assessor is uncertain about assessment of suicidal risk, he or she will contact one of the Center on-call clinicians to either consult or speak directly with the patient and family. Similar procedures have been operative in studies of Dr. Brent's including the Familial Pathways study (R01 MH056612), which assessed youth with parental loading of depression and suicide attempt and the EDSTARS study (U01 MH104311), which assessed adolescent's suicide risk within pediatric EDs. If the interviewer is uncertain about how to proceed, the PI, Dr. Stepp or Co-I, Dr. Brent, will be available as a back up.

All aspects of the research interaction with participants will be private. Research staff will complete the phone assessments in a private, confidential location. In addition, research staff will ask the parent and youth prior to the start of the phone assessment if they are in a private location where they feel comfortable reporting sensitive information to the interviewer. Additionally all identifiable information will be held either in a locked filing cabinet or in a secure online database with security and confidentiality measures implemented and maintained by the University of Pittsburgh IT department.

In the event that additional risks are found out, participants will be notified

immediately of any risk it may pose to them. A copy of the verbal consent script will be provided to participants in the form they request (i.e. mailed, emailed).

16.0 Potential Benefits to Subjects*

This research project provides an immediate app-guided intervention to reduce suicidal distress.

Participants may also derive a sense of accomplishment from participation in research and contributing to the knowledge of screening, triage, and management of adolescent/young adult depression and suicidal ideation and behavior.

17.0 Data Management* and Confidentiality

A stepped wedge design was selected for both ethical considerations and feasibility. A stepped- wedge cluster randomized trial design involves the sequential random rollout of an intervention over multiple time periods following a "baseline" period when no cluster has been exposed. The crossover is typically in one direction, from control to intervention, and continues until all of the clusters receive the intervention with observations taken from every cluster and at each time period. All 3 studies in the ETUDES Center, and specifically, BRITEPath, will utilize this design. Prior to study start, each site will be randomly assigned to switch from.

Treatment As Usual (TAU) to the intervention. In the proposed stepped wedge design, all practices start with TAU (i.e.,PCP referral to embedded MH care) and are randomized to transition to implement BRITEPath at different times. All clinics will be initially monitored for at least 2 months during TAU, followed by a staggered adoption of BRITEPath. During each time period, a new clinic will begin to use BRITEPath (order determined by block randomization. A webbased system will randomly assign the next clinic to begin.

With regard to the stated hypothesis: We will perform multilevel modeling to explore time- and intervention-level factors associated with BRITEPath's use. We will first conduct t-tests for continuous variables and chi-square tests for categorical variables to examine baseline differences in demographic and clinical variables. We will use generalized linear mixed models (nesting for site) to examine between intervention differences in readiness. Distinguishing characteristics will be included as covariates in models examining treatment effects.
Due to the pilot nature of this study, sample size and power considerations center around the precision of confidence interval (CI) width estimation for feasibility outcomes. In this development phase (Aim 1), a sample size of 50 affords us a 95% CI width of no more than 0.28.

We will evaluate uptake of BRITEPath by community pediatric clinics utilizing the RE-AIM framework and determine implementation outcomes as follows: Reach: Compare demographic and clinical characteristics of those patients who do versus do not (opt-out) get BRITEPath in practice for sample representativeness. Efficacy: Measure the percentage of patients for whom clinically significant reductions in depressive symptoms and suicidality as well marked improvements in functioning are obtained. Adoption: The percentage and characteristics of MH clinicians who participate in the BRITEPath study. Implementation: The percentage and characteristics of MH clinicians who follow through with BRITEPath use procedures (examining different components of app use). Maintenance: Extent BRITEPath is utilized and predictors of utilization after research support has been withdrawn.

Identifiers that will be collected via electronic data management include: name, email address, phone numbers, medical record numbers, and social security numbers for payment only. We will be collecting location data (addresses), date information (Date of Birth, admission dates, etc), and sensitive data (such as protected health information, etc).

The data will be collected on a web-based database. Data will not be stored with participant identifiers and will be coded with a participant ID #. Data may be stored on UPMC owned or University owned computers in research offices. Documents containing data will be deidentified and encrypted with a password to which only the research staff have access. The following storage devices will be used:

- Google cloud storage will be used for deidentified summary data collected from NuRelm's webportal only. NuRelm is the app developer of BRITEPath suite of tools.

- University or UPMC owned laptops and desktops
- Amazon Web services stores deidentified data of one of the measures University of Pittsburgh collects through the cat-mh.com adaptive measures. Only deidentified data will be stored here.
- UPMC MyCloud/One Drive will be used to release only identifiable data and deidentified data that is necessary for ceded/partner sites to complete data analysis per Data Use Agreements with the University of Pittsburgh
- Pitt Box will be used to share data between investigators and will only contain deidentified data.
- University of Pittsburgh CSSD Network Operations Center Managed Server: Participant questionnaire data and interview data collected during baseline and follow up phone visits will be stored on the web database created by the Center for Clinical Trials Data Collection (CCDC) on the University of Pittsburgh managed server. NuRelm will create the portal and application tables that store intervention data and communicate to the CCDC web database will be stored on this server. Only authorized users to the tables and portals/websites developed and stored on this server have access with specific login and password information given to them by study administrators/PIs. Only particular views to the data are given to particular individuals on the study. Individuals are only given access to what they absolutely need to complete their role on the study.

Any hard copy or paper data will be stored by ID # in a locked cabinet in a locked office to which research staff only have access. No research data will be stored with identifiers on it. The key/link between the ID# and participant identifiable information will be kept separately in locked cabinets in locked research offices or in encrypted electronic documents on a Pitt or UPMC owned computer behind the firewall.

18.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

Data Safety Monitoring Plan

The study is designed to carefully monitor patient and participant safety and the PI is ultimately responsible for ensuring the safety of participants enrolled. During weekly project meetings, the principal investigator and the project coordinator will meet with all staff associated with the research study to monitor reports of abuse, neglect, suicidality, data entry, safety and maintenance of confidentiality for all active participants, course of adverse events, and ongoing symptoms of suicidality. They will review participant enrollment, instrument completion and data collection and determine if any breaches of confidentiality have occurred, or if participants have disclosed concerns that have warranted referral for further assessment or treatment, or if participants have made any complaints related to the conduct of the study. The PI and Project Coordinator will review the appropriate procedures for further assessment and referral in cases where clinical issues have been identified. In the event of a breach of confidentiality, the principal investigator will inform the involved participant and his/her parents that the breach occurred. The affected participant will be assigned a new ID number. The staff involved will continue to be counseled by the principal investigator and retrained on confidentiality principles. Any breaches of confidentiality will be reported to the IRB by the principal investigator. All serious adverse events (SAEs) will be reported to the WPIC Institutional Review Board according to the regulations set forth by the IRB. As defined by the FDA, an SAE is any adverse experiencing occurring during the study or within 30 days from termination of the patient/participant from the study that results in the following outcomes: death, a life-threatening experience, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, results in a congenital anomaly/birth defect, or based upon appropriate medical judgement, may jeopardize the participant's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

Data Safety Monitoring Board

A DSMB committee will be formed to periodically (semi-annually) review data, management of data and patient safety, reporting procedures and any UAPs and SAEs that emerge from the research. All UAPs and SAEs will be documented and reported to the DSMB & Pitt IRB, once a participant’s immediate safety and welfare are addressed.

Board members will include at least 3 qualified MD's and/or PhD's experienced in clinical care and research in adolescent suicidal behavior and uptake of technological interventions to address management and treatment of suicidal and/or depressed adolescents, all of whom have been identified upon funding of the ETUDES Center grant. The DSMB will make final conclusions regarding changes to risk-benefit ratio of the study and final recommendations related to continuing, changing, or terminating the study at each of the semi-annual meetings.

Overall data monitoring will be the responsibility of the PIs. During the course of the study, the PIs will follow the progress of the clinical study and data entry to ensure utmost accuracy of the data and to detect any possible errors at an early timepoint. The study coordinators will generate weekly reports, which will include suicidality and adverse events for each subject for review during weekly project meetings as well as an ongoing CONSORT diagram. The data manager, the CCDC at University of Pittsburgh, will also compile DSMB reports, which will include recruitment data, demographic information, serious adverse events, early termination, and protocol deviations, as well as any other information requested by the DSMB.

19.0 Provisions to Protect the Privacy Interests of Subjects

Study procedures have been designed to protect the privacy and confidentiality of the research participants. Throughout the study all data, including that collected during the recruitment phase, will only be identified by a unique identification (ID) number and participant/subject codes using letters and numbers to protect against invasion of privacy. The data will be blinded correspondingly in all data analyses. Only authorized staff will have access to patient information. All study information containing identifying information will be stored separately from the study data and will be stored in a locked filing cabinet. On the other hand, we notify the patient at the beginning of the study if we detect information that could indicate that a participant's life or health is in danger, we will need to bring his/her parents and/or primary care physician and/or outpatient physical or mental health care provider into the discussion.

20.0 Compensation for Research-Related Injury

n/a

21.0 Economic Burden to Subjects

There are no costs to insurance or otherwise to participants if they choose to volunteer for this study.

22.0 Consent Process

INFORMED CONSENT/ ***Subjects who are not yet adults (infants, children, teenagers)***

Trained research/site staff will complete verbal informed consent with participant over the phone and provide a copy of the document via email or mail. Upon obtaining informed consent, the site staff will initiate the BRITEPath intervention. Following the intervention, Pittsburgh/ETUDES Center research staff will follow up and complete research phone calls for which participants will be paid.

During the informed consent discussion, the site staff will speak with the parent to obtain permission to enroll the teen in this study and consent for her or his own participation. The staff will also speak with the adolescent to obtain her or his assent. The assessor will ask the family to take the phone call in a private location to decrease confidentiality breaches and discomfort about talking about sensitive topics.

During the consent process, research/site staff will make it clear that participation is voluntary to both the parent and child participants or adult participant if they are 18 at the time of enrollment. If a minor turns 18 years old during the course of the study an additional consent process will occur via the phone to ensure ongoing willingness to participate that Pittsburgh/ETUDES trained research staff will conduct. During each baseline and follow up phone call, Pittsburgh/ETUDES trained research staff will ascertain if the parent and child are still interested in participating in the study questions prior to collecting or updating data. Both the site staff and Pittsburgh/ETUDES trained research staff will make the family aware that they do not have to immediately make the decision to consent and can take the time to think and discuss participation after they receive all the necessary consent and risk information. The staff may also say that their participation will not influence their care or relationship with care providers. The staff will encourage the family to discuss their participation and provide several minutes for adequate reflection time.

Staff from both Pittsburgh and multi-sites are trained to ascertain if a participant is adequately understanding what is being said during the informed consent discussion and the research questions. Staff will describe the study in wording to reflect appropriate literacy level of a teen and parent. Staff will ask if the family has questions throughout the process and provide responses to questions as they arise.

Non-English Speaking Subjects

n/a

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

The research involves minimal risk. No changes will be made to the adolescents' standard clinical care. The BRITEPath intervention and passive sensors augments their care. Further, questions asked as part of study assessments are consistent with those asked at standard visits to their doctor. Project staff trained in the process of informed consent will obtain informed consent for study participation and document that they certify they gave informed consent.

Due to the nature of research activities, which occur within a variety of sites across Western Pennsylvania, NY, Seattle, WA, and Dallas TX, and other states

in the United States, an investigator cannot practicably be available to participate in the consenting process of each subject. An investigator will be made available to those subjects who wish to speak to them.

Research staff will inquire if a parent is biological or adoptive and it will be documented. Adults without this status must present paperwork to the research staff who will filter it to the respective IRBs and legal counsel for review and verify if an adult is legally able to consent for the child, if there is question over legal status.

23.0 Process to Document Consent in Writing

Research staff at the site will document the consent/assent response of each the parent and child during this process and the date and time it was obtained in the secure study database. Please see attached "Fact Sheet" for minors and adult participants which will be emailed/mailed and read aloud to the participants over the phone.

24.0 Setting

24.1 Describe the sites or locations where your research team will conduct the research.

The setting where all research procedures will take place except screening and informed consent and the intervention will be at the University of Pittsburgh ETUDES phone center.

Potential participants will be identified in the site's clinical settings via telehealth appointments (or in person if the COVID-19 pandemic permits). Trained clinicians will have access to a specific view in the CCDC/ETUDES database referenced in data management procedures to enter participant information to confirm eligibility and document date/time/response of participants during informed consent discussion.

25.0 Resources Available

25.1 Describe the resources available to conduct the research:

During already scheduled appointments, clinicians trained at the site will approach and "pitch" the study to between 10-20 patients to pilot the BRITE app and suite of tools. This will be done over the phone via telehealth appointments during the COVID-19 pandemic. Site clinicians will be engaged in regular team meetings to review work and problem solve on the ground at their site.

26.0 Multi-Site Research*

26.1 Study-Wide Number of Subjects: 50

26.2 Study-Wide Recruitment Methods*

All recruitment methods will be under the control of the local site. Specific clinicians who are trained at each site will ask patients on their own caseload at the time of scheduled appointments if they want to participate in using the app and the associated research phone calls. Site clinicians may use BRITEPath advertising material to provide additional information to patients before they agree to answer screening questions and complete the informed consent over the phone. No community sampling or other methods will be used to advertise for participants at the site.

26.3 All participating sites will be engaged on bi-weekly team meeting conference calls to review procedures, problems, and enrollment targets.